EUROPEAN UNIVERSITY

Journal of Biomedical and Medical Sciences

2022, Volume 1, Number 4

ISSN 2667-9507

PROJECT AUTHOR

Tamar Zarginava, European University, Tbilisi, Georgia

EDITORS (INTERNATIONAL AND NATIONAL ASSOCIATES)

Georgia

Tinatin Gognadze, Faculty of Medicine, European University

Aleksandr Khelaia, Tsulukidze National Center of Urology

Natalia Maglakelidze, Aversi Clinic

Naomi Hoyle, Eliava Phage Therapy Centre

Shorena Tsiklauri, Depratment of Otorhinolaryngology, Aversi Clinic

Maia Zhamutashvili, Infectious Diseases, AIDS and Clinical Immunology Research Center

Nana Momtselidze, Department of Fundamental and Applied Researcher, Multidisciplinary Science High School

Giorgi Kuchava, Department of Rheology and Diagnostic Analytical Services, Ivane Beritashvili Experimental Center of Biomedicine

Shota Janjghava, Department of Andrology, National Institute of Endocrinology

Content

DOI 10.51231/2667-9507-2022-001-03-6-7

Letter from the Editor-in-Chief

Dear authors, reviewers and readers, the Journal of Biomedical and Medical Sciences is an international open access, peer-reviewed scientific research journal that provides rapid publication of articles in all disciplines of medicine and biomedicine and also in adjacent and their connected basic and applied sciences such as engineering including biomedical engineering, food engineering, material science, nanotechnology, medical pedagogy, medical jurisprudence, law, financing and management, etc. It gives me great pleasure as the Editor-in-Chief to welcome you to the second journal of 2022. I am aware of the responsibilities that the editor's role entails after almost a two-year period of strict pandemic restrictions. This period was linked to limited laboratory work and experiments, also contact meetings and discussions between researchers were limited too. Naturally, now people will be involved in scientific work with even greater interest, and we will be able to see more and more actual original publications on pages of our magazine. This will further increase interest in publishing it and citing articles from it. All of this obliges us to constantly raise and improve the level of the magazine. The policy of top priority of the Journal of Biomedical and Medical Sciences is to publish high-quality researches in basic sciences and applied sciences. Original research articles, experimental, methodological articles, systematic reviews, case reports form the content, also once to the volume we publish a particularly interesting historical excursion. Preference has been given to multidisciplinary papers by authors representing different areas of research.

We encourage all authors who present new and the newest needed information to readers, which can be used for the development of a new diagnostic, prevention or treatment model. A special place of honor will be given to meta-analytical articles. The editors are especially grateful for the articles of honorary academicians and professors. Several times a year we publish particularly interesting papers by young researchers. In this way, we expand the circle of readers. We have strong consensus that accepted articles are often improved by peer review after referees' comments and criticisms are dealt with. This explicit appraisal process also helps to engender trust of the reader. Such an approach is vital to ensure the recognition and importance of the Journal of Biomedical and Medical Sciences in this biomedical generation in the world. Also, it's crucially important for conclusions reached from publications contained in the magazine to be valid and reliable. Peer review processing remains a vital component of our assessment of submitted articles to the Journal of Biomedical and Medical Sciences as well. Our magazine offers an exceptionally fast publication schedule including prompt peer-review by experts in the

field and immediate publication upon acceptance. This is achieved by our cooperation with large powerful corps of qualified reviewers. It is impossible not to note the great merit of experienced scientists and high-ranking medical doctors, who are co-editors and members of the scientific committee. All editorial board aims to fast review and evaluation of the submitted articles for forthcoming issues. The quality and pace of publication along with the anti-plagiarism campaign is our credo. We would not be able to provide a scientific product of such a format as the Journal of Biomedical and Medical Sciences if not for the constant moral and financial support from Lasha Kandelakashvili and Tamar Zarginava. On my behalf, on behalf of the co-editors and editors as well as on behalf of the authors of publications, and readers, we thank them.

Best regards,
Sincerely,
Prof. Maka Mantskava

Focus and Scope

We refer, peer-review and publish science articles about original study and clinical trial, theoretical reviews, preview and report of researcher project, preliminary data and the description of new and the newest hypothesis, essay in next directions.

- Epidemiology methods. Infection Diseases and Non-infection Diseases. Vaccinations
- Prevention of Epidemic. Prevention of Pandemic
- Multidisciplinary Approaches of Modern Science
- Polyprofile Medicine
- Biomedicine, Biorheology and Biotechnology
- Biochemistry and Biophysics in Fundamental and Applied Medicine. Micro – and Nanobiomechanics
- Innovative Methods. Bioinformatics. Biological Models. Mathematical Models
- Economic and Strategic Aspects of Biomedicine
- Blockchain and programming languages in Medicine. Digital Medicine. Chatbots
- The Role of Biomaterials in Biomedicine
- Theoretical, Clinical and Environmental Toxicology
- Radiology and Radiation Safety
- Nutritionology. Food, Biologically Active Substances, Medicines and Health. Enzyme
- Balneology, Wellness and SPA. Physical Education
- Beauty Industry
- Medical Physics. Medical chemistry
- Evidence Medicine. Medical and Biological Statistics
- Health Care and Policy
- Clustering in Biomedicine. Management systems in Biomedicine Areal. Strategic Communication in Biomedicine
- Ethics. Informed Consent. Doctor-Patient Relationship. Strategy and Using Instruments for Conflict Avoidance
- Grant application. Grant Management. Funding Science. Donors. Sponsors
- Mental Health. Defectology. ADD and ADHD

- Pharmacy and Pharmacology
- Reproductive Sciences and Sexual Medicine
- Cell Membranes, Structures and Function. Genome. Mechanisms of Aggregation and Deformation. Genome
- Blood, Blood Flow. Anatomy, Physiology and Pathophysiology of Blood Circulation
- Mechanisms of Thrombus and Stasis Formation
- Theoretical Hemodynamics and Hemorheology
- Clinical Hemorheology
- Rheology of Petroleum Products, Oils, Food and Construction Materials
- Neonatology. Pediatrics
- Gerontology and Geriatrics
- The Brain and its Functioning
  - ◊ Sleep-wakefulness Cycle
  - ◊ Pain and Analgesia
  - ◊ Behavioral and Cognitive Functions
  - ◊ Stress
  - ◊ Experimental and Clinical Neurology
  - ◊ Neurophysiology
  - ◊ Ultra – and Nanoarchitectonics
  - ◊ Alzheimer's Disease
  - ◊ Parkinson's Disease
  - ◊ etc.

- Kinesiology and Biomechanics
  - ◊ Rehabilitation
  - ◊ Sports Medicine
  - ◊ Prosthetics
  - ◊ Occupation Disease
  - ◊ etc.

- Alternative medicine
  - ◊ Chinese medicine
  - ◊ Acupuncture
  - ◊ Chinas Medicine
  - ◊ etc.

- Surgery
  - ◊ Planned Operations
  - ◊ Urgent Operations
  - ◊ Postoperative Shock
  - ◊ Plastic Surgery
  - ◊ Reconstructive Surgery
  - ◊ etc.

- Medical Linguistics
  - ◊ Medical Terms
  - ◊ Adaptation of Medical Literature
  - ◊ Translation Problems of Medical Literature
  - ◊ etc.

- New Approaches and Challenges for the Medical Education System
- Authorization, Certification, Licensing Issues in Health Care Institutions, University
- History of medicine
- Philosophy and medicine
- Medical Tourism
- Medical Low
- All about COVID-19
- etc.

DOI 10.51231/2667-9507-2022-001-04-11-17

Modern aspects of chronic rhinosinusitis treatment

M. Lomaia[1,2], Sh. Tsiklauri[3,4], T. Khechinashvili[4], M. Tsabadze[5], N. Nakudashvili[3]

[1]TSMU G. Zhvania Pediatric Academic Clinic, Tbilisi, Georgia
[2]Tbilisi JSC "Curatio", Tbilisi, Georgia
[3]European University, Tbilisi, Georgia
[4]LTD "Aversi Clinic", Tbilisi, Georgia
[5]National Center of Otorinolaringology, Japaridze-Kevanishvili Clinic, Tbilisi, Georgia

Abstract

In this work, we discuss the development of a new method of immunogenesis and treatment of infectious and infectious-allergic chronic sinusitis and its effectivness, based on new targeted methods of immunocorrection, taking into account the severity of the inflammatory process, current complaints and duration. 52 patients were under observation. The results of treatment with an aerosol of recombinant interferon αa-2b (in the form of Gripferon drops) in different types of chronic rhinosinusitis were studied. It has been shown that aerosol therapy with Gripferon gives promising results – subjective condition of patients and rhinoscopic and endoscopic data, as well as improvement of nasal olfactory function and regulation of mucociliary clearance, which indicates the effectiveness of this method of treatment.

KEY WORDS: rhinosinusitis; gripferon; aerosol therapy; neutrophils; eosinophils

Introduction

In the last ten years, a significant increase in the number of patients with nose and sinus pathologies, first of all, chronic rhinosinusitis, has been observed, at the same time, the tendency of these pathologies to worsen is noted [1,2,3,4,5,6,7,8].

Chronic rhinosinusitis is a chronic inflammatory disease of the upper respiratory tract, the treatment methods of which include drug treatment or surgical intervention. Surgical treatment in many cases does not exclude the relapse of the disease that is why the main goal of our research was to combine conservative treatment and physiotherapeutic methods and search for efficient methods of treatment of the mentioned nosology.

The aim of the study was to study the effect of Gripferon intranasal aerosol therapy on clinical, functional and laboratory parameters of patients with chronic infectious rhinosinusitis and chronic allergic-infectious rhinosinusitis.

Materials and Methods

52 patients between the ages of 17 and 60 were examined, 30 of them had chronic infectious rhinosinusitis (CIRS), and 22 had chronic allergic-infectious rhinosinusitis (CAIRS).

All patients participating in the study were subjected to general clinical examinations against the background of studying the anamnesis of the disease and living conditions.

When studying the complaints of these patients, special attention was paid to the nature of nasal discharge, the function of smell and the state of nasal breathing, rhinoscopy was performed with the Medical 5W LED (ENT) Head Light and the Flexible Nasopharyngolaryngoscope Pentax FNL-10RP3, while we evaluated the condition of the mucous membrane of the nasal cavity and the nature of nasal discharge.

To determine the state of the nasal olfactory function, we used odorous solutions of various increasing strengths, namely, 0.5% acetic acid solution (weak odor), wine alcohol (medium odor), and valerian tincture (strong odor).

If the patient could not smell the weak acetic acid solution, he was considered to have olfactory function disorder I degree (hyposmia I degree), if the patient could not

smell the acetic acid solution, but could smell the alcohol of wine, he was considered to have hyposmia II degree. If the patient could smell only valerian tincture from the above-mentioned odorous substances, it was considered that he had hyposmia of the III degree.

Absence of olfaction to odorous solutions of acetic acid, alcohol, and valerian indicated anosmia.

We were investigating mucociliary clearance in G.I. Markov's [9] method, when charcoal powder based on starch-agar gel was used as an indicator (starch 0.2 g, agar-agar 0.60 g, charcoal powder – 1 g, water – 10 ml).

At the beginning of the study, a gel was prepared to which indicator powder was added, and we applied the obtained compound to the surface of the lower turbinate and controlled its entry into the nasopharynx. We evaluated the driving function of the ciliated epithelium with the following parameters: norm – 15 minutes; First degree violation – 16-30 minutes; II-degree violation – 31-45 minutes; III-degree violation – 46-50 min.

Before treatment, all patients participating in the study underwent Radiography of the paranasal sinuses in the frontal-nasal and lateral projections. Cytological and Bacteriological examination of nasal discharge, F.I. Chumakov's recommendations [10] and microscope ″Biolam-P" (LoMo, Russia).

During the performed cytological examination, the number of neutrophils and eosinophils with phagocytic bacteria was determined. To determine the number of neutrophils and eosinophils, we used criteria provided by A. Yalovaiski and R. Zeiger [11] with our modification. In particular, if the average number of neutrophils and eosinophils in 10 fields of vision at 1000 times magnification did not exceed one, it was evaluated as 1 point. The average number of neutrophils and eosinophils in 10 fields of view under conditions of 1000 times magnification from 1.1 to 5 was evaluated as 2 points, from 5.1 to 15 as 3 points, from 15.1 to 20 as 4 points and more than 20 – as 5 points.

During the bacteriological examination, special attention was paid to the size (diameter) of colonies of homogeneous cultures of microbes. Colonies whose diameter did not exceed 2 mm were considered as small colonies, and colonies whose diameter ranged from 2.1 to 4 mm were considered medium. Colonies greater than 4 mm in diameter were considered large colonies.

Treatment of patients included 15 procedures of intranasal aerosol therapy.

As an aerosol, a 10 ml solution of Gripferol 10,000 IU/ml was used in the form of 1 ml diluted with 3 ml of distilled water. Procedures were carried out every day, except Sunday. The duration of a separate procedure was 15 minutes. We used the ″OMRON C102″ device (Italy) to conduct aerosol therapy.

Results and Discussion

It was revealed that before the treatment, patients' complaints, their frequency and nature depended on the form of rhinosinusitis. Complaints were more diverse in chronic allergic-infectious rhinosinusitis.

Gripferon intranasal aerosol therapy led to a reduction, sometimes even disappearance, of the complaints present before the start of the study. These positive processes were more detected during CIRS.

During rhinoscopy, the nasal mucosa of 23 practically healthy persons examined by us was moist, pink, with a smooth surface. Blood vessels located on the surface can be seen anywhere.

Patients with chronic infectious rhinosinusitis, before the start of treatment, during the previous rhinoscopy, showed irregular thickening and swelling of the nasal mucosa, especially in the area of the lower nasal turbinate, which caused narrowing of the common nasal passage. The surface of the nasal turbinate was smooth. There was also hyperemia and cyanosis of the nasal mucosa. Against this background, 16 (53.33%) examined had single, initiated, superficially located blood vessels. Thick and viscous white serous discharge was also observed in the lower part of the nasal cavity.

In the case of allergic-infectious rhinosinusitis, before the intranasal aerosol therapy of Gripferon, rhinoscopy revealed a whitish-gray coloration of the mucous membrane of the nasal cavity in 4 (18.18%) patients, 12 (54.54%) had pale pink, 5 (22.72%) pink and 3 (13.63%) – red.

19 (86.36%) patients had swelling of the nasal mucosa, 5 (22.72%) – its hyperemia and cyanosis, and 4 (18.18%) – it’s bumpy. All subjects with CAIRS had narrowing of the nasal passages and liquid-mucous discharge from the nose.

Intranasal aerosol therapy with Gripferon led to improvement of the condition of the nasal mucosa, in some cases to complete normalization. This positive process was more pronounced – during CIRS.

It should be noted that after intranasal aerosol therapy with Gripferon, 17 (56.66%) patients with chronic infectious rhinosinusitis completely improved their rhinoscopic data: the thickening and swelling of the nasal mucosa disappeared, cyanosis and hyperemia, which returned pink; the nasal passages were widened. The discharge from the nose stopped. In 13 (43.33%) of the subjects examined by CIRS, after intranasal aerosol therapy with Gripferon, the condition of the nasal mucosa improved; thickening of discharge and swelling of the mucous membrane; The hyperemia and cyanosis of the nasal mucosa decreased, the discharge from the nose decreased, and the nasal passages expanded to some extent.

In the case of allergic-infectious rhinosinusitis, after treatment with Gripferon aerosol, 16 (72.72%) patients had pink mucous membrane in the nasal cavity, 18 (81.81%) patients had smooth nasal cavity mucosa. Mucosal thickness decreased in 4 (18.18%) patients and did not change in 2 (9.09%) patients. Swelling of the nasal mucosa disappeared in 8 (36.36%) and decreased in 10 (45.45%) subjects with CAIRS. 15 (68.18%) patients were diagnosed with enlargement of the nasal passages. After treatment with Gripferon aerosol, none of the patients with CAIRS had cyanosis and hyperemia of the mucous membrane of the nasal cavity. At the same time, intranasal aerosol therapy with Gripferon did not cause any changes in rhinoscopic data in 2 (9.09%) patients with CAIRS.

The mentioned intranasal aerosol therapy method at the same time led to the improvement of the nasal olfactory function and the mucociliary clearance of the ciliated epithelium of its mucous membrane, almost even to normalization. These positive changes were more pronounced during chronic infectious rhinosinusitis.

For example, absence of smell (anosmia) was detected in 6 (17.64%) patients with CIRS and 9 (40.90%) patients with CAIRS; violation of the olfactory function of the first degree, according to the forms of the pathology, 2 (6.66%) and 1 (4.54); 2nd degree violation of olfactory function – 5 (16.66%) and 2 (9.09%); 3rd degree violation of olfactory function – 5 (16.66%) and 8 (36.36%) examined.

4 (13.33%) patients with chronic infectious rhinosinusitis and 2 (9.09%) patients with allergic-infectious rhinosinusitis had no olfactory dysfunction before treatment.

After treatment with Gripferon intranasal aerosol, olfactory dysfunction degree I was detected in 7 (23.33%) patients with CIRS and 5 (22.72%) patients with CAIRS; violations of the olfactory function of the II degree respectively were detected in 2 (6.66%) and 4 (18.18%) cases; III-degree violation of olfactory function – 1 (3.33%) and 3 (13.63%) examinees.

Before treatment, 14 (46.66%) patients with CIRS and 6 (27.27%) patients with CAIRS had first-degree mucociliary clearance disorders. 9 (30%) and 11 (50%) had second-degree mucociliary clearance violation, according to the pathology forms; Level III disturbance of mucociliary clearance – 1 (3.33%) and 3 (13.63%) examinees.

6 (20%) patients with CIRS and 2 (9.09%) patients with CAIRS had normal mucociliary clearance before treatment.

Cytological examination, which was performed on the nasal mucosa, revealed a significant number of neutrophils with phagocytic neutrophils was in the smear in patients with CIRS and a significant number of eosinophils was CAIRS, and after treatment with Gripferon intranasal aerosol, a decrease in the number of these cells were noted. The positive process was more pronounced during CIRS. In particular, the positive impact of Gripferon intranasal aerosol treatment was more pronounced in chronic infectious rhinosinusitis.

It should be noted that before treatment with Gripferol intranasal aerosol, the content of neutrophils with phagocytosed microbes in the nasal discharge smear in case of CIRS was averaged 3.883 points ± 0.1177 points (N-1.00 points), the number of eosinophils in the same smear – 1.00 points (N-1.00 points). The values of the mentioned indicators during the CAIRS, after intranasal aerosol therapy with Gripferon, were respectively – 1.144 points ± 0.3565 points and 4.466 points ± 0.9599 points.

After conducting intranasal aerosol therapy with Gripferon, the content of neutrophils with phagocytosed microbes in the nasal discharge smear during CIRS was already 1.589 points ± 0.1345 points ($P<0.001$), and the number of eosinophils in the same smear was equal to – 1.00 points. In the case of CAIRS after Gripferon aerosol treatment, the values of the indicators were equal to 1.00 points ($P<0.05$) and 2.144 points ± 0.2452 points ($P<0.001$).

Bacteriological examinations of nasal discharge showed that all patients with chronic rhinosinusitis were carriers of bacteria. Staphylococcus aureus was the most frequently cultured, which was detected in all patients with CRS: epidermal staphylococcus, 16 (47.05%) in CIRS and 12 (42.85%) CAIRS, diphtheria corynebacterium respectively 10 (29.41%) and 8 (28.57%).

Treatment with Gripferon intranasal aerosol had a bacteriostatic effect, which was revealed by a decrease in the diameter of the colonies of microbial cultures sown in the majority of patients.

In particular, before treatment, small colonies of seeded microbes were detected in 3 (10%) patients with CIRS and 1 (4.54%) patient with CAIRS; Colonies of medium size, according to the forms of pathology – 12 (40%) and 9 (40.9%); Large colonies – 15 (50%) and 12 (54.5%) examined.

After treatment with Gripferon intranasal aerosol, small colonies were detected in 18 (60%) patients with CIRS and 11 (50%) patients with CAIRS; Colonies of medium size, according to the forms of pathology – 12 (40%) and 11 (50%) of the examined.

From the obtained studies, it was determined that Gripferon intranasal aerosol therapy in patients with the mentioned forms of chronic rhinosinusitis leads to a marked improvement of both subjective condition and rhinoscopic data, nasal olfactory function and mycociliary clearance condition, in some cases even to complete normalization; reduction or complete disappearance of neutrophils and eosinophils in the mucous discharge of the nasal cavity; It causes a bacteriostatic effect, which is manifested in the reduction of the size of the colonies of the sown infected cultures.

References

1. Krutikhina SB, Yablokova EA. Acute respiratory viral infections in children: current possibilities for the use of homeopathic medicines. 2016; 18:1191-1195 [in Russ]
2. Osidak LV, Golovacheva EG, Afanasiev OI, Gorelov AV, Geppe NA, Yanina MA. Evaluation of the therapeutic effectiveness of two domestic preparations of recombinant interferon α-2b for intranasal introduction (genferon® light and grippferon®) for sars in infants and young children. J Drugs in pediatrics, 2017 [in Russ]
3. Yushchuk ND, Khadartsev OS. The use of interferons in the prevention and treatment of respiratory viral infections in adults and children. Medical scientific and practical journal attending physician 2018; 3. – 67 [in Russ]
4. Kozlov MN. Clinical and immunological characteristics of some forms of chronic rhinitis. Abstracts Book. Science.– M.: 1998; – 21 [in Russ]
5. Osidak LV, Golovacheva EG, Afanasyeva OI, Gorelov AV, Geppe NA, Yanina MA. Evaluation of the therapeutic efficacy of two domestic preparations of recombinant interferon α-2b for intranasal administration (Genferon® Light and Grippferon®) in ARVI in infants and young children. Journal of Pediatrics named after G.N. Speransky, 2017; 96(2) [in Russ]
6. Anon JB, Jacobs MR, Poole MD. Sinus and allergy health partnership. Antimicrobial treatment guidelines for acute bacterial rhinosinusitis. Otolaryngol. Head Neck Surg. 2004; 130(1):1-45
7. Druce HM. Chronic sinusitis, rhinitis and asthma. Rhinitis and asthma. Similarities and differences. – Copenhagen: Mlunksgaart. 1990; 150-155
8. Chow AW, Benninger MS, Brook I. Infectious Diseases Society of America. IDSA clinical practice guideline for acute bacterial rhinosinusitis in children and adults. Clin. Infect. Dis. 2012; 54(8):e72-e112
9. Markov G. Differential diagnosis and sparing methods of treatment of inflammatory diseases of the nose and paranasal sinuses: Abstract of the thesis. diss. Dr. med. Sciences. – M.: 1987. – 31 [in Russ]
10. Chumakov FI. Diagnostic and therapeutic methods in the clinic of diseases of the ear throat and nose. – St. Petersburg: Peter. 2000; – 218 [in Russ]
11. Yalovaisky A, Zeiger R. The study of scrapings from the nasal mucosa and conjunctiva. Clinical Immunology and Allergology (translated from English). M.: Practice. 2000; 682-683 [in Russ]

DOI 10.51231/2667-9507-2022-001-04-18-26

Neurocognitive functions and some electrioencephalographic changes in preadolescent children with different degrees of primary hypothyroidism and mild iodine deficiency

N. Natroshvili[1,2], N. Beridze[2,3]

[1]*N. Kakhiani Central Clinical Hospital Under The Georgian Railway, Tbilisi, Georgia*
[2]*European University, Tbilisi, Georgia*
[3]*"Expressdiagnostics" LTD, Tbilisi, Georgia*

Abstract

Neurologic and electrophysiologic changes in children with mild hypothyreosis and euthyroid goiter at the background of mild ID are not well understood at present. Our goal was to evaluate of some cognitive disturbances and alteration of some EEG parameters in preadolescent children at early stages of the development of primary hypothyreosis and euthyroid goiter. 55 somatically healthy preadolescent children, aged 8-12 years with the 1st degree of diffuse goiter underwent clinical and neurological investigation of cognitive functions: "copy", "time to copy" and "recognition" using Rey Complex Figure Test and recognition trial as well as Rochester fatigue Diary test; Motor Fatigue index, PASAT – 3 (second version) and lassitude was evaluated. Digital 21 channeled EEG study was also performed. Study groups were randomized to: children with overt mild hypothyreosis; children with subclinical hypothyreosis; euthyroid children; healthy controls. Mediana of UIE 64 was in the lower 3rd in the range for mild ID. Children of the study group more often had non-specific neurologic symptoms. All indices of neurocognitive dysfunction were more frequent in

patients with overt hypothyreosis (P<0,001) and in lesser extent were present in subclinical hypothyreosis and euthyroid goiter, compared to controls. This was accompanied by the changes of EEG parameters. The pathologic visual version of EEG had 90% of children with overt hypothyreosis. In turned out that in prepubertal children is accompanied by cognitive disorders represented by Mild Cognitive Impairment; among neurologic subclinical signs of manifestation of ID the Fatigue test is of great sensitivity; even mild ID is characterized by specific changes of the frequency and amplitude of physiologic spectrum of EEG activity, mainly of aA; pathologic consequences of ID are manifested both in overt and subclinical hypothyroidism and in lesser extent in patients with euthyroid goiter.

KEY WORDS: Neurocognitive functions; "copy"; "time to copy"; "recognition"; hypothyroidism

Introduction

Generally, among regional population with iodine deficiency (ID) there is a high prevalence of various types of thyroid dysfunction, especially, primary hypothyroidism (PH) which is regarded as one of the most important causes of mental retardation. Therefore, population from these regions has lower IQ as compared to those from iodine-sufficient areas [1]. This was explained by the profound effect of thyroid hormones on developing brain and anatomy and physiology of peripheral nerves and dramatic consequences of even mild thyroid insufficiency on mental function in future life [2].

From ancient past Georgia belongs to the group of countries where significant regions are represented by ID regions. Epidemiologic studies carried out at the end of the last century revealed high prevalence of goiter among pre-adolescents 31-93% [3] at the background of moderate and severe ID and 64% in 2004 [4]. Things have changed at the beginning of XXI century after introduction of mandatory salt iodization in Georgia with the help of WHO and UNICEF in 2005. Since then severe ID has been eliminated [5].

Recent academic papers are full of information concerning clinical manifestations of overt and severe PH in newborns, children and adults [6]. But less is known about psycho-neurological and electrophysiological changes in preadolescent children with moderate and latent forms of PH and euthyroid goiter developed in the regions with mild ID. Present data are scarce and equivocal. At the same time most authors con-

cluded that even minimal ID in vulnerable periods of life: pregnancy, neonatal and early childhood period, puberty, stress, etc. may give impetus to the development of minimal thyroid insufficiency or so-called asymptomatic hypothyroxinemia with FT4 at low normal level and TSH at high normal [7]. Prolonged ID may also cause decrement of the ability of thyroid gland to synthesize and produce thyroid hormones [8].

Our aim was to study aims at finding peculiarities of neuroendocrine functions in preadolescent children aged 8-12 from mild ID areas of Georgia with different degrees of PH to reveal early latent symptoms of the disease.

Materials and methods

The work has been performed with the help of the Ministry of Health and Welfare and assistance of the Georgian charity organization ″SOCO″.

Overall, 100 preadolescent otherwise healthy children underwent complex clinical investigation. Consilium of pediatricians, neurologists, endocrinologists and surgeons made a decision concerning their health.

Clinical investigations were performed as a part of epidemiological studies in the schools of 15 regions of Georgia. Laboratory and EEG investigations were conducted in corresponding department's hospitals in Georgia.

Urinary iodine excretion (UIE) was measured by the biochemical method with the use of special KITs. The values were taken in Mkg/L. Blood FT4 and TSH levels were measured by the immune-ferment method using apparatus ELISA taken in ng/dl and mU/L, respectively.

The degree of goiter was evaluated using WHO criteria, last version.

Ultrasound investigation of thyroid gland with the apparatus ALOKA – 210.

Rochester Fatigue Diary (RFD) test was used to reveal the fatigue phenomenon.

Electroencephalographic (EEG) investigation was performed on digital 21 channel encephalograph ″Braintest″.

Mnestic – Cognitive function of the brain was studied by Rey Complex Figure Test and Recognition Trial [9].

Three components of the test were evaluated:

1. ″copy″ – ability to copy geometrical construction;
2. ″time to copy″ evaluation of time for ″copy″;
3. ″recognition″ tests the visual-spatial perception ability, attention and visual-spatial memory.

Evaluation of functional neurological status was made with the use of Rochester Fatigue Diary. Namely, its three components:

1. Motor Fatigue index;
2. Paced Auditory Serial Addition test (PASAT3.2). The test evaluates attention and the fast line of information processing by calculating correct and incorrect answers following listening of information during three minutes. More than 10% of incorrect answers are indicative for cognition tiredness;
3. ″Lassitude″. Is subjective and is evaluated by persons investigated. Answers are compared to the control group.

Motor fatigue index was calculated only for extensor ulnar muscle and for flexor muscle of the hand.

Electroencephalography (EEG) was performed with 21-channal digital apparatus ″Braintest″. Both visual and computer analysis were made. Brane electromagnetic potentials were divided according to their frequency ranges measured in – Hz: D – Delta wave – 2-4 Hz; T-Theta wave – 4,0-8,0 Hz; A – Alpha wave – 8,0-13Hz; B – Beta wave 14,00-30,0 Hz EEG of healthy children of 0-12 months are represented by slow waved D rhythm and till six-year-old children with slow waved T rhythm.

As for healthy adolescents, nearly 90% of their basic EEG rhythm revealed in sober state at rest with closed eyes or in dark is regular – synchronized A rhythm, of 8-13 Hc frequency with 20-90 mcv^2 range and Index of distribution (i)>50%.

So, a rhythm is the basic rhythm of six or more aged persons and it is associated with intuitive-conscious thinking psycho-emotional stability. Decrement of iA on more than 50% and significant deviation of its amplitude from the normal level is directly associated with psychomotor development retardation and the development of pathological behavior.

Amplitude (a) is magnitude, expressed in MKV^2, of measured from pic to pic and normally aA rhythm is 20-110 mkv^2.

Index (iA and iT) is a time, expressed in %, of being of given EEG activity in given EEG epocha.

Visual evaluation of EEG data was made by classification of Zhirmunskaia [10]), which relies on Alfa rhythm data, and five groups were identified:

- Normal variant – organized type. The A rhythm is predominant in the occipital region with Normal amplitude (aA>40 and iA>50%) small low wave activity with amplitude less than of basic A rhythm;
- Disintegrated type (disorganized), characterized by the presence of A rhythm, but with significantly lesser index, compared to norma (<30% iA<50%) slow waves are represented in more amount;
- Desynchronized type-with less amplitude oscillations (<30mkv^2) and frequent various low amplitude rhythmic activities. iA is very low (<30%).

- Mixed – desynchronized-disintegrated type is pathologic type with the absence of A rhythm and presence of slow activity in the form of T and D rhythms.

Statistical analysis was made by multicentre variable method chosen from computer management system EPINFO.

Results and Discussion

From the whole cohort of prepubertal children we choose 55 with 1st degree goiter, aged 8-12 years and randomized them in three groups and controls:

1. Group I – 12 children with mild overt PH (FT4 0.7 – TSH – 10.5);
2. Group II – 22 children with subclinical hypothyreosis – (FT4 1.1 – TSH – 4.2);
3. Group III – 21 children with euthyroid state (FT4 1.3 – TSH-3.1);
4. Group IV – 15 control healthy children with normal (FT4 1.5 – TSH – 2.8).

Medina of UIE in the areas they leaved was 60.4; 10th percentile – 50.20 and 90th percentile 74.5. This numbers are in the lower third of the range for mild ID.

Study groups had following complaints. Their percentage distribution you can see in Table 1. ″Copy″ test results clearly illustrate that a considerable amount of children of group I and group II 23.8% and 18.6% ($P<0.01$ and $P<0.05$), respectively had mnestic cognitive dysfunction. It was less common in the group III 15% and 4.76 in controls.

Motor Fatigue Index in group I and group II was the highest in group I as compared to control and did not differ substantially between the study groups ($P>0.5$). This indicates that not only patients with overt hypothyreosis but also those with lesser degree of thyroid insufficiency and even euthyroid group show deterioration of cognitive functions.

PASAT test indicating of cognitive tiredness was more frequently altered in group I 16.6% as compared to group II and III 10.5 and 9.0%, $P<0.01$ and $P<0.001$, respectively, and controls 4.54%, $P<0.001$.

″Time to copy″ was disturbed in 12% of group I, 9% of group III, 7% of group III and 3.12% of controls ($P<0.00$, $P<0.011$, $P<0.05$, respectively).

″Recognition″ test also revealed altered cognition in 15.6% of group I and to a Lesser extension in groups 2 and 3 – 10.1 and 8%, respectively, as compared to controls 3.12% ($P<0.001$).

Thus, from the results observed alterations of cognition functions in preadolescent children can be considered as ID induced early neurological equivalents that precede manifestation of clinical neuroligical symptoms.

Data achieved are consistent with the results of experiments which presented the evidence that Hypothyroxinemia of pregnant women causes cognitive dysfunction in their children [11] and even mild iodine deficiency of mothers is followed by cognitive and psychomotor changes in progeny.

According to the results of EEG investigation, 66.6% of controls had a normal type of the curve with predominant A rhythm of 9-12 Hc frequency and moderate level of amplitude 90-110 mcv2. Besides, single T waves in central and occipital areas were found. 27.7% of healthy children had disorganized EEG type and 9.09% desynchronized type.

No child with overt PH had a normal type EEG. 33.3% show the disorganized type, 33.3% demonstrate a desynchronized one and 33.3% showed a mixed type.

The same picture was found in patients with subclinical hypothyreosis with significant lower levels of EEG types 18.1%, 20.2% and 17% P<0.01, P<0.01, P<0.01), respectively.

Children with euthyroid goiter had a normal type of EEG in16.66% of cases, 23.3% disorganized type and 60% desynchronized. Obtained data show the highest prevalence of pathologic EEG types in overt hypothyreosis. These changes were less common in subclinical hypothyreosis and patients with euthyroid goiter. So, overt hypothyreosis has more pronounced negative effect on the brain functional ability and is manifested by the prevalence of desynchronized EEG.

Computer analysis of EEGI revealed a significant p<0.01 increase of interrelation of iT/iA 2.54 in overt hypothyreosis, compared to controls – 1.9 and decrease P<0.01 of aA max 103.4 mkv2 compared to controls 110.10 mkv2. These changes were less pronounced in subclinical hypothyreosis and eutyroid group – 100 and 105 respectively.

So, EEG confirms the damaging effect on the brain function of preadolescent children not only in overt hypothyreosis but also in a subclinical form and euthyroid goiter. These data are consistent with [12] presenting experimental evidence of significant and proportional decrement of cerebral blood flow in severe hypothyroidism of short duration followed by direct effect on the overall brain activity.

Table 1. *The percentage distribution of complaints in patients*

Headache	18.6%
Neurotic state (irritability, emotional lability, squeamishness)	17.5%
Sthenic syndrome (adynamia, weakness, easy tiredness)	14.1%
Sleep disturbances (anxiety, restless sleep)	22%
Memory impairment	8.6%
Palpitation	7.7 %
Coldness and numbness of the limbs	7.5%

Conclusion

So, based on our data, we can conclude that mild ID in prepubertal children is accompanied by cognitive disorders represented by Mild Cognitive Impairment; among neurologic subclinical signs of manifestation of ID the Fatigue test is of great sensitivity; even mild ID is characterized by specific changes of the frequency and amplitude of physiologic spectrum of EEG activity, mainly of aA; pathologic consequences of ID are manifested both in overt and subclinical hypothyroidism and in lesser extent in patients with euthyroid goiter.

The significance of such studies is of a basic and applied nature, therefore, coordinated studies of representatives of different specialties in this direction are very important. To this end, we continue similar studies, including a large number of patients, involving specialists from related fields.

References

1. Assessment of Iodine Deficiency Disorders and monitoring their elimination: A Guide for program managers – 2nd Editions. Geneva 2001
2. Delange F. Iodine deficiency as a cause of brain damage. Postg. Med. J. 2001; 77:217-220
3. Metreveli D, Mikadze N. Endemic goiter – a public health problem; Ministry of Health of Georgia. Epidemiological Bulletin. 1996; 4(1).
4. Sekhniashvili Z, Gordeladze M, Svanidze M. Iodine deficiency diseases, Science, Tbilisi, 2000
5. Gordeladze M, Abdushelishvili N, Sechniashvili Z, Kvanchaxadze R. The structure of the thyroid disease in childhood and adolescence. Expanding endocrinology. Abstract book. Eoropean congress of endocrinology. 2005; 2-267
6. Lai CLI, Liu CK, Tai CT. A study of central and peripheral nerve condition in patients with primary hypothyroidism: the effect of thyroxin replacement. Kaohsiung J. Med Sci. 1998; 14(5):294-302
7. Glinoer D. The thyroid and environment: Merk European Thyroid Symposium. Budapest. 2000; 21-133
8. Delange F. The role of iodine in brain development. Proc. Nutr. Foet. 2000; 59(1):75-79

9. Meyers E, Meyers R. Rey Complex Figure Test and recognition Trial. Psychologic Assesment Resourses. Inc.1995
10. Zhirmunskaya E.A. Atlas of EEG classification. – M., 1996
11. Trump F, De Shepper J, Tafforean J. Mild Iodine Deficiency in pregnancy in Europe and its cosequencies for cognitive and psychomotor development of children, a review. J. Trace elemet in Med, Biol. 2013; 27:174-183
12. Constant EL. Cerebral blood flow and Glucose metabolism in hypothyroidism: A positrom emission tomography study. J.Clin. Endocrinol. Metab. 2001; 86:3864-3870

DOI 10.51231/2667-9507-2022-001-04-26-28

Clinical case of neutropenia, juvenile idiopathic arthritis in infant

T. Kutubidze, E. Naxucrishvili, K. Pagava

Department of Child and Adolescent Medicine, Tbilisi State Medical University, Tbilisi, Georgia

Abstract

Neutropenia is known to result from decreased production, ineffective granulopoiesis, shift of circulating polymorphonuclear cells (PMN) into the vascular endothelium or tissue pools, or increased peripheral destruction. Juvenile idiopathic arthritis (JIA) is a chronic idiopathic inflammatory disease that predominantly affects the joints. The article presents a clinical case of a patient 13 month old. The condition was evaluated as JIA, and glucocorticosteroid therapy was with high doses of intra venous. There was no exacerbation of the disease.

KEY WORDS: juvenile idiopathic arthritis; neitropenia; inflammation

Background

Neutropenia is a challenging issue for pediatricians. The absolute neutrophil count (ANC) is equal to the product of the white blood cell (WBC) count and the fraction of polymorphonuclear cells (PMNs) and band forms noted on the differential analysis. The absolute neutrophil count (ANC) is equal to the product of the white blood cell (WBC) count and the fraction of polymorphonuclear cells (PMNs) and band forms noted on the differential analysis. The causes of isolated neutropenia can be classified

by mechanism or by etiologic agent. Neutropenia results from four basic mechanisms: decreased production, ineffective granulopoiesis, shift of circulating polymorphonuclear cells (PMNs) to vascular endothelium or tissue pools, or enhanced peripheral destruction. Juvenile idiopathic arthritis (JIA) is a chronic idiopathic inflammatory disorder primarily involving joints. The pathogenesis and etiology of JIA are unclear. As with most autoimmune disorders, interactions among genetic factors, immune mechanisms, and environmental exposures are thought to contribute in most cases.

Most of the genetic predisposition to JIA is determined by the major histocompatibility complex (MHC) loci. Although at least some genetic component is evident in all clinical forms of JIA, the environmental component appears to be stronger for some forms [1,2]. Potential environmental influences that may improve or worsen disease include infection, antibiotic use, breastfeeding, maternal smoking, and vitamin D/sun exposure [3].

In classical manifestation sJIA White blood cell (WBC) counts are almost always elevated, and counts in the 20,000 to 30,000/mm 3 range are not uncommon, Antinuclear antibodies (ANA) and rheumatoid factor (RF) are almost always negative in sJIA.

Clinical case

Here we are presenting the case of the infant with severe neutropenia, anemia and arthritis. Patient is 13 months old. Second child in the family, born full term, weight 3300gr. Mother's pregnancy was complicated by severe gestosis of early pregnancy (NVP); COVID-19; at 12 weeks of gestation, hypercoagulation, with short term use of anticoagulation therapy. At the age of 6 months (10/2021) after vaccination, the patient experienced high fever which lasted for 1 month, later she developed moderate anemia, agranulocytosis. Child was hospitalized in December 2021 in the hematology department for anemia (Hg – 6.8 mg/dl). Numerous investigations were performed, including bone marrow aspirate which showed no abnormalities.

Treatment included antibiotic therapy with ceftriaxone IV, and according to protocol for neutropenia, cefixime p.o was prescribed for following 4 months. From March 2022, the patient expressed pain and swelling in both knees, after short period of time the both ankles were involved. Immunodeficiency was ruled out by the conducted labs. Peripheral blood analysis revealed severe anemia and agranulocytosis, Hg – 7.0 mg/dl, ANC – 0.42, Ferum – 2.47 mcm/l, C-reactive protein (CRP) – 76 mg/l, erythrocyte sedimentation rate (ESR) – 70 mm/hr. Intravenous antibiotic therapy (tazobactam/piperacillin 80mg/kg/d) was initiated, hemotransfusion was performed. During the last

hospitalization there were episodes of fever, severe malaise, swelling, pain, limitation of movement in both knees, both ankles, right hip, elbow, wrist joint, PIP joint of the third finger on the right hand. A mass deficit; – 2SD was observed. Laboratory and instrumental studies were conducted – WBC – 5.5 10.6, RBC – 4.0 – 10 12 /l, HGB – 9.2 g/l (after hemo transfusion), HCT – 29.5, MCV – 60.0, MCH – 18.8; MCHC – 32,2; bands – 2, Seg – 15 (ANC-0.93); ESR – 40mm/hr, CRP – 43.9g/dl. Antinuclear factor 1:2560, homogeneous type fluorescenece in high titer.

The condition was evaluated as sJIA, and glucocorticosteroid therapy with high doses of i.v. was prescribed. Intensity of arthritis decreased in dynamics, inflammatory markers – positive dynamics, fever was no longer observed. The patient is currently 1 year and 5 months on 7.5 mg prednisolone daily. There is no exacerbation of the disease.

Conclussion

As resume we can say, there are two very important questions about this patient: Is neutropenia lasting for more then 5 months the beginning of the Juvenile Idiopathic Arthritis (JIA), and could the maternal COVID-19 infection lead to innate immune dysregulation and as the result an unusual presentation of JIA and neutropenia.

References

1. Dong Y, Mo X, Hu Y, Qi X, Jiang F, Jiang Z, Tong S. Epidemiology of COVID-19 Among Children in China. Pediatrics. 2020;145(6). doi: 10.1542/peds. 2020-0702
2. Ellis JA, Munro JE, Ponsonby AL. Possible environmental determinants of juvenile idiopathic arthritis. Rheumatology (Oxford) 2010; 49(3):411-425. doi: 10.1093/rheumatology/kep383
3. Hinks A, Marion MC, Cobb J. Brief Report: The Genetic Profile of Rheumatoid Factor-Positive Polyarticular Juvenile Idiopathic Arthritis Resembles That of Adult Rheumatoid Arthritis. Arthritis Rheumatol 2018; 70:957
4. Gracia-Ramos AE, Martin-Nares E, Hernández-Molina G. New Onset of Autoimmune Diseases Following COVID-19 Diagnosis. Cells. 2021; 10(12):3592. doi: 10.3390/cells10123592

DOI 10.51231/2667-9507-2022-001-04-29-36

Dacriocistorhinostomy and Screening of the Recurrence

G. Petriashvili[1], Sh.Tsiklauri[1,2], N. Nakudashvili[3], M. Lomaia[4], A. Akhalaia[5]

[1]LTD "Aversi Clinic", Tbilisi, Georgia
[2]European University Tbilisi, Georgia
[3]Tbilisi State Medical University, Tbilisi, Georgia
[4]TSMU The First University Clinic, Tbilisi, Georgia
[5]Tbilisi JSC "Curatio", Tbilisi, Georgia

Abstract

The relevance of the pathology of the lacrimal ducts to date remains extremely important, as it leads to disability and loss of professional fitness for a significant number of the working population. Complaints of lacrimation are presented by 6 to 25% of all patients who visit an ophthalmologist. Diseases of the lacrimal ducts are not only the cause of disability, but also lead to serious complications. Creeping corneal ulcer, leading to persistent visual impairment or even loss of vision, is associated with the presence of dacryocystitis in 40-50% of cases. Severe complications may also arise if purulent dacryocystitis remains unrecognized before surgery on the eyeball.

KEY WORDS: dacriocistorhinostomy (DCR); endonasal approach

Introduction

Treatment of patients with diseases of the lacrimal ducts is one of the difficult tasks of ophthalmology and requires intense and painstaking work from a doctor. The pathology of the vertical part of the lacrimal duct is still an ungrateful problem in ophthalmology, since often, despite of the therapeutic measures, relapses of the disease occur.

According to various authors, in the total mass of eye pathology, diseases of the vertical part of the lacrimal ducts range from 2 to 21.9%. In women, dacryocystitis occurs 6-10 times more often than in men, which is explained by the anatomical and physiological features of the lacrimal ducts.

The social significance the rehabilitation of the patients with pathology of the lacrimal ducts lies in the fact, that the proportion of this pathology in people of working age is quite high.

Lachrymation that occurs with dacryocystitis or stenosis of the nasolacrimal duct is not only a ″discomfort″ disease, but also a factor that reduces the ability to work, especially in people of certain professions that require high vision. It is an aesthetic defect, and when an infection is attached, it can be a prerequisite for a number of eye diseases (conjunctivitis, keratitis, corneal ulcers, scleritis), which poses threat to vision and creates unfavorable conditions for intraocular operations, and can cause ophthalmic and intracranial inflammation.

Diseases of the lacrimal ducts are polyetiological pathology, where diseases of the nose and paranasal sinuses, adverse environmental factors (professional and climatic), the consequences of infectious diseases, injuries, and congenital malformations are important. Modern research methods reveal the predominance of the role of rhinogenic pathology in the occurrence diseases of the vertical part of the lacrimal duct in 67.6 – 100% of patients. In case of injuries of the facial skull lacrimal ducts are also often damaged.

The main method to successfully eliminate irreversible changes in the vertical part of the lacrimal ducts caused by various surgical reasons. Almost 100 years have passed since the Florentine rhinologist A.Toti [1] proposed external dacryocystorhinostomy. External dacryocystorhinostomy according to Toti, being, at one time, a major achievement in ophthalmic surgery, had its imperfections. In ophthalmic practice, external dacryocystorhinostomy is used in various modifications aimed at reducing trauma, simplifying the execution technique and preventing infection of the new fistula.

In otorhinolaryngology, modifications of endonasal dacryocystorhinostomy proposed by West, intranasal microdacryocystorhinostomy and laser dacryocystorhinostomy are used. Often, endonasal operations are performed with simultaneous removal of

the so-called unfavorable rhinogenic factors. However, the use of the "two in one" tactics, even with the use of modern surgical equipment, causes an increase in the inflammatory reaction of the altered nasal mucosa, which is unable to adequately respond to damage during surgical exposure, which leads to a protracted course of healing.

In clinical practice, to form an anastomosis between the lacrimal sac and the nasal cavity during external dacryocystorhinostomy, are used suture and sutureless fistula plastics with mucous membranes.

One of the ways to simplify the formation of the anastomosis and prevent the recurrence of obstruction after the operation of dacryocystorhinostomy is the intubation of the anastomosis with various alloplastic implants.

According to various authors, the results of dacryocystorhinostomy with permanent intubation with alloplastic implants are worse than the results of the same operation with temporary intubation [2,3,4,5].

However, known implants have their drawbacks, namely: they are not easy to manufacture and often do not take into account the anatomical features of a particular person due to the lack of the possibility of intraoperative modeling, and they also have shapes that do not allow to stay in the anastomosis for a long time optimally necessary for the formation of a full-fledged rhinostomy.

After surgery, relapses of the disease occur in 0.6 to 23% of cases at different times the efficiency of repeated surgical interventions ranges from 58 to 80%.

These circumstances make it relevant to search for the most optimal surgical treatment methods aimed at improving the efficiency and simplifying the method of fistula formation between the lacrimal sac and the nasal cavity.

As is known, at one of the stages of endoscopic endonasal DCR, an incision is made in the mucous membrane of the nasal cavity and it is separated in such a way as to expose the bone in the area.

Future dacryostomy opening when the bone remains uncovered by soft tissues after surgery, granulation tissue is formed in this area, which is subsequently remodeled.

Surgery remains the main treatment for dacryocystitis. The operation of choice for this pathology is dacryocystorhinostomy, the purpose of which is to create conditions for the outflow of tears into the nasal cavity by forming a dacryostomy.

In ophthalmic practice, the most common and effective operation for dacryocystitis is external dacryocystorhinostomy. However, the method is not without very significant drawbacks, the essence of which lies in the fact that dacryocystitis etiologically often closely associated with diseases of the nasal cavity and paranasal sinuses.

Dacryocystorhinostomy with an endonasal approach has significant advantages and a number of undoubted advantages, namely: low trauma, cosmetic, less disruption of the physiological system of lacrimal drainage, the ability to eliminate adverse rhinological factors that contribute to the recurrence of the disease during the operation.

During external dacryocystorhinostomies, in 34.3% of cases, certain complications are observed. One of the main factors in preventing and reducing the percentage of these complications is a thorough preoperative clinical examination of the patient, especially the condition of the nasal cavity and paranasal sinuses [6,7,8,9].

Currently, in solving the problem of restoring the patency of the lacrimal ducts, there is a close convergence of interests and efforts of ophthalmologists and otorhinolaryngologists.

In our opinion, the development and introduction of diagnostic and therapeutic endoscopic interventions into clinical practice in recent years, in our opinion, greatly facilitates the task of otorhinolaryngologists and allows them to more widely engage in endonasal surgery for lacrimal duct pathology, as well as to transfer endonasal interventions to the microsurgical level using endoscopic techniques [10,11,12,13,14,15].

The recurrence rate after dacryocystorhinostomy varies from 1 to 15% for endonasal operations and from 0.6 to 25% for external access. The effectiveness of repeated surgical interventions ranges from 58 to 80%. The development of preventive measures aimed at preventing scarring of dacryostomy in the postoperative period goes in different directions. However, the proposed innovations are used in a small number of cases and are not widely used.

Based on the foregoing, we have identified the purpose and objectives of the study.

Materials and Methods

20 patients who underwent endonasal dacryocystorhinostomy were observed. There were 17 female and 3 male patients. Their age ranged from 18 to 85 years. We divided the patients into 2 groups. 10 patients in the first group and 10 patients in the second group. In the first group, 6 months after the operation, we called all patients once a week and washed the tear ducts, while in the second group, no washing was done.

Drains were removed from patients in both groups on the 8th month after surgery.

Results

As a result of our observation, it was revealed that despite the difference in age and gender, all operations were performed with the same technique, none of the patients had intraoperative or postoperative complications, postoperatively all patients were prescribed antibiotic therapy with amoxicillin and clavulanic acid for 7 days and also antibiotic eye drops 1 drop per day 4 times for 7 days.

Only one of the patients with weekly lavage needed a repeat operation, while in the second group we had four relapses.

It is necessary to pay attention to such reliable facts, despite the fact that the groups studied by us are small.

Discussion

Regardless of age and sex, as well as concomitant diseases, during the weekly visit of the second group of patients for 2 months of observation, it was revealed that in the initial period, some of them had some tears and during washing, we obtained the inflammatory exudate in the lacrimal sac, and in some cases, despite the presence of drainage, the tears flowed freely in the newly formed foramen and therefore did not Patients did not experience tearing or any other discomfort.

After several procedures, the inflammatory exudate was washed away and the inflammatory swelling was removed, and the channel became freely flowing.

Based on our observation, in the postoperative period, 6 months after the surgery, weekly washing of the lacrimal canal for 2 months without removing the embedded drainage reduces the probability of artificially obtained lacrimal canal closure and the need for reoperation, although the said process, carrying out the same intensity as the procedure, is quite uncomfortable and has certain difficulties connected.

Conclusion

Taking into account our observations, we believe that if the patient does not have any complaints (tears, redness, stuffy nose) in the postoperative period for 1-6 months, he does not need additional washings. In the presence of the above-mentioned complaints, in order to prevent restenosis, it is necessary to periodically flush the lacrimal canal before the drainage is removed.

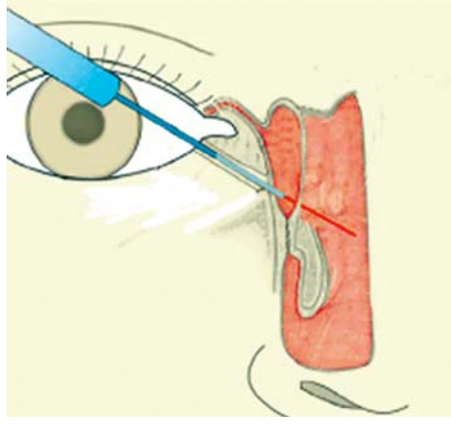

Fig.1. Schematic illustration of laser cystectomy. Nd:YAG laser probe is introduced through the lower punctum and lower canaliculus to evaporate epithelium of the lacrimal sac.

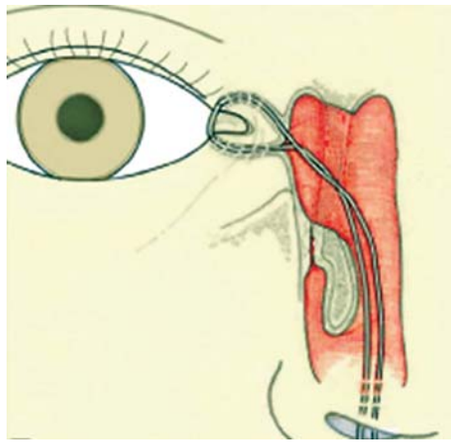

Fig 2. Schematic illustration of laser cystectomy. Final appearance of the laser cystectomy. Note the complete removal of the lacrimal sac.

References

1. Toti A. Nuovo metodo conservatore di cura radicle delle suppurazoni croniche del sacco lacrimale (Dacriocistorinostomia). Clinica Moderna Firenze, 1904, 10; 385-387
2. Rice DH. Endoscopic intranasal dacryocystorhinostomy-A cadaver study. American Journal of Rhinology & Allergy. 1988; 2(3):127. https://doi.org/10.2500/105065888781693122
3. McDonogh M, Meiring JH. Endoscopic transnasal dacryocystorhinostomy. The Journal of Laryngology & Otology. 1989; 103(6):585-587. https://doi.org/10.1017/s0022215100109405
4. Wormald PJ. Powered endoscopic dacryocystorhinostomy. The Laryngoscope. 2002; 112(1):69-72. https://doi.org/10.1007/978-0-387-35267-1_21
5. Majumder A, Singh M, Das C, Das S, Hazra TK. Endonasal dacryocystorhinostomy with mucosal flaps: our experience. Indian J Otolaryngol Head Neck Surg. 2013; 65(2):371-375
6. Becker BB. Dacryocystorhinostomy without flaps. Ophtalmic Surg. 1988; 19:419-427. https://doi.org/10.1007/s12070-012-0541-6
7. Sonkhya N, Mishra P. Endoscopic transnasal dacryocystorhinostomy with nasal mucosal and posterior lacrimal sac flap. J Laryngol Otol. 2009; 123(3):320-326. https://doi.org/10.1017/s0022215108003897
8. Trimarchi M, Giordano Resti A, Bellini C, Forti M, Bussi M. Anastomosis of nasal mucosal and lacrimal sac flaps in endoscopic dacryocystorhinostomy. Eur Arch Otorhinolaryngol. 2009; 266(11):1747-1752. https://doi.org/10.1007/s00405-009-1002-z
9. Jawaheer L, MacEwen CJ, Anijeet D. Endonasal versus external dacryocystorhinostomy for nasolacrimal duct obstruction. Cochrane Database Syst Rev. 2017; 24(2):CD007097. https://doi.org/10.1002/14651858.cd007097.pub3
10. Beloglazov VG. Alternatives to recovery of lacrimal duct patency. Vestnik oftal'mologii. 2006; 122(1):8-12. (In Russ.).
11. Baek JS, Jeong SH, Lee JH, Choi HS, Kim SJ, Jang JW. Cause and management of patients with failed endonasal dacryocystorhinostomy. Clinical and Experimental Otorhinolaryngology. 2017; 10(1):85. https://doi.org/10.21053/ceo.2016.00192
12. Gupta N. Improving results in endoscopic DCR. Indian Journal of Otolaryngology and Head & Neck Surgery. 2011; 63(1):40-44. https://doi.org/10.1007/s12070-010-0112-7
13. Ji QS, Zhong JX, Tu YH, Wu WC. New mucosal flap modification for endonasal endoscopic dacryocystorhinostomy in Asians. Int J Ophthalmol. 2012; 5(6):704-707

14. Fayet B, Bernard JA. A monocanalicular stent with self-stabilizing meatic fixation in surgery of excretory lacrimal ducts. Initial results. Ophtalmologie. 1990; 4(4):351-357
15. Drnovsek-Olup B, Beltram M. Transcanalicular diode laser-assisted dacryocystorhinostomy. Indian J Ophthalmol. 2010; 58(3):213-7. doi: 10.4103/0301-4738.62646. PMID: 20413924; PMCID: PMC2886252

DOI 10.51231/2667-9507-2022-001-04-37-41

Plasma radiation treatment influence in the process of infected postoperative wounds

M. Daraselia[1,2], S. Jaiani[2], E. Mgaloblishvili[2], B. Tsutskiridze[2]

[1]*European University, Tbilisi, Georgia*
[2]*Acad. V. Bochorishvili Clinic, Tbilisi, Georgia*

Abstract

In the work have discribed methods of the treatment of purulent wounds by plasma rays during post-caesarean section sepsis in gynecological patients group. It was established that along with the basic treatment, the use of plasma rays as an auxiliary method relatively reduces the wound healing time in that group. Also, it was appealed on the simplicity and budget of the method as effective.

KEY WORDS: plasma flows; caesarean section; infected wound; sepsis

Introduction

Nowadays one of the most acute problems in modern medicine postoperative complications remain, to be more specific, one of them is wound infection after caesarean section. It is notificated that caesarean delivery is one of the most frequent surgical interventions performed worldwide accounting for up to 60% of deliveries in a number of countries [1,2]. It carries the risk for various short-term ostoperative morbidities, including surgical site infection (SSI), which is one of the most common complications

following caesarean section, and has an incidence of 3%-15%. It depends on prevalence of the accompanying deseases, general condition of the patient, blood loss during operation, complication after operation-septic condition [2,3,4].

It places physical and emotional burdens on the mother herself and a significant financial burden on the health care system. Moreover, SSI is associated with a maternal mortality rate of up to 3%. With the global increase in caesarean section rate, it is expected that the occurrence of SSI will increase. Given its substantial implications, recognizing the consequences and developing strategies to diagnose, prevent, and treat SSI are essential for reducing postcaesarean morbidity and mortality. It may prolong maternal hospitalization, increase health care costs, and lead to other socioeconomic implications. Optimization of maternal comorbidities, appropriate antibiotic prophylaxis and evidence-based surgical techniques are some of the practices proven to be effective in reducing the incidence of SSI. The problem is exceedingly actual because of increasing resistance of microflora and consequently, reduced efficiency of antibiotic therapy. Sometimes the treatment of infected wounds lasts months [2,5,6] and affects psycological condition of the patient, therefore it is related to great financial expences. It is very important to find new supplementary methods for the treatment of infected wounds with basic treatment with antibiotics and pathogenic and ethiologic treatment.

At present, in medicine broad varied physical methods were identified, as thermal and laser radiations. The experience of their using has shown perspective of this method in different pathologys. One of the most perspective ways of admission of heat energy to centtre of the pathological changes, as well, as biologicaly active zone and point is use the temperature plasma flow. The plasma – the most widespread, the most power-consuming and very slopy from four conditions of material. The plasma consists of ionof any element of the periodic system. The material moves over to condition of the plasma under expence of the greater energy from outside. In the process of destruction is accompanied by a big splash of energy (light, gravitating to ultraviolet spectrum and heat up to 15000^{o}C [2,7,8].

The plasma impact is compact, reliable and technically simple, easy for functioning and service. Its flexible design allows working practically in any area. The flows of plasma do not cause negative effect on the patient and medical personel. Using plasma presents itself essential breakout in the field of physical methods of the influence on biological fabrics and many authors commite perspective of use of plasma in modern medicine [1,7,9,10,11,12]. One of the advanteges of this method is the possibility of reducting the overall expences of treatment and the length of treatment.

Goal and objectives

The reason of the study was to show the results of using plasma flow as a suplementary method in patients with an infected wound after caesarean section sepsis. The purpose of the study was to define the perspective of using the plasma in treatment of infected wounds in patients with gynecological sepsis – after caesarian section.

Materials and methods

We studied the influence of plasma radiation in treatment of infected wounds.

The study was conducted in Acad. V. Bochorishvili Clinic – gynecological department. The method was applied to 10 patients (group 1) and compared to 10 patients without plasma radiation (group-2).

We used argon plasma radiation. 10 procedures were made 2 times a day during 5-7 minutes. The temperature plasma ray on wound surface cover was in the range of 40-42^{o}C.

The method was safe, did not require preliminary preparation and did not depend on severity of the pathology. All patients received standard treatment.

Results and discussion

1. A quick healing of the wound because of bactericide and drying effect of the plasma;
2. More swift regenerative processes in the wound;
3. Improvement by reducting the intensity of post operational pain during the postoperative period;
4. Reduction of average length of treatment by 5-7 days;
5. Reduction of hospital stay days;
6. Reduction of average cost of treatment.

Conclusion

Positive effects of the use of plasma radiation for treatment of infected wounds in patients with post caesarean sepsis were reported during the study period. Data received by this study gives us the opportunity to recommend the method of plasma irradiation as a supplementary method in the treatment of infected wounds in patients with postcaesarean sepsis.

References

1. Gibbons L, Belizán JM, Lauer JA, Betrán AP, Merialdi M, Althabe F. The global numbers and costs of additionally needed and unnecessary caesarean sections performed per year: overuse as a barrier to universal coverage. World Health Rep. 2010; 30:1-31
2. Belizan JM, Althabe F, Barros FC, Alexander S. Rates and implications of caesarean sections in Latin America: ecological study. BMJ. 1999; 319 (7222):1397-1400
3. Olsen MA, Butler AM, Willers DM, Devkota P, Gross GA, Fraser VJ. Risk factors for surgical site infection after low transverse caesarean section. Infect Control Hosp Epidemiol. 2008; 29(6):477-484
4. Jaiani S, Tsutskiridze B, Kheladze Z, Kheladze Zv. Aspects of application of plasma streams in treatment of the explosive wounds of finiteness. Criticale Care and Catastrofe Medicine 2005; 45-49
5. Kheladze Z, Jaiani S, Tsutskiridze B, Kheladze Z. The experience of the using plasma radiations at treatment of the pulmonary breachesbesidesick with critical conditions. Critical Care and Catastrophe Medicine. 2007; 76-83
6. Roex AJ, Puyenbroek JI, van Loenen AC, Arts NF. Single – versus three-dose cefoxitin prophylaxis in caesarean section: a randomized clinical trial. Eur J Obstet Gynecol Reprod Biol. 1987; 25(4):293-298
7. Opøien HK, Valbø A, Grinde-Andersen A, Walberg M. Post-caesarean surgical site infections according to CDC standards: rates and risk factors. A prospective cohort study. Acta Obstet Gynecol Scand. 2007; 86(9):1097-1102
8. Zuarez-Easton S, Zafran N, Garmi G, Salim R. Postcaesarean wound infection: Prevalence, impact, prevention, and management chal-

lenges. International Journal of Women's Health. 2017; 9:81-88
9. Schneid-Kofman N, Sheiner E, Levy A, Holcberg G. Risk factors for wound infection following caesarean deliveries. Int J Gynecol Obstet. 2005; 90(1):10-15
10. Gibbs RS. Clinical risk factors for puerperal infection. Obstet Gynecol. 1980; 55(Suppl 5):S178-S184
11. Horan TC, Gaynes RP, Martone WJ, Jarvis WR. CDC definitions of nosocomial surgical site infections, 1992: a modification of CDC definitions of surgical wound infections. Infect Control Hosp Epidemiol. 1992; 13(10):606-608
12. Jaiani S, Tsutskiridze B, Kheladze Z, Kheladze Zv. Aspects of application of plasma in treatment of the explosive wounds of finiteness/ Critical Careand Catastrophe Medicine. 2007; 45-48

DOI 10.51231/2667-9507-2022-001-04-42-51

COVID-19 and pirfenidone. A case report

K. Tsanava, L. Trapaidze, E. Shengelia

European University, Tbilisi, Georgia

Abstract

Diagnosis and treatment of Idiopathic Pulmonary Fibrosis (IPF) has been greatly influenced by the COVID-19 pandemic. Not only has it impacted the prognosis of the Idiopathic Pulmonary Fibrosis, but also the approach to treating these patients. The aim of this study was to evaluate our patient who got infected with COVID-19 and after hospitalization the underling, not previously diagnosed idiopathic pulmonary fibrosis was suspected in this patient. Due to COVID-19 infection and suspected idiopathic pulmonary fibrosis the patient was administered Pirfenidon to treat the deep fibrotic changes. The case was studied during the period from November 2020 – July 2021 in "Vivamedi" hospital Tbilisi, Georgia. The systemic review was made using available literature from online libraries like PubMed, Google Scholar and UpToDate. The report was prepared after analysing all laboratory results and other radiological investigations that were performed during the course of treatment. The patient was treated mainly with Oxygen therapy, Pirfenidone and anticoagulants. The patient recovered from COVID-19 with minimal pulmonary fibrotic changes. The vitals of the patient were stabilised and the lab results returned to normal. The patient was discharged from the hospital after 10 days and fully recovered from the viral infection. The survival after COVID-19 pneumonia in a patient with newly diagnosed IPF under antifibrotic + treatment without serious deterioration is a novel case. Antifibrotics which are available or developing not only have a role in treating such cases but can also be valuable in treating severe COVID-19 in patients without IPF, and might also be helpful preventing pulmonary fibrosis after SARS-CoV-2 infection.

KEY WORDS: COVID-19; idiopathic pulmonary fibrosis; pirfenidone; co-existing

Introduction

Interstitial lung diseases (ILDs) comprise a wide spectrum of acute and chronic lung diseases that cause progressive fibrosis, scarring and the loss of the lung tissue, causing compromised blood oxygenation and respiratory function. The most common form is the idiopathic pulmonary fibrosis (IPF), which majorly affects the older population. It is a specific form of chronic, progressive, fibrosing interstitial pneumonia of unknown cause. It is defined by the histopathologic and/or radiologic pattern of usual interstitial pneumonia. Viral infections can trigger acute exacerbations, with poor prognosis. ILD with COVID-19 infection is associated with higher rate of acute exacerbations of the disease, the impact was notably significant in males and younger patients. Also, COVID-19 patients with ILD have shown more severe clinical manifestations, including increased mortality than the ones without ILD. There are only a handful of recommendations for patients with IPF when they happen to get infected with COVID-19.

The aim of this study was to understand how COVID-19 affects a patient with suspected idiopathic pulmonary fibrosis and also the possibility of management of such patients with antifibrotics along with other conventional therapies. This case-report has a significant value, as the patient with newly contracted COVID-19 was diagnosed alongside with ILD. So, survival rate for such patient is near impossible but with the treatment with antifibrotic like pirfenidone, anticoagulants and supportive therapies, the patient survived and recovered the viral infection. Due to its rarity, we report this case and check all previous research on it.

Materials and methods

The research included a systemic review and a case of 66-year-old female patient. All the lab reports and test results were thoroughly studied. The literature review was made using the available literature on online libraries like PubMed, Google Scholar, Up-to-date and then the case report was prepared with the patient's anamnesis and the lab results before and after the treatment. The study carried on from November 2020 – July 2021.

Case report

The patient presented with the complains of a few days of sweating, chills, high temperature, dizziness, dry cough and breath insufficiency. RT-PCR was performed and the result came out to be positive for COVID-19. Treatment was started in the COVID special department as per the recommendations. It is also crucial to note that five years ago the patient was diagnosed with Diabetes mellitus. Her diabetes mellitus was managed poorly, as she reported her blood sugar level was almost always elevated. As she reported for the past five to six years, two three times a year she had febrile events with acute shortness of breath, which she treated symptomatically. According to the patient during the previous year she had two or three upper respiratory tract infection and all of them were complicated with severe shortness of breath, fevers and chills. Her family doctor considered above mentioned episodes as acute pneumonia, hence prescribed oral antibiotic treatments. Despite the fact that her fever chills and fatigue resolved, she still experienced shortness of breath that had been progressing for the past year.

Upon arrival the patient was in an acute (moderately severe) distress. She had fever 38ºC, sweating, chills, dry cough, increased respiratory rate 30-32, dyspnoea, blood pressure 135/75, heart rate 90 and oxygen saturation at 89-92% on room air. Upon examination, the patient was found to be well oriented in time and space and her speech was fluent. Bilateral dense vesicular sounds were heard on auscultation and the breath was weakened in the lower lobes of lung. Dry expiratory crackles could be heard, cardiac auscultation revealed dull rhythmic sounds. Patient had light acrocyanosis, otherwise skin inspection showed unremarkable results. The palpation of abdomen was painless, no organomegaly. There was no peripheral lymphadenopathy. CT examination demonstrated no deformity in the chest cavity or any mediastinal deviation. The trachea, main bronchus and the lobar bronchus were not obstructed but their walls were thickened and had dilations on the inner surface (bronchiectasis). Small paratracheal hypodense areas could be noted on the right side. There was reduced pneumatization of both lungs in a diffuse and uneven manner due to pneumofibrosis, more prominently seen in lower lobes. Calcifications of the paraseptal tissues could be seen. Additionally, ground-glass infiltrative changes were seen in both the lungs and rough fibrotic zones were expressed in areas of infiltration. IV contrast showed a more clearly enhanced picture. There was no pericardial or pleural effusion. See Fig.1.

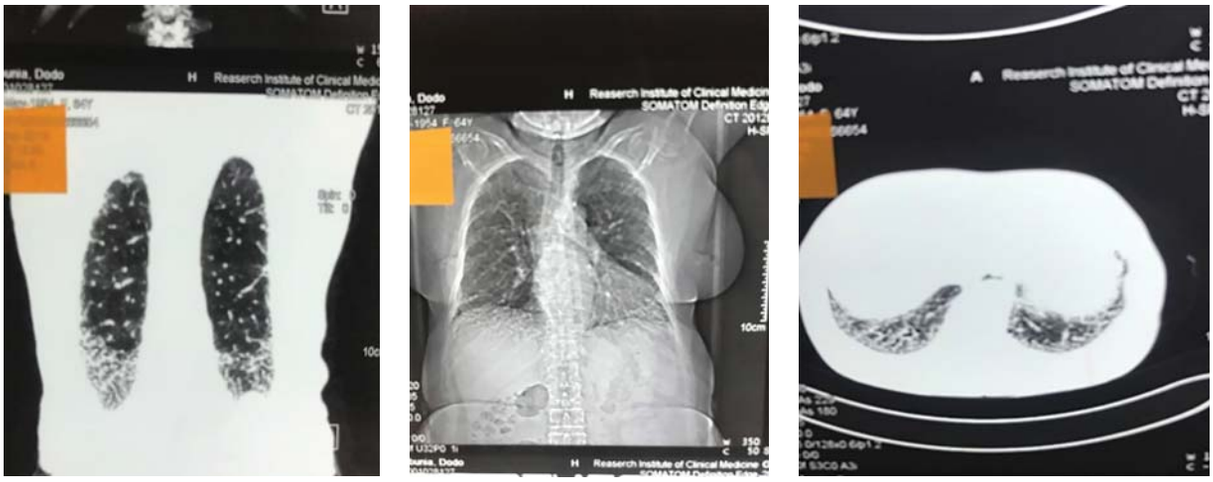

Fig. 1. *Photo from patient's medical history.*

CT data are consistent with the presence of interstitial pneumonia.

The main diagnosis was COVID-19 associated interstitial pneumonia (absorptive phase) and bilateral pneumofibrosis. The patient was treated with pirfenidone, oxygen supplementation and anticoagulants. The vitals were successfully stabilised and she was discharged within 10 days.

Discussion

Interstitial lung diseases are a heterogeneous group of disorders characterized by alveolar septal thickening, fibroblast proliferation, collagen deposition, and, if the process remains unchecked, pulmonary fibrosis. ILDs represent a large number of conditions that involve the parenchyma of the lung-the alveoli, the alveolar epithelium, the capillary endothelium, and the spaces between these structures, as well as the perivascular and lymphatic tissues.

ILDs have been difficult to classify because >200 known individual diseases are characterized by diffuse parenchymal lung involvement, either as the primary condition or as a significant part of a multiorgan process, as may occur in the connective tissue diseases (CTDs).

Idiopathic pulmonary fibrosis (IPF) is the most common form of idiopathic interstitial pneumonia.

Clinical Manifestations include exertional dyspnea, a nonproductive cough, and inspiratory crackles.

The HRCT lung scans typically show patchy, predominantly basilar, subpleural reticular opacities, often associated with traction bronchiectasis and honeycombing. Pulmonary function tests often reveal a restrictive pattern, a reduced DLCO, and arterial hypoxemia.

Histologic findings include interstitial inflammation, foci of proliferating fibroblasts, dense collagen fibrosis, and honeycomb changes [1,2].

Many patients with ILD are on immunosuppressive medications. It stands to reason that patients with ILD would have an increased rate of complications and death from COVID-19 [1,3,4]. Consequently, patients with idiopathic pulmonary fibrosis have poor clinical outcomes with COVID-19 disease.

The risk of serious disease and death in COVID-19 cases increases in people over age 65, in people who smoke or previously smoked, and in people with other serious medical disorders, such as Cancer, Chronic heart, lung, kidney, or liver disease, Diabetes, Stroke or cerebrovascular disease, Immunocompromising conditions, HIV infection, Tuberculosis, Sickle cell disease, Thalassemia, Dementia, Obesity, Pregnancy (up to 42 days after pregnancy), Some types of disabilities, Substance use disorders, Physical inactivity, Some mental health disorders such as depression and schizophrenia.

In addition to respiratory disease that can progress to acute respiratory distress syndrome (ARDS) and death, other serious complications include the following: Heart disorders including arrhythmias, cardiomyopathy, and acute cardiac injury, coagulation disorders including thromboembolism and pulmonary emboli, disseminated intravascular coagulation (DIC), hemorrhage, and arterial clot formation, Guillian-Barre syndrome (rare), sepsis, shock, and multiorgan failure [2,5,6].

Idiopathic pulmonary fibrosis (IPF) in the vast majority of cases affects the older population, in a progressive fibrosing manner, resulting in severe respiratory failure and death within 3-5 years [6].

Public health officials recommend that patients in the higher risk category should reduce the risk of being exposed to SARS-CoV-2 [7,8].

Patients with IPF, sarcoidosis, and other ILDs with known etiology, such as rheumatologic diseases with ILD involvement, could be at particular risk for SARS-CoV-2, since they tend to be older, have multiple comorbidities, and are often immunosuppressed by their disease or therapy. Currently, there is no reliable data regarding the incidence of COVID-19 in the field of ILDs.

Several media reported cases of pulmonary fibrosis resulting from COVID-19 disease. Most importantly, acute exacerbation leads to an in-hospital mortality of more than 50% with a mean survival time of only a few months [9].

Therefore, consideration of complications in IPF is of great importance for the may develop acute exacerbation such as pneumonia and progress to respiratory failure

and acute respiratory distress syndrome (ARDS), which requires life support with a mechanical ventilation.

Acute exacerbation of IPF and severe cases of COVID-19 show similar clinical profile as both affect the elderly, the ones suffering from diabetes, cigarette smoke exposure or ischemic heart disease. Among the underlying diseases, chronic respiratory comorbidities show more significant impact on the clinical picture of COVID-19. Thoracic malignancy and Chronic Obstructive Pulmonary Disease (COPD) are the risk factors for more severe manifestations and poor prognosis of COVID-19. As per studies, asthma does not possess any major risk for severity and susceptibility of COVID-19. There is very limited literature available on clinical course of COVID-19 in patients with ILD [10,11].

The exacerbated inflammatory state, associated with the fibrotic tissue stimulated by SARS-CoV-2, plays a key role in critical clinical cases. As the viral infection progresses to more severe stages, cytokine storm causes lung damage with extensive fibrosis and rapid onset of respiratory distress syndrome.

The possibility of shared mechanisms of fibrosis between ARDS cases and chronic ILDs raises the potential that therapies that treat ILDs could also be beneficial to COVID-19 associated lung disease [12,13]. In this regard, pirfenidone is being used in patients with COVID-19 in Wuhan, China (clinical trial.gov), and a prospective clinical trial with the other antifibrotic drug, nintedanib, is discussed [12], taken in consideration the shared pathogenetic and clinical similarities of COVID-19 and the fibrotic process.

Using antifibrotic agents, such as pirfenidone, can have therapeutic efficacy in addressing fatal lungs complications. Pirfenidone is a class of pleiotropic pyridine compounds with anti-inflammatory, anti-fibrotic and antioxidant properties.

Pirferidone and nintedanib are both pleiotropic anti-fibrotic agents and although both of the drugs are approved for the treatment of idiopathic pulmonary fibrosis (IPF) as a monotherapy [14], pirfenidone is the drug of choice in managing idiopathic pulmonary fibrosis (IPF). It was first approved in Japan for the treatment of patients with idiopathic pulmonary fibrosis after clinical trials, under the trade name of Pirespa by Shionogi, in 2008. Randomised controlled clinical trials and subsequent post hoc analyses have demonstrated that pirfenidone reduces lung function decline, decreases mortality and improves progression-free survival. Long-term extension trials, registries and real-world studies have also shown similar treatment effects with pirfenidone [3,10,15,16].

It is administered orally, 2-3 tablets three times a day, for at least 4 weeks. With a diversity of mechanisms of action reduces the inflammatory and fibrosis of the lung tissue. It downregulates the cytokines, including connective tissue growth factor (CTGF), transforming growth factor (TGF)-β1, tumour necrosis factor (TNF)-α and platelet-derived growth factors (PDGF). Also, pirfenidone is a reactive oxygen species (ROS) scavenger, as well as it suppresses the expression of ACE receptor, the major cellular

receptor for COVID-19. There are also some other features of pirfenidone, including antifibrotic effects and anti-apoptotic effects, which make it a suitable treatment for COVID-19. Moreover, employing a combined therapy of anti-inflammatories with antifibrotics, like pirfenidone could give additional clinical benefits.

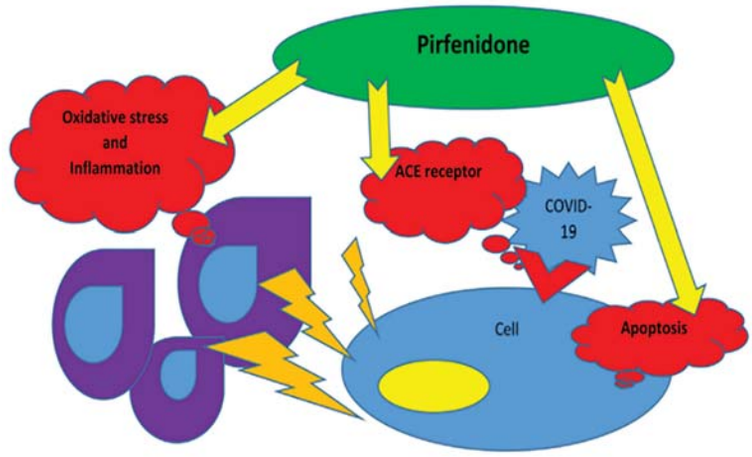

Fig. 2. *Pirfenidone inhibits apoptosis, down regulates the expression of ACE receptors, reduces inflammation through various mechanisms and ameliorates oxidative stress, thereby, protects pneumocytes from the invasion of COVUD-19 and the resulting cytokine storm.*

Pirfenidone has been shown to have a favourable safety profile and was generally well tolerated over the long term in clinical trials and real-world experience. However, side-effect management is critical to help some patients remain on treatment over the long term. The primary treatment-related adverse events associated with pirfenidone therapy are gastrointestinal upset, rash and photosensitivity. Gastrointestinal events may be mitigated by ensuring that pirfenidone is taken with food, while skin symptoms may be reduced by avoiding sun exposure and frequent use of sunblock [17].

There is description of case report about successful concomitant therapy with Pirfenidone and Nintedanib in idiopathic pulmonary fibrosis. They presented the first case of a Caucasian male patient with IPF treated with both pirfenidone and nintedanib following 2 years of treatment with pirfenidone monotherapy. Over a 24-month period, there was a clear decline in the patient's forced vital capacity from 3.5 liter before initiation of treatment to 2.5 liter after 24 months. Concomitant nintedanib treatment was initiated in March 2015. Lung function stabilized, and the two treatments were well tolerated. Treatment with pirfenidone and nintedanib has currently been ongoing for nearly 12 months. This was the first report of a successful long-term treatment with pirfenidone and nintedanib and suggested that in selected cases, concomitant anti-fibrotic therapy may represent a safe and therapeutically valuable escalation option after pirfenidone monotherapy [14].

Conclusion

The survival after COVID-19 pneumonia in a patient with a newly diagnosed, underlying IPF under antifibrotic treatment without serious deterioration is a novel case. The physicians today are facing the challenge to protect and treat the patients with ILD from COVID-19. Telemedicine has played a vital role in dealing with this pandemic. The case of our patient demonstrated that combining pirfenidone with the existing medications would not only cease the progression of the disease but also help with managing the residual pulmonary fibrotic damage in the post healing phase. With its pleotropic action mechanisms, pirfenidone can even be used to treat the COVID-19 patients without IPF. As, we know that in such pandemic situation we all are fond of treatment for COVID-19 and how we can stop it. In our case the patient was already suffering from symptoms of undiagnosed Idiopathic pulmonary fibrosis and the fibrotic changes were ongoing in her respiratory system. Additionally, to this chronic condition, the patient contracted COVID-19 infection and as a result her respiratory symptoms deteriorated rapidly [7,9,13]. The conjoined two chronic and acute fibrotic diseases made us to come to decision to start pirfenidone in this patient. 10 days after we started pirfenidone the patient's symptoms and laboratory results improved. After this she was discharged from the hospital. The patient was prescribed Pirferidone and recommended follow-up visit for 2 months. Follow-up pulmonary CT scan after 2 months revealed positive changes regarding fibrotic areas in the lung, as the intensity of fibrosis was decreased. So, we conclude that using Pirferidone in COVID-19 patients with high comorbidities like in the patients with suspected latent Interstitial Pulmonary fibrosis may lead to beneficial outcome, high survival rate and improved fibrotic areas in the lungs.

References

1. Podolanczuk AJ, Richeldi L. COVID-19 and interstitial lung disease: Keep them separate. 2020
2. https://www.merckmanuals.com/professional
3. Antoniou KM, Raghu G, Tzilas V, Bouro, D. Management of patients with interstitial lung disease in the midst of the COVID-19 pandemic. Respiration. 2020; 1
4. Ferrara F, Granata G, Pelliccia C, La Porta R, Vitiello A. The added value of pirfenidone to fight inflammation and fibrotic state induced by SARS-CoV-2. European Journal of Clinical Pharmacology. 2020; 76(11):1615-1618
5. Uzel FI, İliaz S, Karataş F, Çağlayan B. COVID-19 Pneumonia and Idiopathic Pulmonary Fibrosis: A Novel Combination. Turkish Thoracic Journal. 2020; 21(6):451
6. Raghu G, Remy-Jardin M, Myers JL, Richeldi L, Ryerson CJ, Lederer DJ. American Thoracic Society, European Respiratory Society, Japanese Respiratory Society, and Latin American Thoracic Society. Diagnosis of Idiopathic Pulmonary Fibrosis. An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline. Am J Respir Crit Care Med. 2018; 198(5):e44-68
7. British Thoracic Society Advice for Managing Interstitial Lung Disease Patients during COVID-19 pandemic. Available from: https://brit-thoracic.org.uk/media/455101/bts-management-advice-for-ild-patients-v10-23-march-2020.pdf
8. Halpin DM, Faner R, Sibila O, Badia JR, Agusti A. Do chronic respiratory diseases or their treatment affect the risk of SARS-CoV-2 infection? Lancet Respir Med. 2020; 8(5):436-8
9. Kreuter M, Polke M, Walsh SL, Krisam J, Collard HR, Chaudhuri N. Acute exacerbation of idiopathic pulmonary fibrosis: international survey and call for harmonisation. Eur Respir J. 2020; 55(4):1901760
10. Drake TM, Docherty AB, Harrison EM, Quint JK, Adamali H, Agnew S. Outcome of hospitalization for COVID-19 in patients with interstitial lung disease. An international multicentre study. American journal of respiratory and critical care medicine. 2020; 202(12):1656-1665
11. Seifirad S. Pirfenidone: A novel hypothetical treatment for COVID-19. Medical hypotheses. 2020; 144:110005
12. Spagnolo P, Balestro E, Aliberti S, Cocconcelli E, Biondini D, Della Casa G. Pulmonary fibrosis secondary to COVID-19: a call to arms? Lancet Respir Med. 2020; 8(8):P750-52
13. George PM, Wells AU, Jenkins RG. Pulmonary fibrosis and

COVID-19: the potential role for antifibrotic therapy. Lancet Respir Med. 2020; 8(8):P507-15

14. Hagmeyer L, Treml M, Priegnitz C, Randerath WJ. Successful Concomitant Therapy with Pirfenidone and Nintedanib in Idiopathic Pulmonary Fibrosis: A Case Report Respiration. 2016; n91(4):327-32
15. Behr J, Prasse A, Kreuter M, Johow J, Rabe KF, Bonella F. Pirfenidone in patients with progressive fibrotic interstitial lung diseases other than idiopathic pulmonary fibrosis (RELIEF): a double-blind, randomised, placebo-controlled, phase 2b trial. The Lancet Respiratory Medicine. 2021; 9(5):476-486
16. Lancaster LH, de Andrade JA, Zibrak JD, Padilla ML, Albera C, Nathan SD. Pirfenidone safety and adverse event management in idiopathic pulmonary fibrosis. European respiratory review. 2017; 26(146)
17. Cottin V, Maher T. Long-term clinical and real-world experience with pirfenidone in the treatment of idiopathic pulmonary fibrosis. Eur Respir Rev. 2015; 24(135):58-64

DOI 10.51231/2667-9507-2022-001-04-52-58

Alteration of immune status during treatment with β-blockers in patients with essential hypertension

T. Sharashenidze[1], M. Buleishvili[2], M. Tsimakuridze[2], M. Tortladze[3], T. Sanikidze[2]

David Aghmashenebeli University of Georgia, Tbilisi, Georgia
Tbilisi State Medical University, Tbilisi, Georgia
Caucasus International University, Tbilisi, Georgia

Abstract

The balance of cytokines (IL-2, IL-10, IF-γ) in patients with essential hypertension before and after treatment with β-blockers was studied. 20 patients aged 45-65 years and diagnosed with essential hypertension (12 women, 8 men) were investigated. For the treatment of hypertension, patients received second-generation beta-selective β-blockers Egilok and Betalok Zok, and third-generation β-blocker Nebilet for one month. Patients performed their blood pressure measurements daily in the morning during I month. The content of interleukins (IL-2, IL-10, IF-γ) in the blood by the immune enzymatic ELISA method on a semi-automatic reader Stat Fax 3200 with RayBio, (USA) reagent was measured. The results of our studies show an increase in the level of CD4+ (IL-2) cytokines in the blood of the studied hypertensive patients, which coincides with the literature data on the important role of CD4+ pro-inflammatory cytokines in the pathogenesis of hypertension. After 1 month of treatment with β-blockers, the patient's arterial pressure and IL-2 level content in the blood decreased. These data indicate the important role of inflammation in the pathogenesis of hypertension and the anti-inflammatory effects of β-brokers, used in the treatment of hypertension.

KEY WORDS: essential hypertension; interleukins; β-blockers

Introduction

Epidemiological and experimental studies revealed a relationship between biochemical markers of systemic inflammation and diseases of the cardiovascular system, such as atherosclerosis, heart failure, and hypertensive disease [1]. The relationship between the regulatory systems of arterial hypertension, such as the renin-angiotensin system, the sympathetic nervous system, and proinflammatory cytokines, has been determined. As is known, pro-inflammatory cytokines affect vascular function, cause structural and functional changes in endothelial cells, regulate the release of vasoactive factors by the endothelium (endothelin, nitric oxide, NOS-mRNA [2] and in this way participate in blood pressure regulation.

Stimulation of sympathetic neurons innervating secondary lymphoid organs suppresses inflammation in various chronic diseases by regulating cytokine secretion [2]. This mechanism is quite important and has been used in the treatment of various chronic inflammatory diseases. Neuro-immune mechanisms involve adrenergic receptors, including β-adrenoreceptors, which are expressed on various (innate and adaptive) immune cells. In order to control ″inflammation″, the neuro-signaling system through β-adrenoreceptors limits the release of inflammatory cytokines by macrophages and dendritic cells, as well as the activated T cells.

We studied the balance of cytokines (IL-2, IL-10, IF-γ) in patients with essential hypertension before and after treatment with beta-blockers.

Materials and Methods

20 patients aged 45-65 years and diagnosed with essential hypertension (12 women, 8 men) were studied.

Inclusion criteria for hypertensive patients – elevated blood pressure (with a sitting position ≥140/90±10 mm Hg) during 3 consecutive measurements over 4 weeks.

Exclusion criteria from the study were polycystic ovary syndrome, ovariectomy, hormone therapy, excessive alcohol consumption (more than 20 g per day), taking estrogen replacement drugs, glucocorticoids, aspirin, calcium channel blockers, diabetes mellitus, and kidney diseases.

For the treatment of hypertension, patients received second-generation be-

ta-selective β-blockers Egilok and Betalok Zok, and third-generation β-blocker Nebilet for one month.

Patients performed their blood pressure measurements daily in the morning; Initial (before treatment) and final (after treatment) blood pressure values were analyzed.

We collected blood from patients before treatment and 1 month after treatment. Collected blood samples were stored at – 80°C and just before analysis thawed at 4°C in a refrigerator. We measured the content of interleukins (IL-2, IL-10, IF-γ) in the blood by the immune enzymatic ELISA method on a semi-automatic reader Stat Fax 3200 with RayBio, (USA) reagent.

Statistical Analysis

Statistical analysis was performed using the ″Statistical Package for Social Sciences (SPSS) for Windows (SPSS version 11.0)″. Results were expressed as means ± SD. A confidence limit of 0.05 ($P<0.05$) was selected for statistical confidence.

Results

Fig. 1. shows the blood pressure values of the studied patients with essential hypertension before and after treatment with β-blockers. As can be seen from diagram 1, blood pressure indicators of the studied patients tend to decrease after treatment with β-blockers.

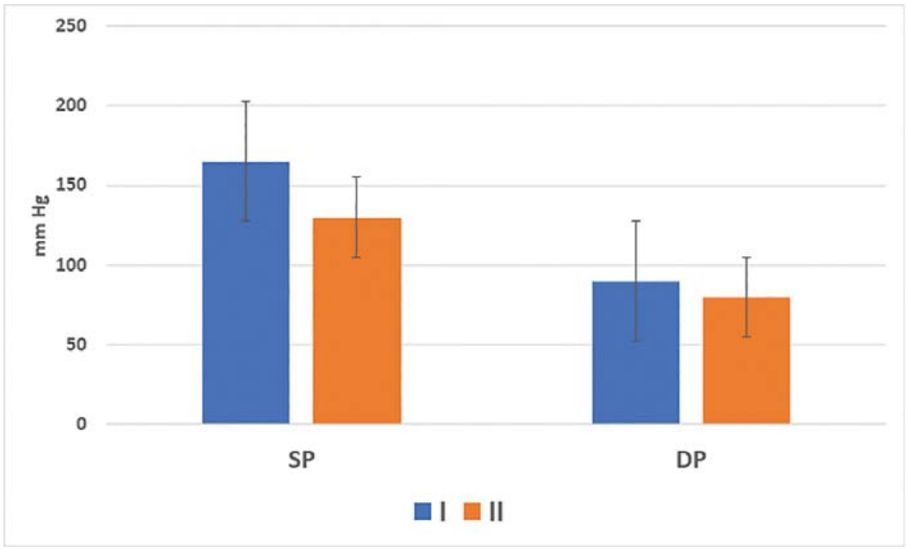

Fig. 1. *Blood pressure indicators of studied patients before and after treatment with β-blockers. (Series 1 – hypertensive patients before treatment; Series 2 – hypertensive patients after treatment).*

Fig. 2. shows the magnitude of the deviation from the maximum value of the normal content of cytokines (IF-γ, IL-2, IL-10) (optimal index – IF-γ – 0-5pg/ml; IL-2 – 0-10pg/ml; IL – 10 – 0-31pg/ml) in the blood of the studied patients before and after treatment with β-blockers.

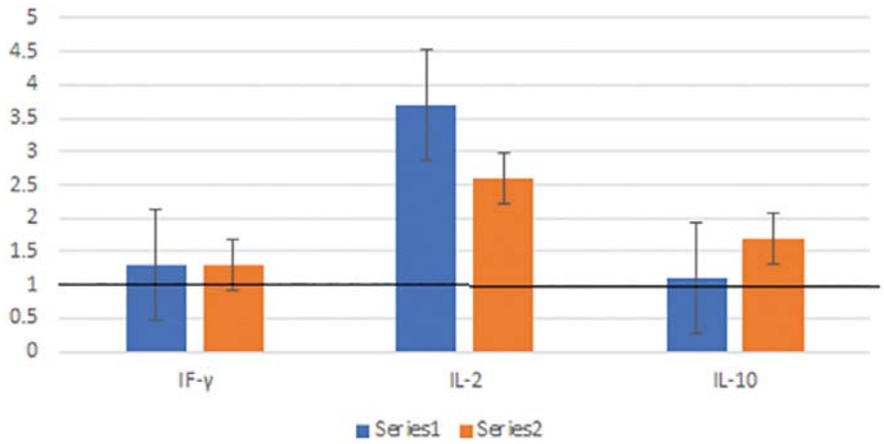

Fig. 2. *The magnitude of the deviation from the maximum value of the normal content of cytokines (IF-γ, IL-2, IL-10) (optimal index – IF-γ – 0-5pg/ml; IL-2 – 0-10pg/ml; IL – 10 – 0-31pg/ml) in the blood of the studied patients before and after treatment with β-blockers. (Series 1 – hypertensive patients before treatment; Series 2 – hypertensive patients after treatment). – optimal index of the cytokines.*

As can be seen from the figure, in the blood of the hypertensive patients studied by us before the treatment the levels of IF-γ and IL-10 did not importantly vary from the optimal levels, while IL-2 was 3-4 times higher than the optimal level. After 1 month of

treatment of hypertensive patients with β-blockers, the content of F-γ and IL-10 in the blood almost did not change compared to the initial values, while the content of IL-10 statistically significantly decreased by 30% compared to the initial values.

Discussion

As is known, inflammation is a key component in the pathophysiology of hypertension, it determines not only hypertension development and/or progression but also leads to end-organ damage [3,4]. Metabolic/chemical, mechanical (wall stretch), or infectious endothelial aggressions trigger complex immune reactions, leading to a pro-inflammatory state [5]. There are data that patients with essential hypertension have an altered profile of pro – and anti-inflammatory cytokines [6].

In studies dedicated establishment of the role of subtypes of T cells in hypertension and the mechanisms by which they contribute to this disease, was shown that mice lacking CD8+T cells were protected from hypertension, whereas mice lacking CD4+T cells or MHC class II were not [7]. An interesting study by Youn et al. [8] compared circulating T cell phenotypes in newly diagnosed hypertensive patients to age – and sex-matched controls and found that the number of circulating pro-inflammatory CD8+T cells is increased in humans with hypertension. These cells produce increased amounts of IFN-γ, TNF-α, and the cytotoxic molecules granzyme B and perforin compared with CD8+T cells from normal subjects. There is also evidence that CD4+T cells are activated in hypertension and likely play an important role.

The regulation of the functional activity of lymphocytes, the protective and damaging effect of T cell antibodies in the immune system, is based on the interaction of immune cells with mediators of the nervous and endocrine systems. Several autoregulatory mechanisms have been developed that ensure the maintenance of homeostasis of these systems and regulation of the immune response in various diseases [9,10]. These regulatory mechanisms include the modulation of the cellular membrane-surface receptors, in particular, β-adrenergic receptors. Early data of radioligand binding analysis confirmed the expression of the β-adrenergic receptor on both the human and the murine T cell populations, of which the β2 adrenergic receptor subtype is predominant; scarce evidence supports the expression of a high-affinity β1 adrenergic receptor on T cells [11,12]. It was shown that β-adrenergic blockers can alter the mitogenic response of lymphocytes [13,14], increase their proliferation and differentiation rate, and therefore change the distribution of lymphocyte subclasses [15].

The results of our studies show an increase in the level of CD4+ (IL-2) cytokines in the blood of the studied hypertensive patients, which coincides with the literature data on the important role of CD4+ pro-inflammatory cytokines in the pathogenesis of hypertension [6,7]. Possibly, it is related to the regulatory effect of IL-2 associated with the synthesis and secretion of other cytokines (IL-4, IL-6, IFN-γ, CSFs, TNF-α) [16]. After 1 month of treatment with β-blockers, the patient's arterial pressure and IL-2 level content in the blood decreased. These data indicate the important role of inflammation in the pathogenesis of hypertension and the anti-inflammatory effects of β-blokers, used in the treatment of hypertension.

References

1. Granger Joey P. An emerging role for inflammatory cytokines in hypertension J Physiol Heart Circ Physiol. 2006; 290:H923-H924
2. Sharma D, Farrar JD. Adrenergic regulation of immune cell function and inflammation. Seminars in Immunopathology. 2020; 42:709-717
3. Jain V, Choudhary J, Pandit R. Blood Pressure Target in Acute Brain Injury. Indian J Crit Care Med. 2019 Jun; 23(Suppl 2): S136–S139. DOI: 10.5005/jp-journals-10071-23191
4. Wenzel UO, Bode M, Köhl J, Ehmke HA. pathogenic role of complement in arterial hypertension and hypertensive end-organ damage. Am J Physiol Heart Circ Physiol. 2017 Mar; 1;312(3):H349-H354. DOI:10.1152/ajpheart.00759.2016. Epub 2016 Dec 16. PMID: 2798666
5. Tanase DM, Gosav EM, Radu S, Ouatu A, Rezus C, Ciocoiu M. Arterial Hypertension and Interleukins: Potential Therapeutic Target or Future Diagnostic Marker? International Journal of Hypertension, 2019; 3159283. PMID: 31186952. PMCID: PMC6521461. DOI: 10.1155/2019/3159283
6. Peeters AC, Netea MG, Janssen MC, Kullberg BJ, Van der Meer JW, et al. Pro-inflammatory cytokines in patients with essential hypertension. Eur J Clin Invest. 2001; 31(1):31-6. PMID: 11168436. DOI: 10.1046/j.1365-2362.2001.00743
7. Norlander AE, Madhur MS, Harrison DG. The immunology of hypertension. J. Exp. Med. 2018; 215(2):21-33. PMID: 29247045. PMCID: PMC5748862. DOI: 10.1084/jem.20171773
8. Youn, JC, Yu HT, Lim BJ, Koh MJ, Lee J, Chang DY. Immunosenescent CD8+T cells and C-X-C chemokine receptor type 3 chemokines are increased in human hypertension. Hypertension. 2013; 62:126-133

9. Kin NW, Sanders VM. It takes nerve to tell T and B cells what to do. Leukoc. Biol. 2006; 79:1093-1104. PMID: 16531560. DOI: 10.1189/jlb.1105625
10. Kohm AP, Sanders VM. Norepinephrine and β2-Adrenergic Receptor Stimulation Regulate CD4+ T and B Lymphocyte Function in Vitro and in Vivo, Pharmacol Rev. 2001; 53(4):487-525. PMID: 117346169
11. Du Y, Li X, Yu H, Yan l, Lau WB, Zhang S. Activation of T Lymphocytes as a Novel Mechanism in Beta1-Adrenergic Receptor Autoantibody-Induced Cardiac Remodeling. Cardiovascular Drugs and Therapy. https://doi.org/10.1007/s10557-019-06856-2
12. Fan X, Wang Y. β2 adrenergic receptor on T lymphocytes and its clinical implications. Progress in Natural Science. 2009; 19: 17-23. PMID: 2013726411
13. Sharashenidze T, Mamamtavrishvili N, Enukidze M, Machavariani M, Gabunia T, Sanikidze T. [Effect of propranolol on cytokine profile in an experimental model of human t lymphocytes (jurkat cells) in vitro]. Med News. 2021; 311):169-172 [in Georgian]
14. Sharashenidze T, Enukidze M, Machavariani M, Otarishvili N, Gabunia T, Sanikidze T. β-Adrenergic receptor blockers as a regulator of t cell viability (in the model system of the jurkat cells. Experimental and clinical medicine. 2020; 9(6):14-29
15. Krasnikova TL, Kozlova MV, Kalentchuk VU, Suvorov Y, Parfenova EV, Radiukhin VA. Beta-blocker action on lymphocyte proliferative response in essential hypertension. Cor Vasa. 1988; 30(2):110-4. PMID: 2899017
16. Lip GY, Hall JE. Comprehensive Hypertension. 1st ed. Mosby/Elsevier. 2007; – 1222

DOI 10.51231/2667-9507-2022-001-04-59-75

The role of computed tomography in a diagnostic approach to cystic lung diseases and their differential diagnosis

N. Gabashvili[1,2], Z. Avaliani[1,2]

[1]*European University, Tbilisi, Georgia*
[2]*National Center for Tuberculosis and Lung Diseases, Tbilisi, Georgia*

Abstract

In everyday routine, lung cysts are commonly seen in Computed Tomography, as far as many different conditions and diseases are associated with air cysts. Thus, correct diagnosis of cystic lung diseases, which show a wide spectrum, is a challenge for radiologists. For diagnosis and differential diagnosis, first of all, cysts should be distinguished from such other air filled lesions, like cavities, bullae, pneumatocele, emphysema, honeycombing and cystic bronchiectasis. Second, cysts can be categorized as single/localized versus multiple/diffuse. Solitary/localized cysts include incidental cysts, congenital cystic diseases and cystic cancers. Multiple/diffuse cysts can be further categorized according to the presence or absence of associated radiologic findings. Multiple/diffuse cysts without associated findings include lymphangioleiomyomatosis and Birt-Hogg-Dubé syndrome. Multiple/diffuse cysts may be associated with ground-glass opacity or small nodules. Multiple/diffuse cysts with nodules include Langerhans cell histiocytosis, cystic metastasis and amyloidosis. Multiple/diffuse cysts with ground-glass opacity include pneumocystis pneumonia, desquamative interstitial pneumonia and lymphocytic interstitial pneumonia. The stepwise radiologic diagnostic approach can be helpful in reaching a correct diagnosis for various cystic lung diseases.

KEY WORDS: lung diseases; lymphangioleiomyomatosis; Birt-Hogg-Dubé syndrome; histiocytosis; langerhans cell; emphysema; cystic bronchiectasis; cystic cancer

Introduction

Many different cystic diseases or conditions can be encountered in chest, because of frequent use of CT scans in daily clinical practice. Lung cysts appear as round parenchymal lucencies or low-attenuating areas with a well-defined thin wall, surrounded by normal lung parenchyma [1]. For radiologic assessment of cystic lung diseases, it is important to differentiate true lung cysts from other air-filled lung lesions in the first step of the diagnostic process. Radiologic characteristics of lung cysts, including size, wall thickness, number, location, and distribution, and the associated radiologic findings provide the most helpful diagnostic clues for diagnosing specific cystic lung diseases. A definite diagnosis may require clinical correlation and, occasionally, biopsy. However, although a multidisciplinary approach is necessary to make the correct diagnosis, a radiologic-CT approach is particularly important in narrowing the differential diagnosis.

The purpose of this review is to provide a stepwise radiologic diagnostic approach for cystic lung diseases.

STEP 1. Air cyst identification

Cysts

A cyst appears as a round parenchymal lucency or low attenuating area with a well-defined interface with normal lung parenchyma. Cysts are usually thin-walled (<2mm) and occur without associated pulmonary emphysema on CT scans (Fig. 1A). Single or several cysts in a localized area of the lung should be distinguished from a cavity, pneumatocele, or bullae. Moreover, multiple cysts diffusely distributed in both lungs should be distinguished from emphysema, honeycombing and cystic bronchiectasis.

Cyst-like lesions

Cavity

Cavity is a gas-filled space that is observed as lucency or low-attenuated area within pulmonary consolidation, a mass, or a nodule (Fig. 1B) [1]. Cavity wall thickness may vary, but the wall is usually relatively thick [2,3]. Many different diseases present as cavitary lesions. This spectrum of diseases includes acute to chronic infections, chronic systemic diseases and primary or metastatic malignancies [3,4,5]. A cavity is differentiated from a cyst by the presence of a thicker wall and a more irregular shape.

Bulla

A bulla is an airspace measuring more than 1 cm that is sharply demarcated by a thin wall [1]. Radiologically, it appears as a rounded focal lucency or decreased attenuation more than 1 cm in size, and is bounded by a thin, usually almost undetectable wall that is not greater than 1 mm (Fig. 1C). Bullae are usually located in the subpleural lung rather than within the lung parenchyma. Multiple bullae are usually accompanied by adjacent paraseptal and centrilobular emphysema [1]. Bullae can be distinguished from cysts by their almost imperceptible thin-wall, subpleural location, and accompanying adjacent emphysema.

Pneumatocele

A pneumatocele is a transient, thin-walled, gas-filled lesion, usually caused by pneumonia, trauma, or aspiration of hydrocarbon fluid [1]. The mechanism underlying their formation is believed to be a combination of parenchymal necrosis and check valve airway obstruction. Radiologically, a pneumatocele appears as an almost round, thin-walled airspace in the lung (Fig. 1D) [1]. Pneumatoceles can be accompanied by adjacent consolidation or ground glass opacity as a result of recent pneumonia; they may progressively increase in size over the following days or weeks, and then resolve after weeks or months [6].

Emphysema

Pulmonary emphysema can be classified into three major subtypes based on disease distribution within secondary pulmonary lobules: centrilobular or centriacinar emphysema, panlobular or panacinar emphysema, and paraseptal or distal acinar emphysema [1,7,8]. Centrilobular emphysema is the most common type of pulmonary emphysema, and is pathologically defined by the presence of destroyed centrilobular alveolar walls and enlarged respiratory bronchioles and associated alveoli [1]. Centrilobular emphysema typically appears in focal areas of decreased lung attenuation, usually without visible walls, and it has a predilection for the upper lungs [1,8,9]. Centrilobular emphysema is usually combined with a central dot which is a central bronchovascular bundle in the secondary pulmonary lobule (Fig. 3B). However, centrilobular emphysema may appear similar to thin-walled cysts. Paraseptal emphysema involves the more distal part of the secondary pulmonary lobule, and usually presents as a single row of elongated, thin-walled, air-filled structures that are distributed within the subpleural

lung. Panlobular emphysema involves the destruction of the entire secondary pulmonary lobule, and it involves lung parenchyma more diffusely, especially in the lower lungs [8]. Cysts are larger, fewer in number, lack a centrilobular location, lack a central core vessel, and have more visible walls compared with centrilobular emphysema.

Honeycombing

Honeycombing represents destroyed and fibrotic lung tissue containing numerous cystic airspaces with thick fibrous walls, indicative of the late stages of various lung diseases [1]. Radiologically, it appears as clustered cystic lesions with 1-3 mm-thick well-defined walls, which are typically 3-10 mm in diameter but may be occasionally larger (Fig. 3C) [1,9,10]. Honeycombing is characterized by multiple rows of air-filled spaces clustered in the subpleural region, predominantly in the lower lungs. Honeycombing usually accompanies other features of lung fibrosis, such as reticulation and traction bronchiectasis. It is the most distinguishing feature of usual interstitial pneumonia pattern, which is a hallmark radiologic pattern of idiopathic pulmonary fibrosis [10]. Cysts are larger in size, lack a subpleural distribution, do not show associated fibrosis, and are isolated lesions in comparison with honeycombing.

Cystic bronchiectasis

Bronchiectasis is an irreversible, localized, or diffuses bronchial dilatation, usually resulting from chronic infection, proximal airway obstruction, or congenital bronchial abnormalities [1]. Bronchiectasis may be classified as cylindric, varicose, or cystic, depending on the appearance of the affected bronchi [1]. Cystic bronchiectasis can also be mistaken for cysts when a dilated airway is viewed in cross-section (Fig. 3D). Bronchiectasis is usually distinguished from true cysts by careful examination of contiguous CT images. Findings such as tubular rather than spherical dimensions, branching patterns, associated bronchial wall thickening, centrilobular densities, and air-trapping are helpful for the diagnosis of bronchiectasis.

STEP 2. Are lung cysts solitary/localized or multiple/diffuse?

As a second step, after differentiating cysts from cyst mimickers, lung cysts can be categorized as solitary/localized cysts or multiple/diffuse cysts. Single or several cysts

in a localized area are classified as solitary/localized cysts, while multiple or numerous cysts distributed in both lungs are classified as multiple/diffuse cysts.

Solitary/localized cysts

Incidental cyst

A solitary cyst or several small lung cysts can be found incidentally on CT scans (Fig. 3A). Cysts are most likely to appear solitarily in the lower peripheral lungs and remain unchanged or slightly increase in size over time. Cysts are not associated with impairment in measures of spirometry, cigarette smoking, or emphysema. Therefore, incidental lung cysts could be a part of the normal aging process [11,12]. However, a single cyst may also be a remnant of a previous infection or trauma [13]. It is important to differentiate incidental lung cysts from other cystic lung diseases. Solitary or several small thin walled lung cysts incidentally found on CT in the old age group, may be a part of the normal aging process. Thus, old age, smaller number, and a lack of association with other radiologic findings are useful for the differentiation of incidental lung cysts from cystic lung diseases.

Intrapulmonary bronchogenic cyst

The bronchogenic cyst is a developmental anomaly that results from abnormal budding or a branching defect between the 26th and 40th gestation days [14,15,16]. Although a bronchogenic cyst usually presents as a middle mediastinal mass along the tracheobronchial tree, it can also present as a lung mass in about one-third of the cases, with a predilection in the lower lobes [13,16]. Intrapulmonary bronchogenic cysts are usually filled with fluid, and air-filled intrapulmonary bronchogenic cysts are rare [13]. Radiologically, an intrapulmonary bronchogenic cyst appears as a well-defined, homogeneous, spherical lesion with a smooth or lobulated margin on CT. Cysts contain usually fluid and rarely air with or without air-fluid level (Fig. 3C) [13,16,17]. Air-filled intrapulmonary bronchogenic cysts are sometimes difficult to differentiate from lung abscess or infected bullae. Clinical manifestations and previous chest radiographs and CT scans may be helpful for differentiation.

Congenital cystic lung diseases

Congenital Pulmonary Airway Malformation Congenital pulmonary airway malformation (CPAM) is a heterogeneous group of cystic and non-cystic lung lesions that result from abnormal bronchial structure proliferations [14]. CPAM, formerly known as congenital cystic adenomatoid malformation, usually presents during childhood and rarely in adulthood. CPAM is classified into subtypes based on cyst size and location, as well as other associated congenital abnormalities [2]. Most CPAMs derive their blood supply from the pulmonary artery and drain via the pulmonary veins [14]. Radiologically, large cysts, small cysts, and microcystic or solid lesions are observed according to the CPAM subtypes. Radiologic findings correlate well with the underlying histopathological characteristics [17]. CT shows lesions with a solitary well-defined thin-walled cyst or multiple cysts of varying sizes with variable densities, depending on the fluid contents of the cysts (Fig. 3B) [14].

Solitary cystic cancer

Cystic primary lung cancer is often missed or misinterpreted, which is most likely due to their unique imaging appearance, showing overlap with benign entities such as infection.

Cystic lung cancers are predominantly adenocarcinomas in about 80% of cases, with squamous cell carcinomas as the second most common subtype.

A rare number of other tumour types like adenosquamous, neuroendocrine and lymphoma have been reported [18].

Multiple underlying histopathologic substrates (eg. focal tumour proliferation, fibrosis, lepidic tumour growth along alveolar walls, emphysema) relate to the imaging features of cystic lung cancer and are responsible for either the solid component, septations, ground glass, and cystic air spaces. The most widely quoted mechanism of air space formation is ″check-valve″ ventilation. The air can enter in inspiration but cannot return during expiration due to partial obstruction of the terminal airway proximal to the cystic air space due to tumour cells and fibrosis.This leads to development, persistency and enlargement of the cystic air space [5].

STEP 3. Are multiple/diffuse cysts associated with other radiologic findings

Multiple/diffuse cysts can be further categorized according to the presence or absence of other associated radiologic findings. Radiologists should carefully review CT images for cysts as well as identify any other associated findings such as nodules, ground-glass opacity, or extrapulmonary lesions in areas visible in chest CT.

Multiple/diffuse cysts only (without associated other radiological findings) Lymphangioleiomyomatosis

Lymphangioleiomyomatosis (LAM) is a rare disease that predominantly affects the lung parenchyma of women of childbearing age [19,20,21]. LAM can occur sporadically, but is more common in patients with tuberous sclerosis complex (TSC-LAM) [21,22,23]. Cysts in the lung parenchyma may be the result of terminal bronchiole obstruction by LAM cells with associated air-trapping, which is thought to cause progressive dilatation of the distal airspaces leading to cyst formation and/or from degradation of the lung parenchyma due to an imbalance between proteases and protease inhibitors [21]. Cysts are typically round or ovoid and are usually 2-10 mm in diameter, but can occasionally be as large as 30 mm [20,21,22]. The lung parenchyma between cysts is typically normal (Fig. 4A).

Birt-hogg-dubé syndrome

Birt-Hogg-Dubé syndrome (BHD) is an uncommon, autosomal-dominant, multiorgan systemic condition characterized clinically by fibrofolliculomas, pulmonary cysts, and renal neoplasms [24,25,26,27]. On CT, more than 80% of adult patients with BHD have multiple lung cysts, and lung parenchyma except for multiple lung cysts generally appears normal [4,24,28]. The presence of lung cysts is significantly associated with spontaneous pneumothorax [2]. Radiologically, multiple thin-walled lung cysts are predominantly seen in lower, peripheral lung zones and along the mediastinum (Fig.4B) [25,26]. These cysts are surrounded by normal lung parenchyma. The shape and size of cysts are variable; they can be round, oval, lentiform, lobulated, or irregularly shaped, and generally have perceptible thin walls. Large cysts, particularly those in the lower lungs, have a lobulated, multiseptated appearance [26]. Predominant distribution of cysts in the lower medial lung zone is a characteristic finding.

STEP 4. Multiple/diffuse cysts associated with other radiological finding

The next step is to identify radiological findings accompanying the cysts. Multiple/diffuse cysts can be devided into two categories according to associated radiological findings as follows: multiple/diffuse cysts with nodules and multiple/diffuse cysts with ground-glass opacity.

Multiple/diffuse cysts with nodules

Pulmonary langerhans cell histiocytosis

Pulmonary Langerhans cell histiocytosis (PLCH) is a rare interstitial lung disease that typically affects young adults and is associated with cigarette smoking [21,23,27]. PLCH is characterized by peribronchiolar infiltration by Langerhans and inflammatory cells and formation of granulomas, leading to stellate interstitial nodules [23,29]. These stellate nodules can later cavitate, resulting in bronchial dilatation and formation of thin – and thick-walled cysts and cavities. Radiologically, nodules are the predominant features in the early stages, while cysts tend to develop later. In the early stages, small (1-10 mm) irregularly shaped nodules appear in a bilateral symmetric pattern with upper-middle lung dominance and a spared lung base and costophrenic angle. As the disease progresses, cystic degeneration appears as round or oval to bizarre with thin-wall and associated nodules (Fig. 5A) [21,23,29]. Cysts usually measure < 10 mm in diameter but may be as large as 20 mm. Bizarre-shaped cysts associated with nodules predominantly in the upper lung are a key imaging discriminator for PLCH in a young smoker.

Cystic metastasis

Cystic lung metastasis is most frequently seen in patients with angiosarcoma or squamous cell carcinoma mainly in the head and neck [30,32]. Radiologically, multiple solid nodules and multiple thinwalled cysts, often admixed with hemorrhagic change, are common features of metastatic angiosarcoma [31]. Cystic metastasis from angiosarcomas shows variability in the walls, air-fluid levels, and vessels or bronchi penetrating the cysts (Fig. 5B) [30,32]. As with other lung metastases, cystic metastasis tends to show different sizes and a basilar predominance [33]. Pneumothorax is a potential complication of cystic metastasis. A patient’s previous malignancy history is critical for diagnosis. If new lung cysts are detected in patients with a known malignancy,

cystic metastasis should be considered, and adequate tissue confirmation is required for diagnosis.

Amyloidosis

Amyloidosis is a rare disease characterized by extracellular deposition of abnormal insoluble proteins [34,35]. Pulmonary amyloidosis can present with cystic lung disease, and amyloid-associated cystic lung disease is rare. Amyloid-associated cystic lung disease can occur with Sjögren's syndrome and mucosa-associated lymphoid tissue lymphoma [35]. Radiologically, lung cysts are commonly numerous (more than 10), are often peribronchovascular or subpleural and are frequently associated with nodular lesions that are often calcified [35]. Cysts tend to be multiple, round or lobulated, small to moderate in size, and thin-walled [31,35]. Other associated findings include interlobular septal thickening, honeycombing, ground-glass opacity, circumferential thickening of the tracheal wall, and lymphadenopathy [34] (Fig. 5C).

Multiple/diffuse cysts with ground-glass opacity
Lymphoid interstitial pneumonia

Lymphoid interstitial pneumonia (LIP) is an uncommon benign polyclonal lymphoproliferative disease [21]. Idiopathic LIP is categorized as a rare idiopathic interstitial pneumonia. Most cases of LIP are associated with various underlying disorders, including HIV infection, connective tissue diseases such as Sjögren's syndrome, Hashimoto's thyroiditis, and systemic lupus erythematosus [21]. Radiologically, a combination of ground-glass opacity, poorly defined centrilobular nodules, small subpleural nodules, interlobular septal thickening, thickening of the bronchovascular bundles, and scattered cysts in lower lungs are seen (Fig. 6A) [20]. Lung cysts are present in up to 68% of patients; they are usually fewer in number but are distributed diffusely in both lungs, although they are often subpleural and peribronchovascular. Cysts in LIP are generally < 3 cm in diameter, are variable in shape, and may be the sole manifestation of this disease. In most cases, follow-up CT reveals the resolution of groundglass opacity, and cysts are the only residual finding in more chronic cases. Lymphadenopathy can be present, but pleural effusion or airspace consolidation is extremely rare [31]. The diagnosis of LIP should be considered in patients with lung cysts and immunological abnormalities.

Desquamative interstitial pneumonia

Desquamative interstitial pneumonia (DIP) is characterized by the accumulation of numerous pigmented macrophages within most of the distal airspace of the lung [31]. According to the international multidisciplinary classification of idiopathic interstitial pneumonias, DIP is classified as a smoking-related interstitial lung disease. Up to 90% of DIP patients have a smoking history, but other conditions besides smoking, such as occupational exposure to certain inhaled toxins, drugs, viral illnesses, and autoimmune diseases, can also cause DIP [31]. Radiologically, DIP presents with patchy ground-glass opacity with a predilection for the basal and peripheral lungs. Reticular density may also be present. Small (usually < 2 cm), well-defined, thin-walled cysts are seen within ground-glass opacity, which is an important finding in DIP (Fig. 6B) [13,36]. Honeycombing is also possible, but uncommon. Cysts in DIP have imperceptible walls, and they are mostly discrete but occasionally can be clustered and are surrounded by ground-glass opacity. Cysts in DIP are believed to represent dilated bronchioles and alveolar ducts, and in the later stages of DIP, cysts may also represent early centrilobular emphysema or honeycombing [23,34]. The presence of small cysts admixed within groundglass opacity is a unique feature of DIP. This feature is reported in approximately one-third of DIP patients.

Pneumocystis jirovecii pneumonia

Pneumocystis jirovecii pneumonia (PCP) is a fungal infection that has a strong association with immunocompromised conditions such as human immunodeficiency virus (HIV) infection [9,33,35]. Radiologically, ground-glass opacity indicating acute pneumonia is the dominant feature of this condition. The pattern of these opacities is often bilateral, multifocal, and mainly symmetrical, and distributed in the central portions of the lungs. Opacities can predominate in the upper lung zones in patients receiving prophylactic therapy for this infection. Thin-walled cysts are now recognized as a relatively common manifestation of this infection and are reported in as many as one-third of all patients. Cysts are usually variable in size, shape, and wall thickness, and are usually multiple and bilateral, subpleurally or intraparenchymally located, and are predominantly in the upper lung zone (Fig. 6C) [9]. PCP is associated with an increased incidence of spontaneous pneumothorax, which is believed to occur in association with ruptured subpleural cysts.

Conclusion

Many different conditions and diseases can be associated with lung cysts. Computed Tomography is the most informative, noninvasive diagnostic method for not only finding them, but also for their detailed characterization and differentiation. Knowing the main and associated radiological signs of different cystic conditions is very helpful for the correct diagnosis, although final diagnosis may require clinical and laboratory correlation and sometimes biopsy, for morphological diagnosis. The stepwise radiologic approach offers easier solution for accurate diagnosis of different cystic lung diseases. Correct CT diagnosis is also crucial for clinicians, for better management and treatment.

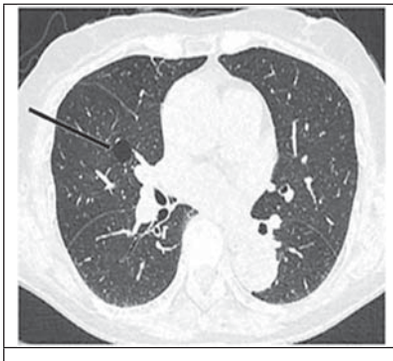

Fig. 1. A

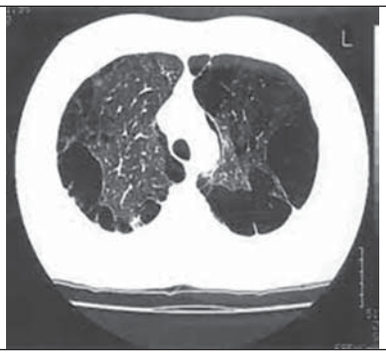

Fig. 1. C

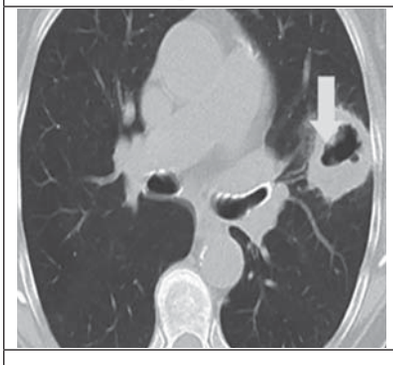

Fig. 1. B

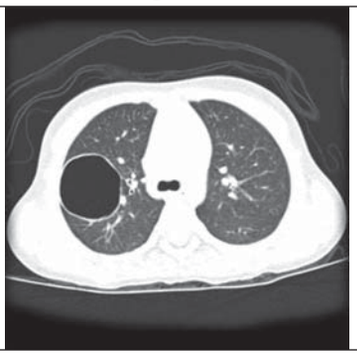

Fig. 1. D

Fig. 1. A. *Cyst: round air-filled lesion with well-defined thin wall surrounded by normal lung (arrow).* ***B.*** *Cavity: air-filled lesion with thick wall within mass.* ***C.*** *Bulla: air-filled lesion, more than 1 cm in diameter, bounded by very thin imperceptible wall and associated with adjacent centrilobular emphysema.* ***D.*** *Pneumatocele: thin-walled, air-filled lesion caused by pneumonia.*

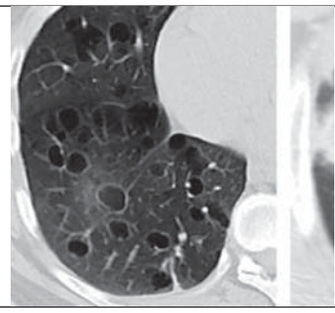

Fig. 2. A

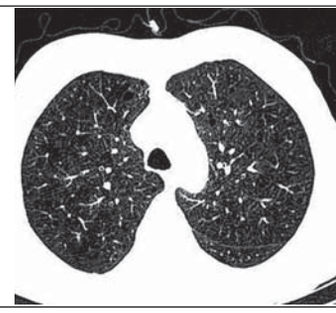

Fig. 2. C

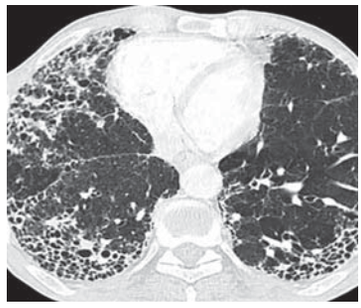

Fig. 2. B

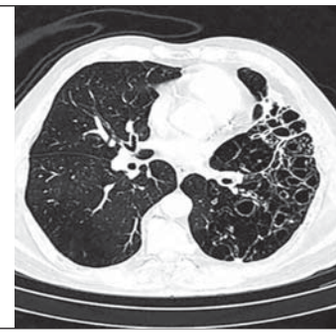

Fig. 2. D

Fig. 2. A. *Multiple or numerous air-filled lesions distributed in both lungs.* ***A.*** *Multiple cysts of variable sizes and shapes with thin wall.* ***B.*** *Centrilobular emphysema: centrilobular lucencies without distinct walls, central dot within lucency represents branch of pulmonary artery.* ***C.*** *Honeycombing: multiple rows of air-filled spaces with thick wall clustered in subpleural region.* ***D.*** *Cystic bronchiectasis: tubular rather than spherical dimensions with branching pattern and associated bronchial wall thickening.*

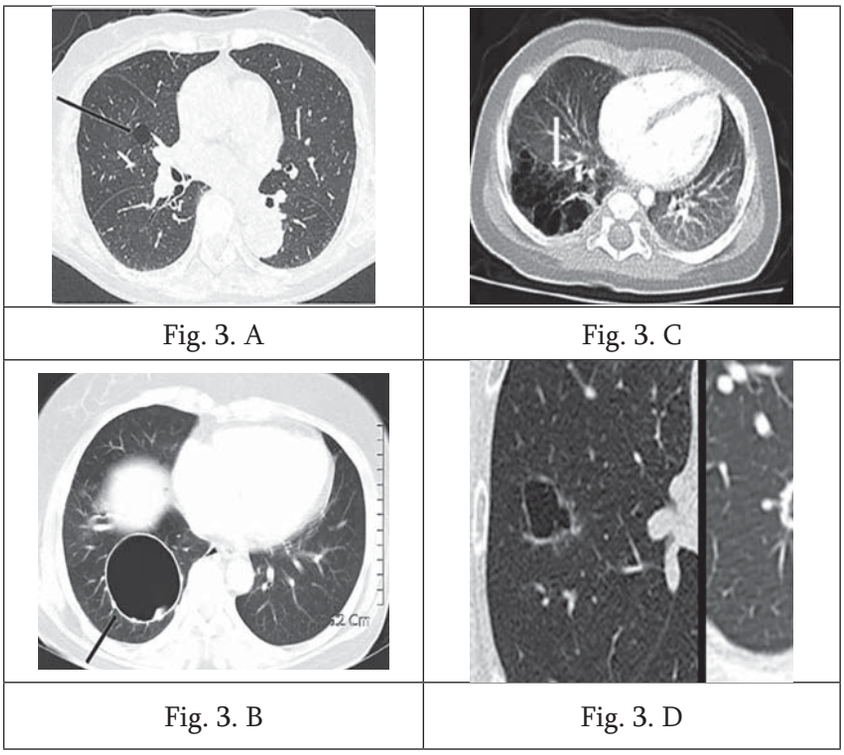

Fig. 3. A	Fig. 3. C
Fig. 3. B	Fig. 3. D

Fig. 3. A. *Incidental cyst in 66-year-old woman. CT shows round 14-mm-sized thin-walled cyst (arrow) in right middle lobe.* ***B.*** *congenital cystic adenomatoid malformation (CPAM) in a 10-month-old infant. several small cysts (arrow) in the right lower lobe.* ***C.*** *Bronchogenic cyst in 55-year-old woman. CT shows well-defined air-filled cyst (arrow) in right lower lobe, suggesting bronchogenic cyst.* ***D.*** *Surgically proved solitary cystic lung cancer.*

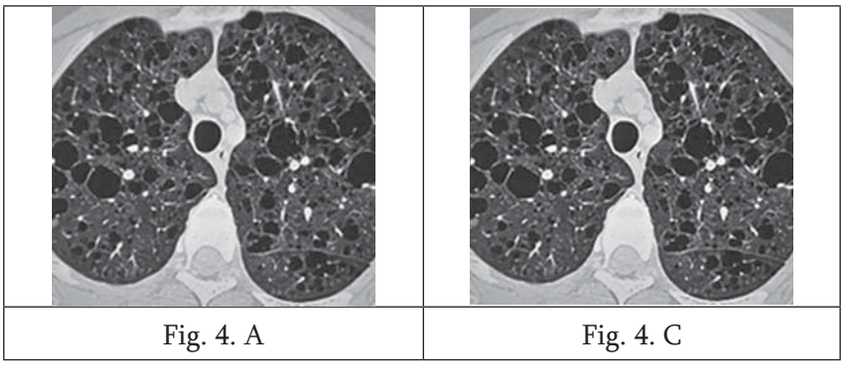

Fig. 4. A	Fig. 4. C

Fig. 4. A. *Lymphangioleiomyomatosis (LAM) CT shows numerous cysts in both lungs. Cysts are round or ovoid and relatively uniform in size and shape. Cysts are diffusely distributed without zone predominance in both lungs.* ***B.*** *Birt-Hogg-Dubé syndrome (BHD) Multiple lower zone predominant thin-walled cysts of varying size, many of which are about the pleura, particularly the paramediastinal pleura.*

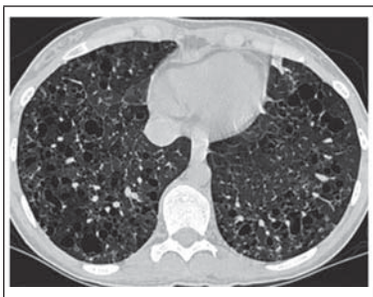

Fig. 5. A

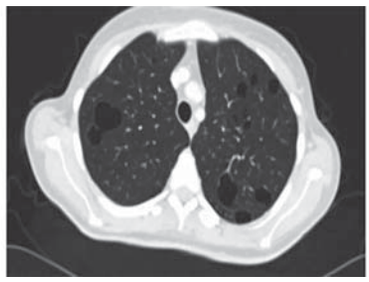

Fig. 5. B

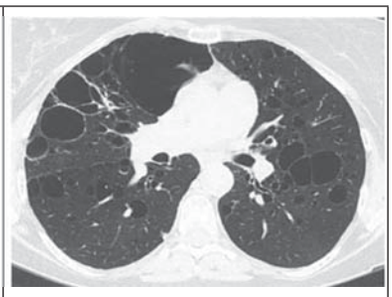

Fig. 5. C

Fig. 5. A. *Histiocytosis X CT shows multiple, irregular and round, thick and thin-walled cysts with small irregular nodules in both lungs, suggestive of PLCH, which was subsequently confirmed histologically.* ***B.*** *Cystic metastases from angiosarcoma. Multuple oval shaped, thin walled cysts are identified in both lungs,* ***C.*** *Amyloidosis High resolution CT scan of a 56-year-old woman, nonsmoker, with AL amyloidosis and lung involvement. Bilateral pulmonary cysts of widely varying sizes and asymmetric distribution are noted.*

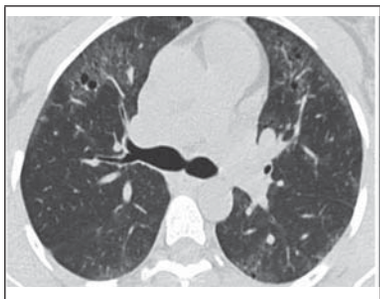

Fig. 6. A

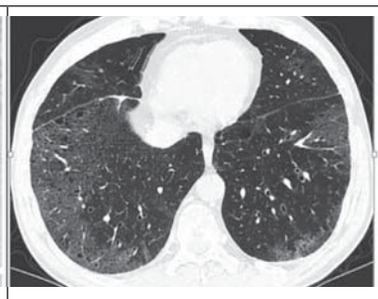

Fig. 6. B

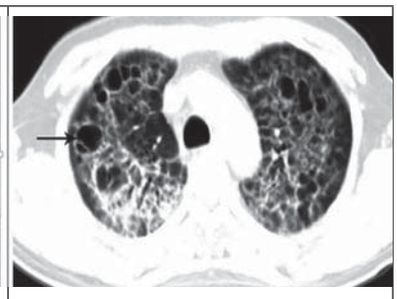

Fig. 6. C

Fig. 6. A. *Axial computed tomography image from a patient with lymphoid interstitial pneumonia showing thin-walled lung cysts in areas of ground glass opacities.* ***B.*** *Desquamative interstitial pneumonia in a 52-year-old smoker. CT shows GGO with tiny cysts in both lungs, mainly lower peripheral lungs, almost symmetrically distributed.* ***C.*** *Chest CT of a PCP in an AIDS patient. Patchy shadows and multiple cysts are shown in the upper lobes of lungs.*

References

1. Hansell DM, Bankier AA, MacMahon H, McLoud TC, Müller NL, Remy J. Fleischner Society: glossary of terms for thoracic imaging. Radiology. 2008; 246:697-722
2. Ryu JH, Swensen SJ. Cystic and cavitary lung diseases: focal and diffuse. Mayo Clin Proc. 2003; 78:744-752
3. Gafoor K, Patel S, Girvin F, Gupta N, Naidich D, Machnicki S. Cavitary lung diseases: a clinical-radiologic algorithmic approach. Chest. 2018; 153:1443-1465
4. Gupta N, Vassallo R, Wikenheiser-Brokamp KA, McCormack FX. Diffuse cystic lung disease. Part II. Am J Respir Crit Care Med. 2015; 1(92):17-29
5. Parkar AP, Kandiah P. Differential diagnosis of cavitary lung lesions. J Belg Soc Radiol. 2016; 100:100
6. Beigelman-Aubry C, Godet C, Caumes E. Lung infections: the radiologist's perspective. Diagn Interv Imaging. 2012; 93:431440
7. Lynch DA, Austin JH, Hogg JC, Grenier PA, Kauczor HU, Bankier AA. CT-definable subtypes of chronic obstructive pulmonary disease: a statement of the Fleischner Society. Radiology. 2015; 277:192-205
8. Takahashi M, Fukuoka J, Nitta N, Takazakura R, Nagatani Y, Murakami Y. Imaging of pulmonary emphysema: a pictorial review. Int J Chron Obstruct Pulmon Dis. 2008; 3:193204
9. Ha D, Yadav R, Mazzone PJ. Cystic lung disease: systematic, stepwise diagnosis. Cleve Clin J Med. 2015; 82:115-127
10. Raghu G, Remy-Jardin M, Myers JL, Richeldi L, Ryerson CJ, Lederer DJ, et al.; American Thoracic Society, European Respiratory Society, Japanese Respiratory Society, and Latin American Thoracic Society. Diagnosis of idiopathic pulmonary fibrosis. An official ATS/ERS/JRS/ALAT clinical practice guideline. Am J Respir Crit Care Med. 2018; 198:e44-e68
11. Copley SJ, Wells AU, Hawtin KE, Gibson DJ, Hodson JM, Jacques AE. Lung morphology in the elderly: comparative CT study of subjects over 75 years old versus those under 55 years old. Radiology. 2009; 251:566-573
12. Araki T, Nishino M, Gao W, Dupuis J, Putman RK, Washko GR. Pulmonary cysts identified on chest CT: are they part of aging change or of clinical significance? Thorax 2015; 70:1156-1162
13. Raoof S, Bondalapati P, Vydyula R, Ryu JH, Gupta N, Raoof S. Cystic lung diseases: algorithmic approach. Chest. 2016; 150:945-965
14. Biyyam DR, Chapman T, Ferguson MR, Deutsch G, Dighe MK. Congenital lung abnormalities: embryologic features, prenatal diagno-

sis, and postnatal radiologic-pathologic correlation. Radiographics. 2010; 30:1721-1738

15. Zylak CJ, Eyler WR, Spizarny DL, Stone CH. Developmental lung anomalies in the adult: radiologic-pathologic correlation. Radiographics. 2002; 22 Spec No:S25-S43
16. Yoon YC, Lee KS, Kim TS, Kim J, Shim YM, Han J. Intrapulmonary bronchogenic cyst: CT and pathologic findings in five adult patients. AJR Am J Roentgenol. 2002; 179:167170
17. Odev K, Guler I, Altinok T, Pekcan S, Batur A, Ozbiner H. Cystic and cavitary lung lesions in children: radiologic findings with pathologic correlation. J Clin Imaging Sci. 2013; 3:60
18. Sheard S, Moser J, Sayer Ch, Stefanidis K, Devaraj A, Vlahos I. Lung Cancers Associated with Cystic Airspaces: Underrecognized Features of Early Disease. Radiographics. 2018; 1527-1323
19. Kalassian KG, Doyle R, Kao P, Ruoss S, Raffin TA. Lymphangioleiomyomatosis: new insights. Am J Respir Crit Care Med. 1997; 155:1183-1186
20. Pallisa E, Sanz P, Roman A, Majó J, Andreu J, Cáceres J. Lymphangioleiomyomatosis: pulmonary and abdominal findings with pathologic correlation. Radiographics. 2002; S185-S198
21. Baldi BG, Carvalho CRR, Dias OM, Marchiori E, Hochhegger B. Diffuse cystic lung diseases: differential diagnosis. J Bras Pneumol. 2017; 43:140-149
22. Umeoka S, Koyama T, Miki Y, Akai M, Tsutsui K, Togashi K. Pictorial review of tuberous sclerosis in various organs. Radiographics. 2008; 28:e32
23. Seaman DM, Meyer CA, Gilman MD, McCormack FX. Diffuse cystic lung disease at high-resolution CT. AJR Am J Roentgenol. 2011; 196:1305-1311
24. Menko FH, van Steensel MA, Giraud S, Friis-Hansen L, Richard S, Ungari S. et al.; European BHD Consortium. Birt-HoggDubé syndrome: diagnosis and management. Lancet Oncol. 2009; 10:1199-1206
25. Tobino K, Hirai T, Johkoh T, Kurihara M, Fujimoto K, Tomiyama N. Differentiation between Birt-Hogg-Dubé syndrome and lymphangioleiomyomatosis: quantitative analysis of pulmonary cysts on computed tomography of the chest in 66 females. Eur J Radiol. 2012; 81:1340-1346
26. Agarwal PP, Gross BH, Holloway BJ, Seely J, Stark P, Kazerooni EA. Thoracic CT findings in Birt-Hogg-Dubé syndrome. AJR Am J Roentgenol. 2011; 196:349-352
27. Toro JR, Pautler SE, Stewart L, Glenn GM, Weinreich M, Toure O. Lung cysts, spontaneous pneumothorax, and genetic associations in 89 families with Birt-Hogg-Dubé syndrome. Am J Respir Crit Care Med. 2007; 175:1044-1053

28. Kitaichi M, Nishimura K, Itoh H, Izumi T. Pulmonary lymphangioleiomyomatosis: a report of 46 patients including a clinicopathologic study of prognostic factors. Am J Respir Crit Care Med. 1995; 151(2 Pt 1):527-533
29. Abbott GF, Rosado-de-Christenson ML, Franks TJ, Frazier AA, Galvin JR. From the archives of the AFIP: pulmonary Langerhans cell histiocytosis. Radiographics. 2004; 24:821-841
30. Yogi A, Miyara T, Ogawa K, Iraha S, Matori S, Haranaga S. Pulmonary metastases from angiosarcoma: a spectrum of CT findings. Acta Radiol. 2016; 57:41-46
31. Tateishi U, Hasegawa T, Kusumoto M, Yamazaki N, Iinuma G, Muramatsu Y. Metastatic angiosarcoma of the lung: spectrum of CT findings. AJR Am J Roentgenol 2003; 180:16711674
32. Tobino K, Gunji Y, Kurihara M, Kunogi M, Koike K, TomiyamaN. Characteristics of pulmonary cysts in Birt-HoggDubé syndrome: thin-section CT findings of the chest in 12 patients. Eur J Radiol. 2011; 77:403-409
33. Cantin L, Bankier AA, Eisenberg RL. Multiple cystlike lung lesions in the adult. AJR Am J Roentgenol. 2010; 194:W1-W11
34. Czeyda-Pommersheim F, Hwang M, Chen SS, Strollo D, Fuhrman C, Bhalla S. Amyloidosis: modern cross-sectional imaging. Radiographics. 2015; 35:1381-1392
35. Zamora AC, White DB, Sykes AM, Hoskote SS, Moua T, Yi ES. Amyloid-associated cystic lung disease. Chest. 2016; 149:1223-1233
36. Georgiades CS, Neyman EG, Barish MA, Fishman EK. Amyloidosis: review and CT manifestations. Radiographics. 2004; 24:405-416

DOI 10.51231/2667-9507-2022-001-04-76-82

The latest approach in planning laparoscopic antireflux surgery for the treatment of gastroesophageal reflux disease in Georgia by single surgical team

D. Elgandashvili[1,2], O. Kepuladze[2], M. Mantskava[1], N. Momtselidze[3], G. Kuchava[4]

[1]*European University, Tbilisi, Georgia*
[2]*Clinic Caraps Medline, Tbilisi, Georgia*
[3]*UNIK-Kutaisi University, Kutaisi, Georgia*
[4]*Georgian Technical University, Tbilisi, Georgia*

Abstract

Gastroesophageal reflux disease (GERD) is one of the most common pathologies of the gastrointestinal tract detected in adults. The implementation of a differential approach in diagnostics is possible through the complex simultaneous application of several examination methods, such as endoscopic and radiological. Standard treatment includes medical and laparoscopic methods of solving problems. The success of laparoscopic surgery depends on many factors. For example, from the knowledge, skill, experience of a group of surgeons. As an innovation for the success of surgical treatment of the patient and his personalization, we proposed additional scientific and experimental approaches, such as modeling and determining the rheology of the masses.

KEY WORDS: gastroesophageal reflux disease; laparoscopic; modeling; rheology; Georgia

Introduction

Gastroesophageal reflux disease (GERD) is a relapsing chronic disease of the lower esophagus. Throwing the contents of the stomach into the esophagus provokes pathological changes in the mucosa and the inflammatory process.

Gastroesophageal reflux disease is one of the most common pathologies of the gastrointestinal tract detected in adults. The percentage of detection of GERD in men and women of middle age is about 13%, however, with an increase in the average age in the study population in gastroesophageal reflux in women, it reaches up to 24%.

Gastroesophageal reflux disease appears due to improper functioning of the lower esophageal sphincter. The systematic ingress of hydrochloric acid from the stomach into the esophagus provokes changes in acidity in the esophagus. In addition, the cause of GERD is a hernia of the esophageal opening of the diaphragm.

Timely diagnosis of GERD allows the patient to choose corrective drug therapy. Eradication and antisecretory drugs are effective, reduce the clinical manifestations of the disease, but do not eliminate the underlying cause. In recent years, antireflux surgery has been considered as a necessary standard for the treatment of complex and complicated forms [1].

Due to the active development of minimally invasive technologies, it became possible to perform antireflux surgery using endovideosurgical access. According to many authors, in almost all cases, surgery to eliminate reflux esophagitis can be performed laparoscopically [2,3]. At the same time, when performing antireflux surgery in a specialized hospital by an experienced highly qualified surgeon, a positive result is achieved in 80-95% of cases [4,5]. The performance of such an operation by a surgeon with little practical experience in their implementation gives a decrease in positive results during the first year to 40-50% [4].

This article will focus on a team of surgeons performing such operations in Georgia.

Patients with a variety of clinical manifestations of reflux esophagitis are often observed with its extraesophageal manifestations. This is confirmed by literature reviews and our observations [4,6,7,8].

The implementation of a differential approach in diagnostics is possible through the complex simultaneous application of several examination methods, such as endoscopic and radiological.

To clarify the presence of functional disorders, their degree and type, the manometric and radioisotope method, intraesophageal pHmetry are important. These survey methods have a fairly high degree of information content.

This contributes to an accurate and correct diagnosis.

This is the foundation for a successful assessment and identification of the causes of the development of reflux esophagitis, on which the treatment tactics depend.

The data obtained on the basis of laboratory and instrumental research methods indicate

- the presence of a degree of shortening of the esophagus;
- peptic stricture of the esophagus;
- concomitant diseases.

This data is to be taken into account when choosing an operative intervention and its volume.

But the modeling proposed by us, as well as the assessment of the rheological properties of the contents of the esophagus, is very informative, which is aimed at the personification of patients.

On the issue of modeling

The compliance of soft tissue walls plays a major role in the transport of biofluids. From the point of view of medicine, a change in motility (i.e., contractile function) is biliary dyskinesia [9].

The motion of a fluid in elastic and compliant channels can be described using different models (in particular, the Windkessel model [10], the model for describing the peristaltic flow, the finite element algorithm of the ″fluid–solid body″ interaction, etc.).

The proposed approach is that the systems that are involved in the formation of reflux are combined into one system as follows:

- Using the Frank model, the dependences of the change in pressure on time [p(t)] and volume on time [V(t)] are determined [11];
- The parameters of the model are experimentally calculated and substituted into the dependence p(t). In this way, you can get on the p(t) dependence for a particular patient, which is necessary to solve the problem;
- Next, the problem of fluid flow is solved, taking into account the interaction ″liquid – solid body″;
- As a result of the solution, we obtain the distributions of velocities and pressures, which will be the initial conditions in the simulation;
- In the end, the problem of fluid flow we must solve a task about the flow of liquid.

On the issue of hemorheology

Rheology is the science of the deformation and flow of various masses.

Deformation is the relative displacement of particles of masses, in which continuity is not violated. If, under the action of finite forces, the deformation increases in time continuously and irreversibly, then this means that the mass is flowing. Deformation usually results in a change in shape or size. However, there are cases in which these phenomena do not exist.

The subject of rheology is the study of various types of deformation depending on their stresses.

The rheology of gastric masses considers the rheological behavior of two – and multi-phase systems depending on the rheological properties of their components. We have studied shear as a determinant of rheology. A simple shear is considered as a plane deformation parallel to a fixed plane due to the action of shear stresses on the faces of an elementary parallelepiped. Simple shear is a special case of laminar flow, in which the mass can be viewed as a set of infinitely thin layers. These layers do not deform, but only slide one over the other.

Stress is a measure of the intensity of internal elastic forces. The magnitude and nature of the deformation depend on the properties. The deformation is accompanied by the appearance of internal forces of interaction between the particles of the body. There are full, normal and shear stresses. That is, the total stress is decomposed into normal and shear stresses.

Hydrostatic pressure is understood as such a stress state in which the normal stresses on the faces of the element are equal to each other, and there are no tangents, as a result of which the volume decreases (or increases), but the shape does not change. In this case, the modulus of volumetric compression EV (expansion) is equal to the ratio of the change in hydrostatic pressure to the corresponding change in volume.

This approach is very relevant. This kind of experimental and theoretical approaches will become the basis for personalizing patients, significantly reducing intra- and postoperative complications in with laparoscopic fundoplication.

Intra-abdominal bleeding during laparoscopic fundoplication ranks first among the complications. According to the literature, the frequency of this complication is diagnosed in 0.3-0.75% of episodes. As a rule, bleeding that occurs during laparoscopic fundoplication is fairly easy to diagnose. The most common source of bleeding is short gastric vessels that are damaged during mobilization of the stomach or at the stage of formation of a fundoplication when an organ is passed into the retroesophageal space.

In addition to damage to short gastric vessels, bleeding can occur when the stomach wall, liver or spleen parenchyma, vessels of the lesser omentum, aberrant hepatic artery, diaphragm and its legs are damaged, as well as from puncture sites of the anterior abdominal wall with trocars. In case of intraoperative bleeding, access conversion provides a clear identification of the anatomical structures of the hepatoduodenal ligament and visualization of the source of bleeding, followed by thorough hemostasis. The consequence of these complications may be insufficient experience in performing endovideosurgical fundoplications by the surgeon [5].

Bleeding arising directly from the wall of the stomach, having previously been captured by a dissector, where the compressed tissue becomes less vascularized and tissue resistance increases, is stopped by the use of point monopolar coagulation. In case of violation of the integrity of a large vessel, then the most optimal solution would be to ligate it with a Z-shaped suture. However, when using the monopolar mode of operation, electrothermal damage (burns of the intestinal wall) in the area of the laparoscopic view is possible, developing with an underestimated anatomical-topographic relationship of organs and when working quite ″close″ to the intestinal wall under visual control.

In case of damage to the vessels of the lesser omentum, with the adjacent vagus nerve, clipping of the vessels is performed with preliminary capture and irrigation of the operation area. Otherwise, it is not excluded that the nerve trunk gets between the clips with subsequent coagulation damage. This will be the basis of complications in the postoperative period.

Based on data published in foreign literature, after laparoscopic fundoplication, the frequency of trauma to the vagus nerve ranges from 10 to 41%. Damage to the posterior vagus nerve, in comparison with damage to the anterior, is less dangerous, since it controls 40% of the motor and secretory function of the stomach. If the anterior nerve or two vagus nerves are damaged in the postoperative period, the patient develops persistent gastroparesis, leading to possible gastric atony, combined with pylorospasm. In the control endoscopic examination and radiopaque examination, hyperdistension of the stomach due to food masses and mucus with a pronounced violation of its motor-evacuation function and pylorospasm is noted [12,13]. The tissues of the left lobe of the liver, as a rule, are damaged during their rough abduction to the right side or when the retractor slips. Stopping bleeding in this case is carried out without any problems by bipolar coagulation of the injured liver parenchyma. Accessory hepatic arteries are also often damaged, which must be clipped before electrosurgical transection to avoid bleeding [14].

In addition to the correct and accurate work of the operating surgeon, adequate assistance is of great importance, since poor visualization of the surgical area, excessive or incorrect traction of the gallbladder can lead to trauma to the bile ducts that occurs

during the intersection or excision of the segment [12]. If damage to the bile ducts is detected, it is possible to execution external drainage; biliary-biliary anastomosis; prosthetic damage; performing a reconstructive operation in the form of a biliodigistic anastomosis.

The most effective results are achieved with an intraoperative diagnosis of lesions with simultaneous correction by a qualified specialist.

Conclusion

Thus, we can conclude that the number of complications directly depends on the team of surgeons, their qualifications and experience, as well as skills. In addition, the scientific approach that we described in the article is very important. On the one hand, we will be able to preliminarily assess the risks, as well as be prepared for unforeseen situations during the operation.

References

1. Myrvold HE. Kirurgi ved refluks [Reflux surgery]. Tidsskr Nor Laegeforen. 2005 Aug 11;125(15):1988. Norwegian. PMID: 16100533
2. Slater BJ, Dirks RC, McKinley SK, Ansari MT, Kohn GP, Thosani N, Qumseya B, Billmeier S, Daly S, Crawford C, P Ehlers A, Hollands C, Palazzo F, Rodriguez N, Train A, Wassenaar E, Walsh D, Pryor AD, Stefanidis D. SAGES guidelines for the surgical treatment of gastroesophageal reflux (GERD). Surg Endosc. 2021 Sep;35(9):4903-4917. doi: 10.1007/s00464-021-08625-5. Epub 2021 Jul 19. PMID: 34279710
3. Myrvold HE. Laparoscopic antireflux surgery; the merits and problems. Ann Med. 1995 Feb;27(1):29-33. doi: 10.3109/07853899509031933. PMID: 7741995
4. McKinley SK, Dirks RC, Walsh D, Hollands C, Arthur LE, Rodriguez N, Jhang J, Abou-Setta A, Pryor A, Stefanidis D, Slater BJ. Surgical treatment of GERD: systematic review and meta-analysis. Surg Endosc. 2021 Aug;35(8):4095-4123
5. Davis CS, Baldea A, Johns JR, Joehl RJ, Fisichella PM. The evolution and long-term results of laparoscopic antireflux surgery

for the treatment of gastroesophageal reflux disease. JSLS. 2010 Jul-Sep;14(3):332-41. doi: 10.4293/108680810X12924466007007. PMID: 21333184; PMCID: PMC3041027

6. Adame E, Mateos-Pérez G, Teramoto Matsubara O, Tawil J, Vallejo-Soto M, Sáez-Ríos A, Vargas-Romero JA, Zárate-Guzmán AM, Galvis-García ES, Morales-Arámbula M, Quiroz-Castro O, Carrasco-Rojas A, Remes-Troche JM. Post-fundoplication symptoms and complications: Diagnostic approach and treatment. Rev Gastroenterol Mex. 2017 Jul-Sep;82(3):234-247. English, Spanish. doi: 10.1016/j.rgmx.2016.08.005. Epub 2017 Jan 5. PMID: 28065591
7. Herbella FA, Patti MG. Laparoscopic Antireflux Surgery: Importance of Patient's Selection and Preoperative Workup. J Laparoendosc Adv Surg Tech A. 2017 Feb;27(2):101-105. doi: 10.1089/lap.2016.0322. Epub 2016 Aug 16. PMID: 27529517
8. Kuchumov AG, Vedeneev V, Samartsev V, Khairulin A, Ivanov O. Patient-specific fluid-structure interaction model of bile flow: comparison between 1-way and 2-way algorithms. Comput Methods Biomech Biomed Engin. 2021 Nov;24(15):1693-1717. doi: 10.1080/10255842.2021.1910942. Epub 2021 Jun 26. PMID: 34176396
9. Herbella FA, Patti MG. Laparoscopic Antireflux Surgery: Importance of Patient's Selection and Preoperative Workup. J Laparoendosc Adv Surg Tech A. 2017 Feb;27(2):101-105. doi: 10.1089/lap.2016.0322. Epub 2016 Aug 16. PMID: 27529517
10. Frank A, Garrelt M. Hydrodynamical models of outflow collimation in young stellar objects. Astrophysical Journal. 1996 472(2): 684
11. Park CH, Lee SK. [Gastroesophageal Reflux Disease]. Korean J Gastroenterol. 2019 Feb 25;73(2):70-76. Korean. doi: 10.4166/kjg.2019.73.2.70. PMID: 30845382
12. Patti MG. An Evidence-Based Approach to the Treatment of Gastroesophageal Reflux Disease. JAMA Surg. 2016 Jan;151(1):73-8. doi: 10.1001/jamasurg.2015.4233. PMID: 26629969
13. King K, Sudan R, Bardaro S, Soriano I, Petrick AT, Daly SC, Lo Menzo E, Davis D, Leyva-Alvizo A, Gonzalez-Urquijo M, Eisenberg D, El Chaar M. Assessment and management of gastroesophageal reflux disease following bariatric surgery. Surg Obes Relat Dis. 2021

Policy

Open Access statement

An open-access mandate is a policy adopted by a research institution, research funder, or government which requires or recommends researchers – usually university faculty or research staff and/or research grant recipients – to make their published, peer-reviewed journal articles and conference papers open access (1) by self-archiving their final, peer-reviewed drafts in a freely accessible institutional repository or disciplinary repository (″Green OA″) or (2) by publishing them in an open-access journal (″Gold OA″) or both.

We have a comprehensive outlook on open access policy

Open access refers to the practice of making peer-reviewed scholarly research and literature freely available online to science and researchers, specialist, students and another persons. This Open access publications are freely and permanently available online. Unrestricted use, distribution and reproduction in any medium is permitted, provided the author/editor/journal is properly attributed.

The articles is universally, freely accessible via the Internet, in an easily readable format. Our periodical (four time/year) are deposited immediately upon publication, without any technical, financial, gender limitations, in an agreed format – current preference is PDF and e-pub version of articles are available, which are the major forms of widely and internationally recognized open access repositories.

All articles are self archiving, with worldwide access through DOI number (Digital Object Identifier) – standardized by the International Organization for Standardization, provided for individual article published. Our journal follows Double Blind peer review process, which means that both the reviewer and author identities are concealed from the reviewers, and vice versa, throughout the review process. The benefits of open access publishing are next: a) Free availability of information; b) Authors retain copyright; c) High quality and rigorous peer review.

We are using the existence of politics of Registry of Open Access Mandatory Archiving Policies http://roarmap.eprints.org.

The quality control system

Our journal follows Double Blind peer review process, which means that both the reviewer and author identities are concealed from the reviewers, and vice versa, throughout the review process.

Plagiarism policy

Manuscripts containing original material are accepted for consideration if neither the article nor any part of its essential substance, tables, or figures has been or will be published or submitted elsewhere before appearing in our journal. Simultaneous submissions of the same article to multiple journals are prohibited. If an author violates this requirement or engages in similar misconduct, our Editorial Board may reject the manuscript.

Plagiarism is when an author passes off the work of someone else as his or her own. This can also include self-plagiarism, which happens when an author reuses portions of his or her previously published work without the proper references. Manuscripts containing plagiarized content will not be considered for publication in our journal. All authors need to take responsibility for their manuscripts. If your name is on a manuscript, make sure all of the material in the paper either is original or is properly cited and has proper permission to be reproduced. If you have a question about the originality of any part of a manuscript, verify it with your coauthors.

All articles are checked by the anti-plagiarism program.

Crossmark policy

Publication of any material in JOURNAL OF BIOMEDICAL AND MEDICAL SCIENCES denotes that all its authors have agreed to its content and have ensured that JOURNAL OF BIOMEDICAL AND MEDICAL SCIENCES's policies have been fully adhered to; adherence to sections 1-4 is compulsory for documents; sections 5 and 6 are strongly encouraged as they present good scientific practice and publishing standards.

We seek to ensure that the documents we publish and for which we provide a platform are responsible and have been selected and produced without bias.

We respect the intellectual property rights of our contributors and seek to avoid unethical publishing behaviors such as plagiarism, defamation and cultural misappropriation.

Our Publication Terms and Conditions set out the publishing standards by which we operate. We require that all work sets out to be fair and accurate, differentiates between fact and opinion, is obtained by straightforward and ethical means, and is promptly corrected where inaccurate or misleading. The acceptability of any document shall be decided by JOURNAL OF BIOMEDICAL AND MEDICAL SCIENCES at its discretion. JOURNAL OF BIOMEDICAL AND MEDICAL SCIENCES reserves the right, at its discretion, to not proceed with publication at any time or to remove the document following publication if there are legal or ethical concerns.

1. Originality

We are happy to publish documents those that are unpublished.

Authors of documents must ensure that they do not breach copyright with any content they post. Authors who wish to reproduce a figure or table from a previous copyrighted publication are responsible for obtaining the permission of copyright holders and for clearly referencing the original source. Figures that were previously published under a creative commons license may be reused under the condition of the specific license that applies to those figures.

2. Authorship on Documents

Any documents whose author’s affiliation is a recognized research centre or clinical institution or organization clearly related to academic research can be posted. At least one author on document must meet this key criterion.

Documents always relate to specific gateways and usually only researchers who are directly affiliated with a gateway and have been invited by the gateway advisers will be able to publish documents.

3. Competing interests

Authors must include a 'Competing interests' statement. A competing interest will not preclude publication, but it provides full transparency for readers. If there are no competing interests to declare, the following standard statement is added: 'No competing interests were disclosed'.

A competing interest may be of non-financial or financial nature. Examples of competing interests include (but are not limited to):

- individuals receiving funding, salary or other forms of payment from an organization, or holding stocks or shares from a company, that might benefit (or lose) financially from the publication of the findings
- individuals or their funding organization or employer holding (or applying for)
- related patents
- official affiliations and memberships with interest groups relating to the con-
- tent of the publication
- political, religious, or ideological competing interests.

Authors from pharmaceutical companies, or other commercial organizations that sponsor clinical trials, should declare these as competing interests on submission. The relationship of each author to such an organization should be explained in the 'Competing interests' section. Publications in JOURNAL OF BIOMEDICAL AND MEDICAL SCIENCES must not contain content advertising any commercial products.

The International Society for Medical Publication Professionals provides good practice guidelines, which are aimed at ensuring that ″clinical trials sponsored by pharmaceutical companies are published in a responsible and ethical manner″.

If an undisclosed competing interest is brought to the attention of the editorial office after publication, JOURNAL OF BIOMEDICAL AND MEDICAL SCIENCES will follow the COPE guidelines (https://publicationethics.org/guidance/Guidelines).

4. Ethical Policies

JOURNAL OF BIOMEDICAL AND MEDICAL SCIENCES adheres to the COPE guidelines (https://publicationethics.org/guidance/Guidelines) relating to ethical oversight.

4.1 Research involving humans

4.1.1 Ethics approval

All studies involving humans (individuals, human data or material) must have been conducted according to the principles expressed in the Declaration of Helsinki. Approval must have been obtained for all protocols from the authors' institutional or other relevant ethics committee to ensure that they meet national and international guidelines. Details of this approval should be provided in the document, including the institution, review board name, and permit number(s).

Human studies categorized by race/ethnicity, age, disease/disabilities, religion, sex/ gender, sexual orientation, or other socially constructed groupings, should include a justification of the choice of definitions and categories, including whether any rules of human categorization were required by the relevant funding agencies. Appropriate non-stigmatizing language should be used when describing different groups.

Ethics approval must be obtained before the research is conducted; retrospective approval can usually not be obtained and it may not be possible to publish the study.

4.1.2 Patient privacy and informed consent for publication

As stated in the Recommendations of the International Committee of Medical Journal Editors: ″Patients have a right to privacy that should not be infringed without informed consent. Identifying information should not be published in written descriptions, photographs, and pedigrees unless the information is essential for scientific purposes and the patient (or parent or guardian) gives written in – formed consent for publication. Informed consent for this purpose requires that the patient be shown the manuscript to be published. When informed consent has been obtained it should be indicated in the published article.″

Consent to participate: For all studies involving human participants, informed written consent to take part in the research must have been obtained, and this should be stated in the document in a section entitled 'Consent'. If only oral consent was obtained (rather than written), the reasons need to be explained, confirmation of IRB approval that oral consent was adequate must be provided, and a statement of how it was documented included in the Consent section.

Consent for publication of identifiable data: For any documents that include information that could potentially identify an individual, please ensure that you have obtained written, informed consent from all patients or healthy participants

(or their legal guardians for minors, or next of kin if the participant is deceased), confirming that the results and any images can be published. This includes large clinical datasets with direct or indirect identifiers (see this article for information), specific details about individuals, images and so on.

If your document contains any identifiable images of individuals, you must include a statement confirming that you have permission to publish these images. If your document contains any clinical images or identifiable data then you must include an explicit consent statement under a separate heading of the 'Consent' section (we suggest: ″We confirm we have permission to use [images/data] from the participants/patients/individuals included in this presentation [conditions under which the permission was obtained]″).

Alternatively, if no consent for publication was required (e.g. the data has been anonymised), then this should be clearly stated and a note should be added confirming that such alterations have not distorted scientific meaning.

Signed consent forms should be made available to the JOURNAL OF BIOMEDICAL AND MEDICAL SCIENCES editorial office if requested.

4.2 Research involving animals

Authors describing studies involving animals must have consulted the 'Animal Research: Reporting in vivo Experiments' (ARRIVE) 2.0 guidelines, developed by the NC3Rs to improve standards of reporting, ensuring that the data from animal experiments can be fully scrutinized and utilized. Studies reporting in vivo experiments must adhere to the ARRIVE Essential 10 checklist as a minimum, and we encourage authors to use the full ARRIVE 2.0 checklist.

Experiments involving vertebrates or regulated invertebrates must be carried out within the ethical guidelines provided by the authors' institution and national or international regulations. Where applicable, a statement of ethics permission granted or animal licenses should be included. If animals were used but ethical approval was not required, a clear statement should be included stating why this approval was unnecessary.

In all cases, a statement should be made to confirm that all efforts were made to ameliorate any suffering of animals and details of how this was achieved should be provided.

Authors should comply with the Convention on Biological Diversity and the Convention on the Trade in Endangered Species of Wild Fauna and Flora.

4.3 Research involving plants

Studies on plants must be carried out within the guidelines provided by the authors' institution and national or international regulations. Where applicable, a statement of permissions granted or licenses should be included. Authors should comply with the Convention on Biological Diversity and the Convention on the Trade in Endangered Species of Wild Fauna and Flora.

5. Registration of trials and systematic reviews

5.1 Trial registration

JOURNAL OF BIOMEDICAL AND MEDICAL SCIENCES uses the WHO definition of a clinical trial to decide what constitutes a clinical trial:

″A clinical trial is any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes. Interventions include (but are not restricted to) drugs, cells and other biological products, surgical procedures, radiologic procedures, devices, behavioral treatments, process-of-care changes, preventive care, etc″.

Trials should be registered prospectively and the trial registration number and registration date must be included in the document.

Although prospective trial registration is preferable, several initiatives (such as the All Trials campaign) have recognized that retrospective trial registration will encourage publication of both positive and negative results.

5.2 Systematic reviews registration

We encourage authors to register their systematic reviews in PROSPERO or another registry for systematic reviews. The registration number should be included in the document.

6. Standards of reporting

For articles in the life sciences there are standards of reporting guidelines devised to help authors to ensure that they have provided a comprehensive description of their research, making it easier for others to assess and reproduce the work; for more detail and a comprehensive overview, see the FAIR Sharing initiative. Comprehensive lists of available reporting guidelines can be found on the EQUATOR network website for health research.

For example, reports of clinical trials should adhere to the CONSORT reporting guidelines. Any deviation from the original trial protocol should be explained.

7. Licenses

Most JOURNAL OF BIOMEDICAL AND MEDICAL SCIENCES documents are published under a CC BY license, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited, and leaves the copyright of the document with the current copyright holder (usually the author or his/her institution). However, in some cases other Creative Commons licenses may apply. The specific license is listed for each document and document.

8. Permanency of content

All documents published in JOURNAL OF BIOMEDICAL AND MEDICAL SCIENCES receive a DOI and are permanently published, so they cannot be withdrawn once a DOI has been issued.

In order to maintain the integrity and completeness of the scholarly record, we will apply the following policies when published content needs to be corrected; these policies take into account current best practice in the scholarly publishing and library communities:

8.1 Correction to Document

All documents may contain errors; authors and readers can point out such mistakes via the Comment system. In the rare instance that a document needs to

be formally corrected, for example, if a change needs to be made to the author list, a Correction statement will be added.

8.2 Retraction

This action is reserved for documents that are seriously flawed. They may be retracted for several reasons, including:

- honest errors reported by the authors (for example, errors due to the mixing up of samples or use of a scientific tool or equipment that is found subsequently to be faulty)
- research misconduct (data fabrication)
- duplicate or overlapping publication
- fraudulent use of data
- clear plagiarism
- unethical research.

For any retracted document, the reason for retraction and who is instigating the retraction will be clearly stated in the Retraction notice. A publication is usually only retracted at the authors' request or by the publisher because serious misconduct has been brought to our attention.

8.3 Removal

The removal of a document would only be undertaken where legal limitations have been placed upon the publisher, copyright holder or author(s), for example, if the documents clearly defamatory or infringes others' legal rights. The bibliographic information for a removed document will be retained on the site along with information regarding the circumstances that led to its removal.

9. Allegations of misconduct

JOURNAL OF BIOMEDICAL AND MEDICAL SCIENCES is a member of the Committee on Publication Ethics (COPE) and provides an ethical publishing framework in accordance with COPE's codes of conduct for editors and pubishers.

All documents are not peer-reviewed or checked before being posted in JOURNAL OF BIOMEDICAL AND MEDICAL SCIENCES; publication of such

shared content in JOURNAL OF BIOMEDICAL AND MEDICAL SCIENCES does not imply endorsement of its content, methods or ethical standards.

If a case of suspected research or publication misconduct is brought to our attention, we will follow guidelines. This may involve contacting the authors' research institution, an ethics committee or other third parties.

Research misconduct includes data fabrication or falsification, or cases where research involving animals or humans has not been carried out within an appropriate ethical framework. Publication misconduct includes duplicate publication of articles or plagiarism. Honest errors or differences of opinion are not considered 'misconduct'.

If you suspect potential misconduct in an article published on JOURNAL OF BIOMEDICAL AND MEDICAL SCIENCES, please contact the editorial office (editor-in-chief@eu.edu.ge).

10. Appeals and complaints

JOURNAL OF BIOMEDICAL AND MEDICAL SCIENCES follows the COPE guidelines (https://publicationethics.org/guidance/Guidelines) in relation tocomplaintsand appeals. If you wish to make an appeal or complaint you should contact the editorial office (editor-in-chief@eu.edu.ge). In the instance that your issue cannot be resolved by the editorial office, the Publishing Director should be contacted.

11. Policy for Comments on Documents

We encourage unsolicited open scientific discussion on all research outputs. Such contributions are published through our Comment system. To ensure that comments contribute to, and focus on, the scholarly debate, we usually only allow comments from readers who have a formal affiliation with a research institution, or other relevant organization. Alternatively, we may also allow comments from readers who have demonstrable expertise in a relevant area of research. Consistent with our commitment to full transparency, the reader's full name and affiliation appear on their public comment.

Comments should focus on the scholarly content presented in the documents with which they are associated.

Comments that appear to be advertising are potentially libelous or legally problematic (including comments revealing patient information) are not permitted. We will not accept Comments that are offensive, indecent or contain negative comments of a personal, racial, ethnic, sexual orientation, or religious character.

All Comments must be written in good English; a Comment may be rejected if it is deemed unintelligible.

Readers who wish to comment are asked to declare any competing interests. Competing interests can be of a financial nature (e.g. holding a patent or receiving fees from a company that may lose or gain financially from the publication of the Comment), or they can be personal, religious, political or other non-financial interests. When completing your declaration, please consider the issues summarized in the Declaration of Competing Interests.

While we welcome open scientific debate and discussion, we will not tolerate abusive behavior towards our authors and reviewers via our Comment system or via social media. In extreme cases we will consider contacting the affiliated institution to report the abusive behavior of individuals.


INTERNATIONAL
STANDARD
SERIAL
NUMBER
INTERNATIONAL CENTRE


doi


Crossref


Google
Scholar


E-LIBRARY


Scope Database
Journal indexing & Citation Analysis