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Features of cystic fibrosis development in a patient with coinfection by *Mycobacterium abscessus* and *Mycobacterium tuberculosis* (clinical case report)

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ABSTRACT

The article presents a clinical case describing a favorable clinical outcome of mycobacterial infection and pulmonary tuberculosis caused by coinfection of *M. abscessus* and *M. tuberculosis* in a patient with pulmonary manifestations of cystic fibrosis one year after delivery. This outcome was achieved due to timely diagnosis and treatment of pulmonary tuberculosis and non-tuberculous mycobacterial infection in the patient with cystic fibrosis. Due to the development of molecular identification of mycobacteria species in the Tomsk region, mycobacterial lung disease was verified, which was challenging in the recent past. Previously, all cases with microscopic examination results positive for mycobacteria were classified as tuberculosis.

Keywords: cystic fibrosis, nontuberculous mycobacteria, M. abscessus, pulmonary tuberculosis, M. tuberculosis, coinfection

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Особенности течения муковисцидоза при сочетании *Mycobacterium abscessus* и *Mycobacterium tuberculosis* (клиническое наблюдение)

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РЕЗЮМЕ

Представлено клиническое наблюдение, описывающее случай благоприятного клинического течения микобактериоза и туберкулеза легких, вызванный микст-инфекцией *M. abscessus* и *M. tuberculosis* у пациентки с легочными проявлениями кистозного фиброза (муковисцидоза) через 1 год после родоразрешения. Данный результат лечения был достигнут с помощью своевременной диагностики, начатому лечению туберкулеза и микобактериоза легких у пациентки с кистозным фиброзом (муковисцидозом). Благодаря развитию в Томской области микробиологической видовой идентификации микобактерий, был верифицирован микобактериоз легких, что еще в недавнем прошлом было проблематично, и все случаи с положительной микроскопией были отнесены к туберкулезу.

Ключевые слова: кистозный фиброз (муковисцидоз), нетуберкулезные микобактерии, *M. abscessus,* туберкулез легких, *M. tuberculosis*, микст-инфекция

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии финансирования при проведении исследования.

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INTRODUCTION

In 1953, the extremely rare opportunistic pathogenic microorganism *Mycobacterium abscessus* that is fast-growing non-tuberculous mycobacteria (NTMB), whose natural environment is soil and water, was isolated from a soft tissue abscess of a patient after a knee injury [1, 2]. Due to the presence of identical biochemical properties, until 1992 they were combined into one species with *Mycobacterium chelonae*, which causes mycobacterial infection of soft tissues in a fish. Subsequently, after genomic analysis, the *M. abscessus* species was divided into three subspecies combined into the MABSc complex: *M. abscessus subsp. abscessus, M. abscessus subsp. massiliense, M. abscessus subsp. bolletii*. These microorganisms have a single sequence of the 16S rRNA gene, but there are differences in specific genes, in particular, those of great clinical importance for resistance to macrolides (*erm41* gene) [3].

Currently, according to foreign sources, NTMB of the MABSc complex are the second most common in patients with various chronic lung diseases after representatives of the *M. avium* complex and the first among all fast-growing mycobacteria [4]. The results of studies conducted in our country similarly show that in patients undergoing differential diagnosis in specialized anti-tuberculosis institutions, *M. abscessus* is most often isolated from fast-growing mycobacteria [6–8]. At the same time, the intraspecies differentiation of *M. abscessus* shows that the subspecies *M. abscessus subsp. abscessus* dominates in Russia (up to 70%), the subspecies *M. abscessus subsp. massiliense* is in the second place in terms of detection frequency (27%), and *M. abscessus subsp. bolletii* is not actually found [9]. In clinical practice, patients undergoing immunosuppressive therapy are mainly at high risk of MABSc infection: recipients of parenchymal organ transplants and patients receiving glucocorticoid and cytostatic therapy for various reasons [2, 10–12].

CLINICAL CASE

We present a clinical case of coexisting mycobacterial infection and pulmonary tuberculosis in a patient with cystic fibrosis. Actually, we narrate a further medical fate of a woman who had complex clinical features of cystic fibrosis during pregnancy and childbirth, described earlier [13].

Medical history. A female patient born in 1997 with a family history of cystic fibrosis (her sister is also ill) had symptoms of the underlying disease from the age of 1.5 months, the diagnosis was verified at almost 5 years old (sweat chlorides – 119 mEq / l). At the

age of 14, lower lobar thoracoscopic lobectomy was performed for bronchiectasis in S 8–10 on the right. In 2017, the patient had chronic vasomotor rhinitis at the vasodilation stage and underwent another surgical intervention – submucosal vasotomy of the lower nasal concha. The patient had one pregnancy and one childbirth. She lives in a comfortable apartment with her parents, husband, and one-year-old child. The patient claims she does not smoke, drink alcohol or use drugs.

The patient is constantly followed up at the Research Institute of Medical Genetics with the diagnosis: cystic fibrosis, mixed form (pulmonary intestinal), moderate severity, continuously recurrent course. Compound heterozygous for Dele 2,3/E92,K. The patient had chronic pancreatic insufficiency, severe course. According to the underlying disease, the patient was granted the status of category 3 disability indefinitely. The patient receives basic therapy: pulmozyme (tigerase) 1 ampoule per day through a nebulizer; bramitob 300 mg 2 times a day through a nebulizer (a cycle of 28 days followed by a break of 28 days) or in a similar scheme colistin 80 mg 2 times a day; creon 25,000 units (based on 6,000 units / kg of body weight) 10 capsules per day with meals; ursofalk 250 mg, 5 tablets per day (3 tablets at lunch after meals and 2 tablets at night); periodically – bronchitol 400 mg 2 times a day. Twice a year, she had scheduled hospitalizations in pulmonology departments, if necessary, with an exacerbation of bronchopulmonary infection, she was hospitalized urgently.

Starting from 20.05.2021, the patient had another scheduled hospitalization in the Pulmonology Department of the City Clinical Hospital No. 3. of Tomsk. She was worried about a constant cough with the release of a small amount of yellow sputum, an increase in body temperature to 38.0 °C. On auscultation, wet wheezing was noted in the lungs, moderate leukocytosis (11.8×10^9 / l) was observed in the CBC, *Staphylococcus aureus* was cultured from the sputum, with sensitivity to meropenem, ertapenem, and imipenem. When the patient was receiving antibacterial therapy, negative changes were established in the form of an increase in symptoms of intoxication and leukocytosis. Lung X-ray upon admission detected focal infiltrative changes in the pulmonary parenchyma around bronchiectasis that were also without significant changes. According to the examination algorithms for patients with chronic pulmonary diseases accepted in clinical practice, the patient's sputum was redirected to Tomsk Phthisiopulmonology Center (TPMC) for testing for tuberculosis by molecular genetic methods. MBTs with preserved sensitivity to rifampicin were detected by the GeneXpert method. On 28.05.2021, for further examination and treatment, she was transferred to the TPMCn to the department for patients with pulmonary tuberculosis.

Upon admission, the condition was of moderate severity, with shortness of breath during physical exertion and cough with mucopurulent sputum discharge. The patient's indicators were as follows: blood pressure 94/63 mm Hg, pulse 118 per minute, body temperature 36.4 °C, saturation 99%. The patient was conscious and alert. The skin was pale, with normal humidity. The body build was hyposthenic, the subcutaneous fat layer was poorly developed. The mucous membranes were normal and pink. Peripheral lymph nodes were not palpable. The heart sounds were clear and rhythmic. The chest was of the correct shape, breathing was harsh with multiple moist fine bubbling rales, respiratory rate was 18 per minute. The abdomen was soft and non-tender upon palpation. The liver was not enlarged. The blistering symptoms were negative. The spleen and kidneys were not palpable. There was no peripheral edema. The bowel movement occurred 2 times, it was liquid without pathological impurities of the usual color, diuresis was normal.

Data from laboratory and instrumental examinations upon admission were as follows. Complete blood count: hemoglobin – 107 g / l, erythrocytes – 4.64×10^{12} / l, leukocytes – 5.09×10^9/ l, neutrophils 30%, lymphocytes 62%, monocytes 8%. Erythrocyte sedimentation rate was 5 mm / h. Blood biochemistry: total protein 72.5 g / l; albumin 40.4 g / l; alanine aminotransferase – 7.1 U / l; aspartate aminotransferase – 17.8 U / l; creatinine – 75.8 mmol / l; urea – 2.9 mmol / l; fasting blood glucose – 5.1 mmol / l; amylase 35.8 U / l; alkaline phosphatase 262.6 U / l. Blood tests for HIV, hepatitis B and C were negative. General urine analysis: light yellow color; relative density 1,015; pH 6; protein, glucose – negative; epithelium 1–2; leukocytes 2–4; erythrocytes 1–2. Spirometry: forced vital capacity (FVC) – 3.53 (70.24%); forced expiratory volume in 1 second (FEV1) – 2.87 (67.79%); FEV1 / FVC – 79.4 (96%). Conclusion: moderate type I obstructive impairment of lung ventilation function. ECG: the position of the electrical axis of the heart was vertical, the rhythm was sinus, the heart rate was 112 beats per minute.

Sputum test results from 31.05.2021: by luminescent microscopy – acid-resistant microorganisms (ARM) (+++). PCR detected MTB DNA (sensitivity to isonazide and rifampicin was preserved), MTB growth was detected using microbial culture on liquid nutrient media (BACTEC MGIT 960), sensitivity to first–line drugs was preserved. Sputum culture on dense media – continuous MTB growth (+++), sensitivity to isoniazid, rifampicin, streptomycin, ethambutol, kanamycin (HRSE Km, respectively) was preserved. When cultured on liquid and then on dense media, NTMB was found, which in two samples were identified as *M. abscessus subsp. abscessus.* Typing was performed at the Novosibirsk Tuberculosis Research Institute using DNA hybridization on strips/time-of-flight mass spectrometry.

Computed tomography (CT) (28.05.2021, Fig. 1) detected infiltrative foci of different size in both lungs with a trend toward a merge into areas of consolidation, in the lower medial part of the right lung, a consolidation site measuring 45 x 35 mm with signs of volume reduction and traction bronchiectasis. In the supra-diaphragmatic zone of the left lung at S 8, 9, 10, there were merging foci and areas of consolidation of a similar nature with partially preserved bronchial patency and traction bronchiectasis. At S5, there was a subpleural consolidation site with signs of volume reduction and cylindrical traction bronchiectasis. Cylindrical and cystic bronchiectasis were determined by separate groups in the upper part of both lungs, more often on the right. Conclusion: focal lung dissemination, signs of bilateral polysegmental pneumonia, areas of local pneumosclerosis in the basal parts of both lungs; bronchiectasis of both lungs.

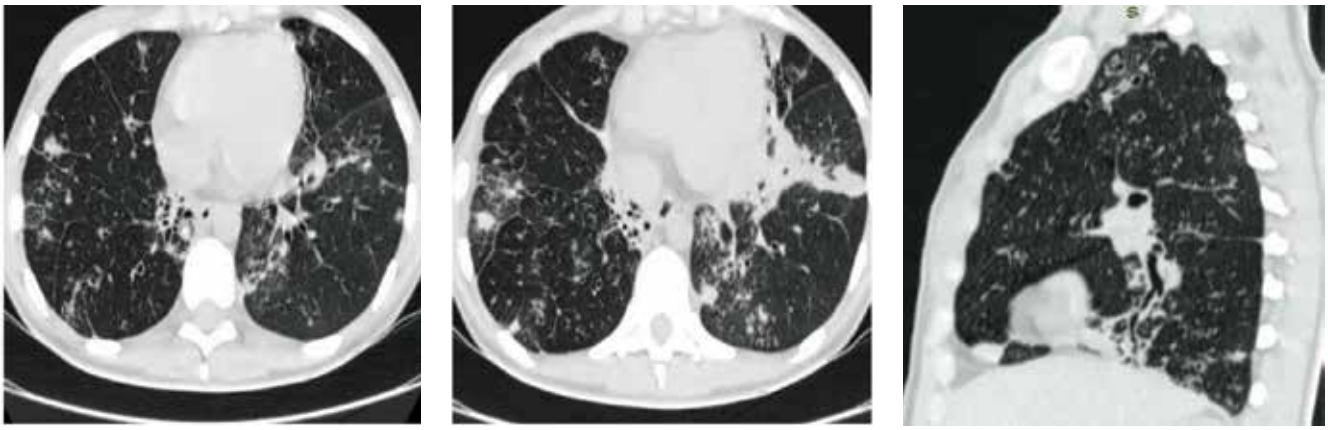

Fig. 1. Chest CT (28.05.2021).Signs of focal dissemination with consolidation around bronchiectasis in moderate pneumofibrosis

The patient was enrolled in the 1st group of follow-up with the diagnosis of disseminated pulmonary tuberculosis, infiltration phase, MTB (+). At the beginning, treatment was prescribed according to the regimen of drug-sensitive tuberculosis with a daily dosage of medicines according to body weight (H 0.6; R 0.6; Z 2.0; E 1.2) with an enhanced regimen for levofloxacin (Lfx) 1.0. After NTMB was identified, clarithromycin 1.0 was added to the treatment regimen.

During treatment, the patient developed adverse reactions to pyrazinamide – joint pain (relieved by the prescription of nonsteroidal anti–inflammatory drugs), and ethambutol decreased visual acuity (it was canceled). Furtheron, the prescribed therapy brought about positive clinical and radiological changes in the form of a decrease (resorption) of focal opacities and areas of consolidation (Fig. 2).

Microbiological analysis data over time: positive microbial culture test for MTB persisted for 8 months until February 2022, positive test for NTMB persisted for 12 months until May 2022. The patient was removed from the register in September 2022. The total course of treatment was 12 months. In the summer of 2023, there was a recurrence of bronchopulmonary infection caused by *Klebsiella pneumoniae,* in the diagnostic titer 10^5. She was examined, including for the recurrence of tuberculosis and mycobacterial infection, no data were obtained. Currently, the patient's condition is satisfactory, she is followed up by a pulmonologist and continues treatment for cystic fibrosis.

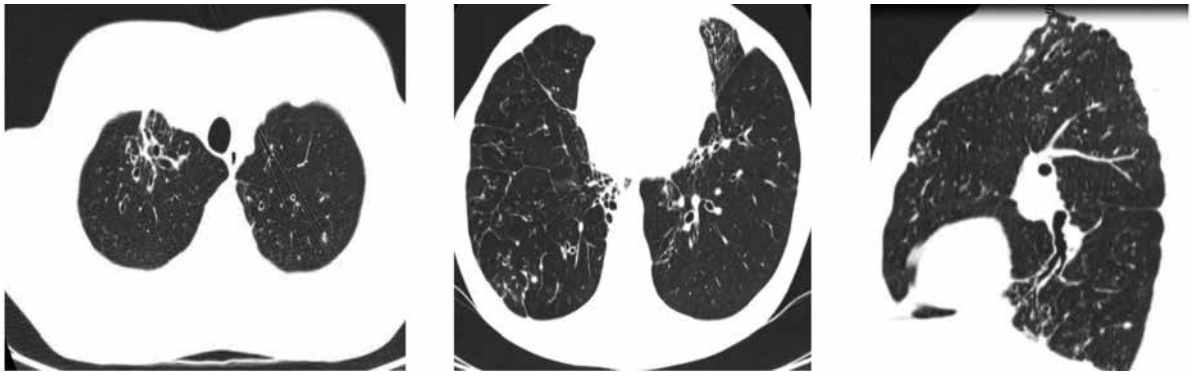

Fig. 2. Chest CT (30.07.2021): in comparison with the CT study of 28.05.2021, there was an improvement in the pulmonary pneumaticity in the lower lobe of the left lung due to a decrease in the number of focal opacities, the area of consolidation, and the severity of the interstitial inflammation

DISCUSSION

Among chronic lung diseases, predisposing factors to the development of mycobacterial infection caused by MABSc include bronchiectasis, cystic fibrosis, chronic obstructive pulmonary disease, primary ciliary dyskinesia, allergic bronchopulmonary aspergillosis, α-1-antitrypsin deficiency, pneumoconiosis, interstitial lung disease, pulmonary alveolar proteinosis, as well as conditions requiring frequent surgical interventions, punctures, injections, prosthetics [6–9, 12, 14, 15]. The symptoms of this pulmonary pathology are nonspecific and very similar to chronic infections of other etiologies, including tuberculosis. Clinical studies have shown that before the diagnosis of mycobacterial infection of the lungs caused by *M. abscessus*, patients in a third of cases have other types of NTMB, in half of cases they had previously experienced pulmonary tuberculosis.

According to CT data, bronchiectasis and single or multiple destruction cavities were detected in more than 50% of cases, and dissemination was detected in every third patient. Almost 70% of the sputum was found to contain acid-resistant bacteria [16]. In addition to the lungs, *M. abscessus* can also cause extrapulmonary infections of the central nervous system, skin, soft tissues, bones, joints, lymph nodes, other parenchymal organs, as well as generalized disseminated processes.

According to available data, mycobacteria of the MABSc complex have numerous virulence factors, ranging from early stages of colonization to intracellular persistence, which actually allow subspecies of *M. abscessus* to be classified as true pathogens, especially in patients with weakened immunity. The hydrophobicity of the mycobacterium cell wall contributes to their strong adhesion to various surfaces with the formation of biofilms, which provide high colonization in natural (bodies of water) and artificial reservoirs of infection, such as various water supply systems at home and in healthcare institutions, for example, on medical devices, surgical instruments / devices, dialysis, ventilators, and other devices [12, 14, 15].

An important feature of MABSc is the high content of lipids and waxes in the cell wall (glycopeptidolipids, GPL, up to 60% of dry weight), which plays a key role in the intracellular survival of microorganisms. GPL *M. abscessus*, like other virulent mycobacteria, form a cord factor and bind microorganisms together in the form of braids and bundles, bypassing the digestion processes [17]. This is facilitated by an advanced expression network of transport proteins (31) of lipid metabolites for GPL cell wall biosynthesis (MmpL and MmpS), which are known to be virulence factors in slow-growing mycobacteria, such as *M. tuberculosis* and *M.bovis*, severe pathogens for humans and animals [18].

In addition to inhibiting phagocytosis processes, the highly immunogenic GPL of mycobacteria of the MABSc complex shifts the effective initiation of cellular adaptive immunity toward an increased humoral response, which leads to increased apoptosis, extracellular replication microorganisms, and the development of acute inflammation and tissue damage with the formation of abscesses in infected people [19]. It has been proven that MABSc possess a whole set of genes (in particular, *GroEL-ES, hsp, ESX-4, EsxU and EsxT*) responsible for survival of

microorganisms inside macrophages. Their functional expression allows them to avoid intracellular oxygen-dependent destruction processes. such as heat shock or oxidative stress, and switch to a phenotype of slower growth, using various sources as energy, for example, fatty acids [20, 21].

Uniqueness of M. abscessus regarding its pathophysiology is confirmed (in addition to weak permeability of the cell wall) by the presence of efflux pumps capable of removing drugs, as well as enzymes that modify both antibacterial agents and their targets (Table).

Table

Biological determinants of *M. abscessus* drug resistance

Factors of natural / acquired drug resistance (enzymes or mutations)	Antibacterial resistance
Rifampicin-ADP-ribosyltransferase	Resistance to rifampicin
Rifampicin-ADP monooxygenase	Resistance to rifampicin
Rifamycin-glycosyltransferase	Resistance to rifampicin
Aminoglycoside-2-N-acetyltransferase	Resistance to aminoglycosides
Aminoglycoside-2-N-phosphotransferase	Resistance to aminoglycosides
β-lactamase	Resistance to β-lactams, including cephalosporins and carbapenems
Flavin-containing monooxygenase	Tetracycline resistance
The presence of the *erm41 gene* in M. abscessus subsp. *Abscessus and M. abscessus subsp. bolletii* (M. abscessussubsp. massiliense does not have it)	Resistance to macrolides
Induced mutations in the *23S* rRNA gene via the functional erm41 *gene*	Acquired resistance to macrolides (clarithromycin induces erm41 *to* a much greater extent than azithromycin)
Induced mutations in the *16S* rRNA gene	Resistance to aminoglycosides (amikacin, kanamycin, and gentamicin)
Induced mutations in the *eMBB* gene	Resistance to ethambutol
Mutations in the regions determining resistance to quinolones (QRDR, *gyr A, gyr* B)	Resistance to fluoroquinolones

According to available data, since the *M. abscessus* genome was decoded in 2009, this mycobacteriosis pathogen has a wide range of natural drug resistance to antibiotics. Taking into account, among other things, their high mutagenic activity, leading to the formation of secondary resistance, this disease is an "incurable nightmare" for clinicians with low treatment effectiveness (less than 50%) in most patients, even after a combination of 4–5 antibacterial drugs during months of therapy [21, 22]. *M. abscessus* has natural resistance to first-line anti-tuberculosis drugs, such as HRZE. In addition, *M. abscessus* is resistant to the main antimicrobial drugs used in respiratory infections, such as β-lactams, aminoglycosides (gentamicin), cyclins (doxycycline), sulfonamides, and macrolides (erythromycin), and induced or mutational resistance to fluoroquinolones is also manifested [2, 23].

As is known, patients with cystic fibrosis are highly susceptible to bacterial and mycotic infections, most often caused by *Staphylococcus aureus, Pseudomonas aeruginosa*, *Burkholderia cepacia* complex, including NTMB [15, 24]. At the same time, transmission of infection caused by mycobacteria of the MABSc complex can be carried out from person to person [25]. The mechanisms of susceptibility to these infections in patients with cystic fibrosis are explained by the pathogenesis of the disease, where due to a mutation in the *CFTR* gene (cystic fibrosis transmembrane conductance regulator), transport of electrolytes between the cell and the intercellular fluid changes, which leads to the formation of thick viscous sputum, secondary ciliary dysfunction of the bronchial mucosa, and inability to effectively eliminate microorganisms from bronchial secretions.

In addition, macrophage dysfunction is also observed in patients with cystic fibrosis, leading to impaired phagocytosis and excessive production of inflammatory mediators. More and more scientific evidence is being accumulated of a certain predisposition of these patients to infection caused by *M. abscessus* [9, 12, 14, 15, 26]. A typical treatment regimen includes intensive therapy using ≥ 2 parenteral antibiotics (options include amikacin, imipenem, tigecycline) for 6–8 weeks, followed by maintenance therapy with clofazimine and inhaled amikacin with or without azithromycin (taking into account its immunomodulatory effect) [27].

Unlike mycobacterial infection, pulmonary tuberculosis is potentially possible, but occurs in single cases of patients with cystic fibrosis. Data obtained

from Russian and French cystic fibrosis centers report 11 cases (8 in Russia, 3 in France) of coexisting pulmonary tuberculosis and cystic fibrosis. It is worth noting that in none of the described cases, the diagnosis was based on clinical and radiological symptoms, but only on the bacteriological examination of sputum, and in almost half of the cases, Russian patients had positive microscopy and multidrug resistance of the pathogen [28].

Simultaneous detection of MBTC and NTMB in mycobacterium cultures is not common, only a few publications are devoted to this issue. One of the latest foreign studies in South Korea determined that out of 6,201 culture samples, 2,456 (59.0%) were identified as MBTC, 2,456 (39.6%) as NTMB, and only 86 (1.4%) as mixed. At the same time, in the last samples, *M. intraculturale* (29.0%) and *M. abscessus* (29.0%) were determined in equal proportions together with *M. tuberculosis* [29]. Data obtained in Russia are similar. In 5,531 patients secreting mycobacteria, *M. tuberculosis* was detected in 3,829 (69.2%) mycobacterium culture samples, while NTMB was detected in 1,638 (29.6%). Mixed populations were found in 64 cases (1.2%), of which four (6.2%) had *M. tuberculosis* + *M. abscessus*[30]. Detailed information on patients secreting mixed mycobacterial cultures has not been published.

CONCLUSION

Thus, a clinical case demonstrates a favorable clinical course of mycobacterial infection and pulmonary tuberculosis caused by coinfection of *M. abscessus* and *M. tuberculosis* in the patient with pulmonary manifestations of cystic fibrosis one year after delivery. In the available publications, there was only one case of such coinfection in an immunocompetent patient without cystic fibrosis, whose favorable outcome would be determined only after pneumonectomy [31].

In our case, it should be noted that the algorithm for diagnosing tuberculosis in patients with chronic infectious processes in the lungs is justified. The development of molecular identification of mycobacteria species in the regions makes it possible to verify mycobacterial infection in the lungs, which was challenging in the recent past, and all cases with positive microscopy were classified as tuberculosis. Despite the fact that drug-sensitive NTMB has not been identified, effective therapy allows to conclude that *M. abscessus subsp. abscessus* were sensitive to macrolides (clarithromycin). It is worth noting that bacteria continue to excrete for a long period of time: MTB – 8 months of treatment, NTMB – 12 months.

REFERENCES

1. Moore M., Frerichs J.B. An unusual acid-fast infection of the knee with subcutaneous, abscess-like lesions of the gluteal region; report of a case with a study of the organism, *Mycobacterium abscessus, n. sp. J. Invest. Dermatol*. 1953;20(2):133–169. DOI: 10.1038/jid.1953.18. PMID: 13035193.
2. Abdelaal H.F.M., Chan E.D., Young L., Baldwin S.L., Coler R.N. Mycobacterium abscessus: It's Complex. *Microorganisms.*2022;10(7):1454. DOI: 10.3390/ microorganisms10071454.
3. Nakanaga K., Sekizuka T., Fukano H., Sakakibara Y., Takeuchi F., Wada S. et al. Discrimination of *Mycobacterium abscessus subsp. massiliense* from *Mycobacterium abscessus subsp. abscessus* in clinical isolates by multiplex PCR. *J. Clin. Microbiol*. 2014;52(1):251–259. DOI: 10.1128/JCM.01327-13.
4. Prevots D. R., Marshall J.E., Dirk W., Kozo M. Global Epidemiology of Nontuberculous Mycobacterial Pulmonary Disease: A Review. *Clinics in Chest Medicine*. 2023;44(4):675–721. DOI: 10.1016/j.ccm.2023.08.012.
5. Dahl V.N., Mølhave M., Fløe A., van Ingen J., Schön T., Lillebaek T. et al. Global trends of pulmonary infections with nontuberculous mycobacteria: a systematic review. *Int. J. Infect. Dis*. 2022;125:120–131. DOI: 10.1016/j.ijid.2022.10.013.
6. Karpina N.L., Egorova A.D., Chesalina Ya.O., Shabalina I.Yu., Ergeshov A.E. Aspects of the stage-by-stage diagnosis of mycobacteriosis of the lungs in real clinical practice. *Tuberculosis and Lung Diseases*. 2023;101(2):30–37 (in Russ.). DOI: 10.58838/2075-1230-2023-101-2-30-37.
7. Starkova D.A., Zhuravlev V.Yu., Vyazovaya A.A., Solovyova N.S., Kulikova O.N., Narvskaya O.V. Species diversity of non-tuberculous mycobacteria in patients with mycobacteriosis in the North-Western Federal District of Russia. *Tuberculosis and Lung Diseases*. 2019;97(6):16–22 (in Russ.). DOI:10.21292/2075-1230-2019-97-6-16-22.
8. Kalimulina K.R., Ismatullin D.D., Lyamin A.V., Kondratenko O.V., Kozlov A.V., Zhestkov A.V. *Mycobacterium abscessus complex* representatives in patients with bronchopulmonary pathology: prevalence, peculiarities of cultivation and identification.*Clinical Laboratory Diagnostics*. 2020;65(5):316–320 (in Russ.). DOI: 10.18821/0869-2084-2020-65-5-316-320.
9. Smirnova T.G., Chernousova L.N., Varlamov D.A., Sochivko D.G., Ergeshov A.E. Intraspecific diversity of *Mycobacterium abscessus* isolated from patients with pulmonary lesions. *Tuberculosis and Lung Diseases.* 2023;101(4) 40–45 (in Russ.). DOI: 10.58838/2075-1230-2023-101-4-40-45.
10. Abad C.L., Razonable R.R. Non-tuberculous mycobacterial infections in solid organ transplant recipients: An update. *J. Clin. Tuberc. Other Mycobact. Dis*. 2016;(4):1–8. DOI: 10.1016/j.jctube.2016.04.001.
11. Ebisu Y., Natori Y., Rosello G., Anjan S., Simkins J., Camargo J.F., Morris M., Martinez O.V., AbboL M. *Mycobacterium abscessus* infections in solid organ transplant recipients: single-center experience in the United States, 2013–2018. *Open Forum Infectious Diseases.* 2022;9(7):254. DOI: 10.1093/ofid/ofac254.

12. Kasimova A.R., Kochish A.A., Gordina E.M., Artyukh V.A., Rukina A.N., Bozhkova S.A. *Mycobacterium abscessus* as a causative agent of periprosthetic infection. *Genij Ortopedii.* 2023;29(5):557–564 (in Russ.). DOI: 10.18019/1028-4427-2023-29-5-557-564.
13. Teteneva A.V., Chernyavskaya G.M., Bespalova I.D., Skorokhodova T.V., Koshavtseva Yu.I., Radionov D.I., et al. Clinical features of the course of cystic fibrosis during pregnancy and childbirth. Bulletin of Siberian medicine. 2022;21(4):205–211 (in Russ.). DOI: 10.20538/1682-0363-2022-4-205-211.
14. Degiacomi G., Sammartino J.C., Chiarelli L.R., Riabova O., Makarov V., Pasca M.R. *Mycobacterium abscessus*, an emerging and worrisome pathogen among cystic fibrosis patients. *Int. J. Mol. Sci*. 2019; 20(23):5868. DOI: 10.3390/ijms20235868.
15. Loebinger M.R., Quint J.K., van der Laan R., Obradovic M., Chawla R., Kishore A. et al. Risk Factors for Nontuberculous Mycobacterial Pulmonary Disease: A Systematic Literature Review and Meta-Analysis. *Chest*. 2023;164(5):1115–1124. DOI: 10.1016/j.chest.2023.06.014.
16. Park J., Yoon S.H., Kim J.Y., Gu K.M., Kwak N., Yim J.J. Radiographic severity and treatment outcome of *Mycobacterium abscessus* complex pulmonary disease. *Respir. Med*. 2021;187:106549. DOI: 10.1016/j.rmed.2021.106549.
17. Sánchez-Chardi A., Olivares F., Byrd T.F., Julián E., Brambilla C., Luquin M. Demonstration of cord formation by rough *Mycobacterium abscessus* variants: implications for the clinical microbiology laboratory. *J. Clin. Microbiol*. 2011;49(6):2293–2295. DOI: 10.1128/JCM.02322-10.
18. Lagune M., Kremer L., Herrmann J.L. *Mycobacterium abscessus*, a complex of three fast-growing subspecies sharing virulence traits with slow-growing mycobacteria. *Clin. Microbiol . Infect*. 2023:S1198-743X(23)00485-8. DOI: 10.1016/j.cmi.2023.08.036.
19. Gutiérrez A.V., Viljoen A., Ghigo E., Herrmann J.L., Kremer L. Glycopeptidolipids, a double-edged sword of the *Mycobacterium abscessus* complex. *Front. Microbiol*. 2018(9):1145. DOI: 10.3389/fmicb.2018.01145.
20. Dubois V., Pawlik A., Bories A., Le Moigne V., Sismeiro O., Legendre R. et al. *Mycobacterium abscessus* virulence traits unraveled by transcriptomic profiling in amoeba and macrophages. *PLoS Pathog.* 2019;15(11):e1008069. DOI: 10.1371/journal.ppat.1008069.
21. Lagune M., Le Moigne V., Johansen M.D., Vásquez Sotomayor F., Daher W., Petit C. et al. The ESX-4 substrates, EsxU and EsxT, modulate *Mycobacterium abscessus* fitness. *PLoS Pathog.* 2022;18(8): e1010771. DOI: 10.1371/journal.ppat.1010771.
22. Tunesi S., Zelazny A., Awad Z., Mougari F., Buyck J.M., Cambau E. Antimicrobial susceptibility of *Mycobacterium abscessus* and treatment of pulmonary and extra-pulmonary infections. *Clin. Microbiol. Infect*. 2023:S1198-743X(23)00482-2. DOI: 10.1016/j.cmi.2023.09.019.
23. Luthra S., Rominski A., Sander P. The кole of antibiotic-target-modifying and antibiotic-modifying enzymes in *Mycobacterium abscessus* drug resistance. *Front. Microbiol.* 2018;9:2179. DOI: 10.3389/fmicb.2018.02179.
24. Filkins L.M., O'Toole G.A. Cystic fibrosis lung infections: polymicrobial, complex, and hard to treat. *PLoS Pathog* 2015;11(12):e1005258. DOI: 10.1371/journal.ppat.1005258.
25. Bryant J.M., Grogono D.M., Greaves D., Foweraker J., Roddick I., Inns T. et al. Whole-genome sequencing to identify transmission of *Mycobacterium abscessus* between patients with cystic fibrosis: A retrospective cohort study. *Lancet.* 2013;381(9877):1551–1560. DOI: 10.1016/S0140-6736(13)60632-7.
26. Bernut A., Nguyen-Chi M., Halloum I., Herrmann J.L., Lutfalla G., Kremer L. *Mycobacterium abscessus*-induced granuloma formation is strictly dependent on TNF signaling and neutrophil trafficking. *PLoS Pathog*. 2016;12(11):e1005986. DOI: 10.1371/journal.ppat.1005986.
27. Daley C.L, Iaccarino J.M., Lange C., Cambau E., Wallace R.J.J., Andrejak C. et al. Treatment of nontuberculous mycobacterial pulmonary disease: an official ATS/ERS/ESCMID/IDSA clinical practice guideline. *Clin. Infect. Dis*. 2020;71(4):e1-e36. DOI: 10.1093/cid/ciaa241.
28. Asherova I.K., Feizhelson J., Amelina E.L., Kashirskaya N.Yu., Kapranov N.I. Cystic fibrosis and tuberculosis. *Pulmonologiya.*2012;(4):34–39 (in Russ.). DOI: 10.18093/0869-0189-2012-0-4-34-39.
29. Hwang S.M., Lim M.S., Hong Y.J., Kim T.S., Park K.U., Song J. et al. Simultaneous detection of *Mycobacterium tuberculosis* complex and nontuberculous mycobacteria in respiratory specimens. *Tuberculosis* (E*dinb*). 2013;93(6):642–646. DOI: 10.1016/j.tube.2013.07.007.
30. Smirnova T.G., Andreevskaya S.N., Larionova E.E., Chernousova L.N., Ergeshov A.E. Mixed populations of mycobacteria in patients with tuberculosis and mycobacteriosis: frequency of detection and spectrum of species. *Tuberculosis and Socially Significant Diseases.* 2023;11(2) (in Russ.): DOI: 10.54921/2413-0346-2023-11-2.
31. Sohn S., Wang S., Shi H., Park S., Lee S., Park K.T. Mixed Infection of *Mycobacterium abscessus subsp. abscessus* and *Mycobacterium tuberculosis* in the Lung. *Korean. J. Thorac. Cardiovasc. Surg*. 2017;50(1):50–53. DOI: 10.5090/kjtcs.2017.50.1.50.

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