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БОЛЕЗНИ ТЕРАПЕВТИЧЕСКОГО ПРОФИЛЯ
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CASE REPORT
КЛИНИЧЕСКИЙ СЛУЧАЙ

Nontuberculous mycobacterial pulmonary disease

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Abstract: The article presents a case report of nontuberculous mycobacterial pulmonary disease. Nontuberculous mycobacterial pulmonary disease is frequently underdiagnosed due to the absence of clinical signs, a nonspecific X-ray picture, as well as the difficulties of using molecular genetic diagnostic tests in primary health care setting. Some patients especially those with underlying respiratory diseases, are at increased risk of developing nontuberculous mycobacterial pulmonary disease. Identification of patients at risk is essential to allow for prompt testing and diagnosis and appropriate management to prevent disease progression.

Key words: nontuberculous mycobacterial pulmonary disease, diagnosis, nontuberculous mycobacteria, computed tomography, case report

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Introduction

Mycobacteria other than *Mycobacterium tuberculosis* and *Mycobacterium leprae* constitute a large group of non-tuberculous mycobacteria (NTM). Representatives of this group are found in water, soil, food products, are opportunistic bacteria, and can live on body surfaces or secretions without causing disease [1–4]. The NTM group includes about 200 species and subspecies of microorganisms, the most common and significant representatives of slow-growing NTM are *Mycobacterium avium complex* (MAC) and *Mycobacterium kansasii*, and fast-growing NTM are *Mycobacterium abscessus.*

Mycobacteriosis of the lungs is an infectious disease caused by NTM in patients with chronic respiratory disease and impaired immunological reactivity [5]. In addition to lung infection, NMTB can cause damage to the skin, lymph nodes, gastrointestinal tract and other organs and systems.

The prevalence of infection with different types of NTMB is unknown, since mycobacterioses are not subject to official statistical reporting, and there are no registries of patients with mycobacteriosis in the Russian Federation and other countries. According to the few published studies, the prevalence of non-tuberculous pulmonary mycobacteriosis (NTML) in different countries ranges from 3.2 to 29 per 100,000 people [1, 2]. At the same time, the 5-year and 10-year survival rates of patients with NTMB caused by MAS are 23.9 % and 46.5 %, respectively [6]. There is a trend towards an increase in the incidence of NTML worldwide, which may reflect both a true increase in the incidence of NTML due to the widespread distribution of NTML in the environment against the background of an increasing incidence of chronic bronchopulmonary diseases, the use of immunosuppressive agents, including inhaled corticosteroids, and better detection of NTML due to more advanced diagnostic tools [3]. The increase in prevalence and incidence is observed mainly due to elderly patients and women. In the United States, the overall annual incidence of NTML from 2008 to 2015 increased from 3.1 to 4.7 per 100,000 person-years, among women the increase was from 4.2 to 6.7 per 100,000 person-years [4]. For individuals aged 65 years and older, the annual incidence increased from 12.7 to 18.4 per 100,000 person-years.

The clinical symptoms of NTML is non-specific, mainly manifested by symptoms of a chronic respiratory disease, against which it occurs and depends on the type of a specific pathogen [5]. In some patients, clinical symptoms may be absent.

The absence of characteristic clinical symptoms often leads to a delayed diagnosis of NTML. According to published data, 88 % of patients were observed by a general practitioner or pulmonologist for 2.3±2.3 years before the diagnosis of NTML was confirmed for various chronic lung diseases [7]. Of these, 55.6 % of patients were registered with a phthisiatrician and received anti-tuberculosis therapy for disseminated, fibrous-cavernous, focal pulmonary tuberculosis.

Given the difficulties in diagnosis and the increase in the incidence of NTML in recent decades, we present a clinical observation of this disease caused by *Mycobacterium avium* in an 80-year-old patient with no previous chronic lung diseases.

Clinical case

Patient R., born in 1944, from St. Petersburg. Body mass index is 19.8 kg/m². Worked as an engineer, retired by age, had no occupational hazards, denies bad habits. Heredity for bronchopulmonary pathology is not burdened. History of ischemic heart disease, chronic gastroduodenitis, bilateral chronic sensorineural hearing loss on the left of grade III, on the right — grade IV.

Denies previous pneumonia, tuberculosis and contacts with tuberculosis patients.

According to the patient, in June 2022, during a routine medical examination, changes in the fluorogram of the chest organs were first detected, which she cannot report. At the time of the examination, she had no complaints. In July 2022, chest X-ray revealed infiltration on the left in C4 and a round formation of 26 * 23 mm against its background. Upon further examination in August 2022, a computed tomography (CT) scan of the chest organs revealed bronchiectasis C4, C5 on the right, bilateral bronchiolitis. During examination at the tuberculosis dispensary in St. Petersburg, no data on the tuberculosis etiology of changes in the chest organs were found. She was consulted at the oncology dispensary; no data on the oncological process in the lungs were found.

From July 2022 to August 2023, she was observed by therapists and pulmonologists in various healthcare institutions in St. Petersburg with the diagnosis: Bronchiectatic pulmonary disease, exacerbation. Bronchiolitis of both lungs. Infiltrates of both lungs. Tracheobronchial dyskinesia stage 1. Chronic bronchitis with an obstructive component, mucopurulent, sluggish exacerbation. Pneumofibrosis.

The clinical manifestations of the disease first appeared in September 2022 in the form of complaints of a rare cough with viscous sputum.

CT scans of the chest organs were performed repeatedly, where various dynamics were noted: migration of compaction areas, changes in their size and shape, changes in the shape and number of dilated bronchi. In general, the dynamics are negative, with a slow increase in the severity of bronchiectasis, the number and size of compaction areas (Table 1, Fig. 1–3).

Laboratory test results from August 2023: DNA *Mycoplasma pneumoniae, Streptococcus pyogenes, Chlamydophila pneumoniae, Mycobacterium tuberculosis complex* — not detected. Microbiological examination of sputum on dense nutrient media for Mycobacterium tuberculosis — no growth. Mycobacterium tuberculosis DNA — not detected. Received courses of antibacterial (Table 2), bronchodilator and mucolytic therapy. Inhalations of thiamphenicol acetylcysteine (fluimucil antibiotic) 500 mg per day, budesonide 2 mg per day, ambroxol 45 mg 1–2 times a day were performed, acetylcysteine 600 mg was taken orally, tiotropium bromide 5 mcg / dose, 1 dose per day was used.

Table 1

Description of the chest computed tomography results of patient R. from August 2022 to March 2024

Date	Computed tomography results
16.08.2022	Bronchiolitis in C2, C4-C5, C8 of the right lung, C3-C5, C6, C8, C10 of the left lung. Cylindrical and varicose Ц bronchiectasis in C4-C5 of the right lung. Pulmonary fibrosis of the basal regions.
02.09.2022	CT- signs of bilateral zones of diffuse infiltrative changes, peribronchial foci of the lower lobe of the right lung, bronchiectasis of the right and left lungs. In comparison to 08/16/2022, there is a regression of changes in the type of «frosted glass» in the lower lobe of the left lung, bronchiolitis in C4-C5, C6 of the right lung.
20.06.2023	Peribronchial foci and rounded infiltrates by type of consolidation in the right lung polysegmental, in the left lung in C3-C5, C6, C8, C10. In comparison to 09/02/2022 — multidirectional dynamics in the form of the appearance of infiltrates in C8 and C6 on the right, a decrease in the size of infiltrates in C3-C5, C6 on the left.
27.12.2023	CT-signs of bilateral zones of diffuse infiltrative changes with predominant lesions of the basal segments, bronchiectasis of the right and left lungs. Chronic bronchitis. In comparison to 07/20/2023, an increase in the size of previously determined infiltration sites and the appearance of multiple new foci of consolidation on both sides is noted. A slight increase in the diameter of the right and left pulmonary arteries.
25.03.2024	CT-signs of bilateral zones of diffuse infiltrative changes with predominant lesions of the basal segments, bronchiectasis of the right and left lungs. Chronic bronchitis. In comparison to 12/27/2023 — diverse dynamics in the form of the appearance of a new infiltration site in the lower lobe of the right lung and a decrease in the size of some foci.

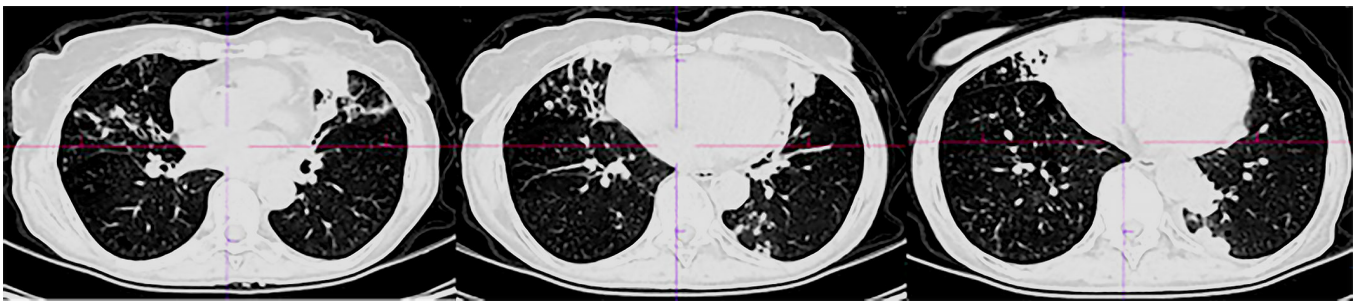

Fig.1. Computed tomography of the chest organs of patient R dated 09/02/2022

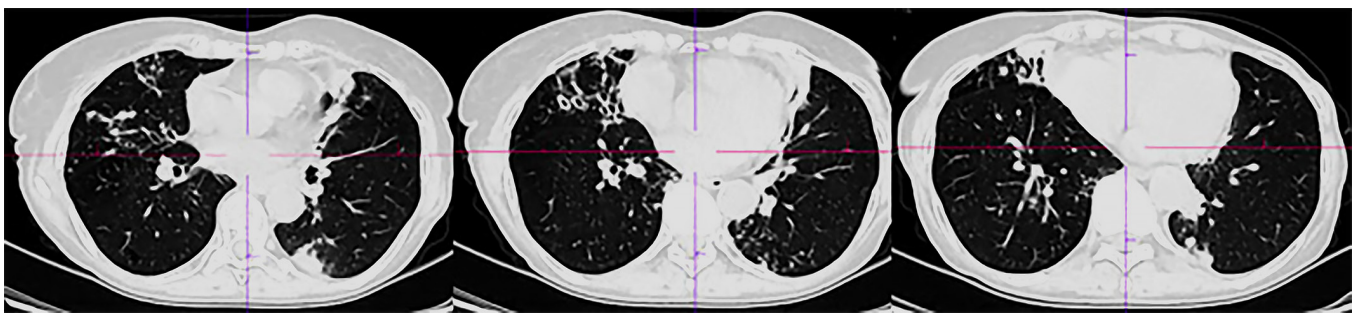

Fig.2. Computed tomography of the chest organs of patient R dated 06/20/2023

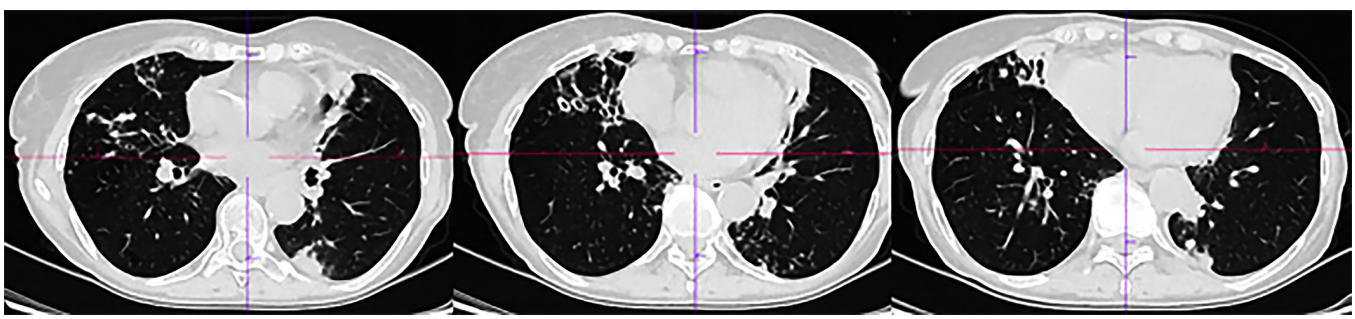

Fig.3. Computed tomography of the chest organs of patient R dated 03/25/2024

Table 2

Antibacterial therapy from July 2022 to September 2023

Date	The drug and the dosage regimen	Duration
July 2022	Clarithromycin 500 mg 2 times a day orally	for 7 days
August 2022	Ceftriaxone 1000 mg 1 time per day intramuscularly, then:	for 7 days
	Moxifloxacin 400 mg 1 time per day orally	for 14 days
August 2023	Levofloxacin 500 mg 1 time per day, then:	for 10 days
	Levofloxacin 500 mg every other day	for 30 days

During the last long course of antibacterial therapy with levofloxacin in August 2023, severe side effects were observed: diarrhea, anorexia, nausea, general weakness, hearing loss, frequent episodes of dizziness. During the period of illness, weight loss of 6 kg was noted.

In September 2023, due to the lack of a positive effect from the therapy, a bronchoscopy was performed. Endoscopic signs of bronchial mucosa atrophy, tracheobronchitis of grade 3 inflammation intensity were revealed. Bronchoalveolar lavage was performed.

In the bronchoalveolar lavage fluid, no growth of bacterial flora was detected during culture, cells with signs of atypia, fungal cells and mycelium, or DNA of *Mycobacterium tuberculosis*. DNA of NTM was detected during a qualitative study. Culture for mycobacteria: growth of NTM was obtained. Result of NTM identification: *Mycobacterium avium*. The study was conducted twice. Result of drug susceptibility testing: clarithromycin R, amikacin S, moxifloxacin R, linezolid R.

Based on the examination results, the patient was diagnosed with focal infiltrative pulmonary mycobacteriosis, *Micobacterium avium*+ with sensitivity to amikacin. Due to the presence of bilateral hearing loss of grade III–IV, the patient and relatives categorically refused treatment with amikacin due to the side ototoxic effect of the drug. The patient was prescribed azithromycin 500 mg once a day for 10 days. The course of treatment with azithromycin also did not lead to an improvement in the clinical manifestations of the disease and positive dynamics according to CT of the lungs dated 12/27/2023. In April 2024, she contacted the JSC Meditsina clinic to determine further diagnostic and treatment tactics. At the time of the visit, the patient was bothered by a slight cough with mucous sputum and general weakness. An additional examination was carried out, including esophagogastroduodenoscopy, colonoscopy, mammography, MRI of the pelvic organs, and a consultation with a gynecologist to exclude an oncological process. According to diagnostic studies, no oncological pathology was detected. Laboratory test results: CRP 7.95 mg / l; antibodies to HIV, HbsAg, anti-HCV — negative. Humoral immunity indicators: total immunoglobulins of class G, M, A (IgG, IgM, IgA) within the reference values. Cellular immunity indicators: decreased cellular immunity indicators, mainly due to regulatory T-lymphocytes (T-helper-T-suppressor system); B-lymphocytes (CD-19), insufficient activity of T-suppressors (increase in CD-4/CD-8 index to 3.48).

Given the low efficiency and presence of pronounced side effects of previous courses of antibacterial therapy, the high risk of ototoxicity and the unknown effect of amikacin, the torpid nature of the disease, the patient was advised to refrain from further antibacterial therapy. Recommendations were given for diet therapy to eliminate nutritional deficiencies, symptomatic treatment (mucolytic, bronchodilator therapy), therapy for intestinal dysbacteriosis, dynamic monitoring was recommended after 3 months. When contacting the clinic doctors after 2 months, the patient noted a significant improvement in her health, regression of cough, weakness, sweating, increased tolerance to physical activity, as well as improved appetite and normalization of stool, weight gain of 3 kg. During physical examination, there are no clinical manifestations of respiratory failure. When studying the function of external respiration, all indicators are normal.

Discussion

Researchers described a certain morphotype of a patient with NTML — relatively healthy women with a low body mass index, no fat deposits, pathology of the skeletal system in the form of scoliosis and funnel chest [5]. In the present clinical case, there are also characteristics of this morphotype — a female patient with a low body mass index, who can be considered relatively healthy for her age. The characteristic features of NTML are the absence of clinical manifestations of the disease in the patient and a long period (one year and three months) from the moment of detection of changes on the chest X-ray to the diagnosis of NTML. Tuberculosis in the patient was excluded, but testing for NTML was not performed.

The diagnosis of NTML is based on the clinical symptoms of the lung disease, the presence of focal or cavitary changes on the X-ray, detection of multifocal bronchiectasis in combination with multiple small foci on CT, and microbiological criteria: two or more positive sputum cultures for NTML from different samples or at least one positive culture for NTML of bronchoalveolar lavage fluid or bronchial washings [5]. In the presented clinical case, the diagnosis was confirmed by examining the bronchoalveolar lavage fluid, NTM DNA was detected, mycobacterium culture yielded NTM growth, and the NTM type was identified. Radiographic changes in NTML are similar to the manifestations of many chronic lung diseases. However, clinical and radiographic syndromes that are highly specific for non-tuberculous mycobacteriosis have been described. Thus, the bronchiectatic disseminated form of NTML is characterized by isolated lesions of the middle lobe and lingual segments of the lungs and a combination of multiple foci and bronchiectasis (Lady Windermere syndrome) [8].

To determine the tactics of patient management, assess the risk and benefit of the prescribed treatment, it is necessary to evaluate the patient's condition and the radiographic picture in dynamics, laboratory markers of inflammatory activity. The need for conservative etiotropic treatment in the form of prescribing multicomponent antibacterial therapy is one of the main controversial issues to which there is no unambiguous answer.

The effectiveness of etiotropic therapy for NTML associated with MAC is 68.1 % (69 % for regimens containing macrolides and 58.5 % for aminoglycoside-containing regimens) [9]. There are published data indicating that multicomponent antibacterial therapy does not prevent complications such as hemoptysis, respiratory infections, development of chronic respiratory failure and does not affect the life expectancy of patients with NTML infected with MAC [10]. Elderly and senile age, concomitant diseases, adverse reactions to the use of antibacterial drugs are factors in favor of dynamic observation [5].

In the present clinical case, in an elderly patient with minimally expressed symptoms that do not reduce her quality of life, with concomitant ischemic heart disease, without clear negative dynamics according to chest CT, the need for and benefit of antibacterial treatment are questionable.

Conclusion

It is quite difficult to diagnose NTML at the early stages of the disease due to the absence of pathognomonic symptoms, non-specificity of the X-ray picture, and difficulties in using modern molecular genetic diagnostic methods at the primary health care stage. Long-term course, frequent exacerbations, ineffective treatment of chronic respiratory diseases are signs of possible NTML. Such patients constitute a risk group for NTML, they must be examined for NTMB for early diagnosis and timely treatment.

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Нетуберкулезный микобактериоз легких

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Аннотация: В статье представлен клинический случай нетуберкулезного микобактериоза легких. Диагностика нетуберкулезного микобактериоза легких на ранних этапах заболевания затруднена в связи с отсутствием патогномоничных симптомов, неспецифичностью рентгенологической картины, а также трудностями применения современных молекулярно-генетических методов диагностики на этапе первичного звена здравоохранения. Признаками возможного присоединения нетуберкулезного микобактериоза легких являются неэффективность лечения хронических заболеваний легких, их длительное течение, частые обострения. Пациенты с этими признаками составляют группу риска нетуберкулезного микобактериоза и нуждаются в обследовании на наличие нетуберкулезных микобактерий.

Ключевые слова: нетуберкулезный микобактериоз легких, диагностика, нетуберкулезные микобактерии, компьютерная томография, клинический случай

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