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A clinical case of central cancer of the lung and infiltrative tuberculosis

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Abstract

The scientific challenge of combining the tuberculosis process and lung cancer has not been fully disclosed in modern literature. This primarily involves the low incidence of these two pathologies at the same time. This may contribute to difficulties in the qualitative and timely diagnosis of these diseases. Tuberculosis "hides" the radiological manifestations of a malignant tumor for a long time that contributing to its progression and the development of high mortality among patients. Lung cancer facilitates hemato- and lymphogenous spread of a specific pathogen. As an example, a clinical case of simultaneous occurrence of pulmonary tuberculosis and lung cancer which was observed in the patient admitted to the Department for patients with respiratory tuberculosis of Nizhny Novgorod regional clinical tuberculosis dispensary, was presented. We concluded that compliance with the algorithm of the mandatory diagnostic minimum when patients admitted to the general healthcare network, as well as compliance with the rules for population screening, especially among people over 45, will minimize the risks of delayed diagnosis in case of coexistence of respiratory tuberculosis and lung cancer.

Keywords: tuberculosis, lung cancer, combination, diagnosis.

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According to the report of the World Health Organization (WHO) [1], the incidence of tuberculosis worldwide was approximately 10 million persons in 2018, including 57% of men, 32% of women, and 11% of children under 15 years of age. The number of deaths from this life-threatening disease among HIV-negative patients amounted to 1.2 million cases, while among HIV-positive patients, it was 251 thousand cases.

Over 80% of all tuberculosis cases occur in 30 countries from the WHO list with a high burden index of tuberculosis, and they are most often registered in India, China, Indonesia, and the Philippines (WHO, 2019). Of the total number of tuberculosis cases worldwide, the countries of America and Europe account for only 3 and 6% of tuberculosis incidence, respectively (WHO, 2018).

Drug-resistant tuberculosis remains a serious problem in the Russian and other international healthcare systems [2,3]. According to WHO (2019), in 2018, resistance to rifampicin (a first-line drug) was detected in half a million people, who were diagnosed with multidrug-resistant tuberculosis in 78% of cases (MDR-tuberculosis). Half of all the cases of *M. tuberculosis* drug resistance to rifampicin and MDR-tuberculosis are registered in three countries, namely India (27%), China (14%), and Russia (9%).

Lung cancer is becoming one of the main causes of mortality compared to all other cancers among the population of many countries [4]. According to I. Roca et al. [5] and J. Furin et al. [6], in the absence of adequate algorithms for the elimination of drug-resistant tuberculosis, mortality from this disease by 2050 will be comparable with that of tumor processes.

According to N.P. Karushchak [7] and V.K. Polyansky [8], tuberculosis and lung cancer can be localized simultaneously in a single set of tissues or manifest themselves as two separate diseases.

Lung cancer and tuberculosis have a lot in common. They are characterized by a lesion of the lung parenchyma, a high prevalence, and a frequently subtle and paucisymptomatic course [9], as well as the occurrence of systemic chronic inflammation with the presence of profound changes in the immune response [10].

As a rule, a progressive and long-term inflammatory response in pulmonary tuberculosis causes

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the emergence of precancerous morphological changes in the epithelium and mucous membranes [11], which creates a favorable background for the development of a malignant tumor.

From the perspective of clinical and morphological classification [12], the following types of tuberculosis and lung cancer combinations are usually distinguished:

1) a tumor may form in the area of scar tissue formation as the inflammatory reaction caused by the causative agent of tuberculosis decreases;

2) a tumor may appear as an independent disease, but cause the reactivation of a previous tuberculosis process (relapse);

3) gross disorders of the tissue architectonics in the cavern can become the basis for the initiation of a tumor disease;

4) in case of deep immunosuppression of the macroorganism, inherent in lung cancer, tuberculosis can be diagnosed as an opportunistic infection.

For illustrative purposes, we present a clinical case of the simultaneous development of tuberculosis and lung cancer, which we monitored in the Nizhny Novgorod Regional Clinical Antituberculosis Dispensary (NNRCAD) in the department for patients with respiratory tuberculosis. Written informed consent was obtained from the patient for the publication of the data.

Patient B., 41 years old, was admitted on 06/06/2019 to the NNRCAD in the department for patients with respiratory tuberculosis with suspected pulmonary tuberculosis combined with cancer of the same localization.

The medical history shows that the patient's illness started since January 2019, when he developed an unproductive cough and atony. He visited the clinic of a primary healthcare facility only on 05/27/2019 with complaints of progressive atony, constant chills, and fever at 39°C. On the plain chest X-ray of 05/27/2019, an inhomogeneous shadow was revealed in the upper and middle fields of the right lung, merging with the root. After examination and consultation with a therapist, he was sent for additional examination at the regional antituberculosis dispensary. In order to rule out a nonspecific pneumonia, he received a broad-spectrum antibiotic ceftriaxone for 7 days, which provided no clinical improvement.

On June 1, 2019, the patient underwent a multispiral computed tomography of the chest organs. Computed tomographic signs of infiltrative tuberculosis of the right lung in the disintegration phase was concluded (Fig. 1), as well as mediastinal lymphadenopathy (Fig. 2) with questionable genesis, questionable bronchial tuberculosis, and a questionable combination with lung cancer.

On 06/03/2019, the patient had his sputum tested three times for microscopy with Ziehl-Neelsen staining. The microscopy results for acid-fast mycobacteria was positive (1+). In the sputum sample collected on 06/04/2019, *M. tuberculosis* deoxyribonucleic acid was detected by the polymerase chain reaction method, with confirmed resistance to isoniazid and rifampicin. An extended drug susceptibility test, obtained from the analysis of the resulting culture of the pathogen on a solid nutrient medium, identified *M. tuberculosis* resistance to two additional antituberculosis antibiotics, namely ethambutol and streptomycin.

Based on the results of the laboratory and instrumental research methods, on 06/06/2019, the Central Medical Control Commission established a diagnosis in accordance with the existing classification, embodied in the order of the Ministry of Health of Russia No. 109 dated March 21, 2003, of A15.0. Infiltrative tuberculosis of the right lung in the phase of destruction, *Mycobacterium tuberculosis* (+), regular medical check-up group 1A, and multiple drug resistance (resistance to H, R, E, S). Questionable lymphadenopathy on the right, questionable bronchial tuberculosis, and questionable lung cancer.

Treatment was started according to the chemotherapy regimen IV, with an intensive phase of up to 240 doses, with six antituberculosis drugs, namely capreomycin 1000 mg, levofloxacin 750 mg, pyrazinamide 1500 mg, ethionamide 750 mg, cycloserine 750 mg, and paraaminosalicylic acid 8000 mg, according to the clinical guidelines for respiratory organ tuberculosis in adults (2020).

On 06/18/2019, the patient underwent diagnostic tracheobronchoscopy under local anesthesia with lidocaine, which revealed the changes, namely a questionable neoplasm of the 6th segmental bronchus on the right, bronchoadenopathy of the bifurcation, tracheobronchial and bronchopulmonary lymph nodes on the right, bronchonodular fistula of the right interstitial bronchus; infiltrative tuberculosis of the 3rd and 6th segmental bronchi and their subsegments, and diffuse catarrhal bronchitis of the inflammation intensity degree III.

A catheter biopsy was obtained from the 6th segmental bronchus on the right for cytological and histological examination. Based on the cytology materials, an accumulation of bronchial epithelium with signs of hyperplasia in some of the cells, moderate neutrophilic infiltration, and fibrin strands were found. Histological examination revealed fragments of fibrous tissue covered partially with bronchial epithelium, and necrotic masses infiltrated by segmented leukocytes with the inclusion of cells with hyperchromic deformed nuclei.

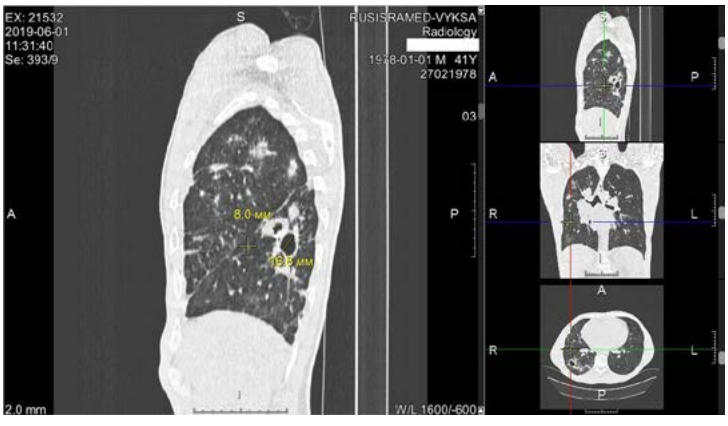

Fig. 1. Multispiral computed tomography of the chest organs. Images of the patient from 06/01/2019: destruction of the pulmonary parenchyma in the lower lobe of the right lung.

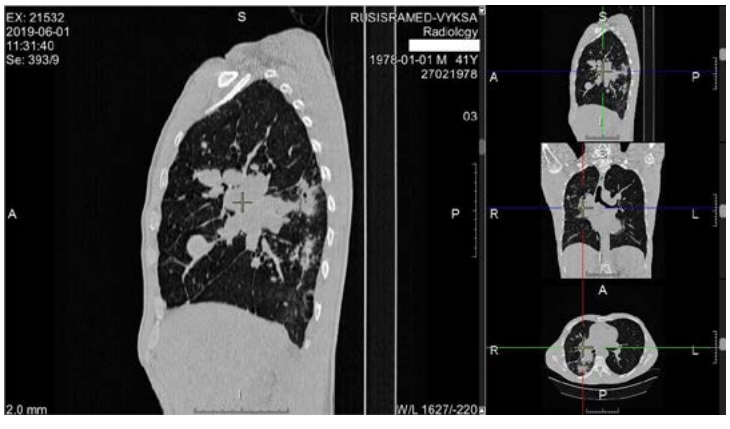

Fig. 2. Multispiral computed tomography of the chest organs. Images of the patient from 06/01/2019: mediastinal lymphadenopathy.

On June 27, 2019, the patient noted a deterioration in the symptoms such as cardiac discomfort. The electrocardiogram (ECG) dated 06/27/2019 showed signs of atrial fibrillation.

Digital fluorogram of the chest organs dated 06/27/2019 revealed focal infiltrates and foci of various sizes with a confluent nature and indistinct contours with decay in some of them in the right lung, and maximally in the root zone. The left lung was clean. The right root was dilated due to enlarged lymph nodes of all the groups, with compression of the bronchi. The heart was expanded in diameter, and displaced to the right. There was a small amount of fluid in the lateral sinus on the right. Compared to the X-ray of the chest organs from 05/27/2019, the focal infiltrative changes in the right lung increased, and the fluid appeared in the pleural cavity on the right. Radiographically, the progression of a specific process in the right lung, complicated by lymphadenitis and exudative pleurisy was registered.

After some time, the patient was transferred to the intensive care unit, where he stayed under supervision from 06/27/2019 to 07/05/2019. The ECG of 06/28/2019 showed a sinus rhythm, tachycardia with a heart rate (HR) of 97 beats per minute; pronounced changes in the myocardium of the apical region, lateral, and lower walls; and disorder of repolarization.

The chest X-ray from 07/01/2019, in comparison with the digital fluoroscopic image from 06/27/2019, revealed an increase in the amount of fluid in the pleural cavity on the right, and an increase in the size of the destruction cavities of the foci in the right lung. There were no changes on the left. Further progression was noted.

ECG from 07/01/2019 showed sinus rhythm with a HR of 75 beats per minute, and pronounced diffuse disorders of repolarization persist.

On 07/03/2019, the patient underwent repeated bronchoscopy under general anesthesia. The conclusion of infiltrative tuberculosis of the 6th segmental bronchus, in combination with endobronchial cancer of the right intermediate bronchus was established. There were metastases in the intrathoracic lymph nodes of all the groups with compression of all the bronchi on the right to a stenosis of degree II–III. Tuberculosis of the intrathoracic lymph nodes was questionable.

A forceps biopsy was performed from the right intermediate bronchus. The histological examination of the material from the right intermediate bronchus revealed the tissue represented by cells with nuclei of oval, elongated, and irregular shape,

forming bundle structures. To rule out connective tissue neoplasms (Kaposi sarcoma), an immunohistochemical study is required.

The immunohistochemical study dated July 16, 2019 enabled to suspect the immunophenotype of primary pulmonary myxoid sarcoma (code 8842/3 according to ICD-O). To confirm the diagnosis, cytogenetic detection of EWSR-1 and CREB-1 gene rearrangements was recommended.

On July 24, 2019, the patient's health repeatedly deteriorated, as severe shortness of breath and an increase in facial edema occurred. The patient was urgently transferred to the intensive care unit, where he stayed until 07/30/2019. The ECG of 07/25/2019 showed persisting pronounced disorders of repolarization with a HR of 150–176 per minute. Ultrasound examination of the chest cavity organs dated 07/31/2019 revealed up to 500 cm^3 of organizing fluid located in the left pleural cavity, while in the right pleural cavity, there were 100–200 cm^3 of organizing fluid.

When comparing X-rays of the chest organs dated 08/01/2019 and 07/01/2019, further negative dynamics were determined in the form of an increase in the shadow of the right lung with a decrease in its volume, and maintaining airiness only in the upper sections, with signs of mediastinal displacement to the right.

On July 31, 2019, the patient was consulted by an oncologist. Central cancer of the right lung with metastases to the lymph nodes of the mediastinum with T2aN2–3M0 was concluded.

As a result of a comprehensive examination and treatment, the final diagnosis was established to the patient on C34.3, central cancer of the right lung with metastases to the lymph nodes of the mediastinum and T2aN2–3M0; A15.0, infiltrative tuberculosis of the right lung, decay phase; infiltrative tuberculosis of the segmental bronchi 3 and 6 and their subsegmental sections on the right, MBT (+), regular medical check-up group 1A, MDR (resistance to H, R, E, S).

The clinical case presented draws the clinicians' attention to a question difficult to resolve, namely how to identify and confirm the diagnosis of tuberculosis and lung cancer in a timely manner? The use in routine practice of medical specialists of various profiles of the current regulatory and legal framework, joint methodological work with antituberculosis and oncological dispensaries, and telemedicine communications will enable to avoid late diagnosis of these types of pathology which are sometimes dangerous and unpredictable in their development, which will lead to a significant decrease in the number of patients in an incurable status.

Authors' contributions. A.G.N. performed analysis and adaptation of the work material; A.V.P. was the work manager; A.Yu.G., N.A.N., K.V.M., and O.E.S. collected the material for work.

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REFERENCES

1. *Global tuberculosis report 2019*. Geneva: World Health Organization. 2019; 283 p.

2. Ergeshov A.E. Tuberculosis in the Russian Federation: situation, challenges and perspectives *Vestnik RAMN*. 2018; 73 (5): 330–337. (In Russ.) DOI: 10.15690/vramn1023.

3. Nechaeva O.B. Socially important infectious diseases posing a biological threat to the population of Russia. *Tuberculosis and lung diseases.* 2019; 97 (11): 7–17. (In Russ.) DOI: 10.21292/2075-1230-2019-97-11-7-17.

4. Silva D.R., Valentini D.F., Borges de Almeida C.P., Dalcin P. de Tarso R. Pulmonary tuberculosis and lung cancer: simultaneous and sequential occurrence. *J. Bras. Pneumol*. 2013; 39 (4): 484–489. DOI: 10.1590/S1806-37132013000400013.

5. Roca I., Akova M., Baquero F. et al. The goal threat of antimicrobial resistance: science for intervention. *New Microbes New Infect*. 2015; 6: 22–29. DOI: 10.1016/j.nmni.2015.02.007.

6. Furin J., Brigden G., Lessem E. et al. Global progress and challenges in implementing new medications for treating multidrug-resistant tuberculosis. *Emerg. Infect. Dis*. 2016; 22 (3): e151430. DOI: 10.3201/eid2203.151430.

7. Karashchuk N.P., Kiseleva M.V. Cancer and tuberculosis of the lung. *Nauchnyy meditsinskiy vestnik Yugry*. 2014; (1–2): 71–73. (In Russ.)

8. Polyanskiy V.K., Savitskiy G.G., Lyatoshinskiy A.V. Lung cancer in patients with tuberculosis. *Tuberkulez i sotsial'no-znachimye zabolevaniya*. 2015; (3): 81–82. (In Russ.)

9. Belova O.S., Komarov I.G. Differential diagnosis of lung cancer and tuberculosis: review. *Sovremennaya onkologiya*. 2018; (3): 56–61. (In Russ.)

10. Cuéllar L., Carstaneda A.C., Rojas K. et al. Características clínicas y toxicidad del tratamiento de tuberculosis enpacientes con cancer. *Rev. Peru Med. Exp. Salud Publica*. 2015; 32: 272–277.

11. Plotnikov V.P., Perminova I.V., Chernykh E.E., Laptev S.P. A case of concurrent lung cancer and fibrous-cavernous pulmonary tuberculosis. *Tuberculosis and lung diseases*. 2019; 97 (1): 35–40. (In Russ.) DOI: 10.21292/2075-1230-2019-97-1-35-40.

12. Cukic V. The association between lung carcinoma and tuberculosis. *Med. Arch*. 2017; 73 (3): 212–214. DOI: 10.5455/medarh.2017.71.212-214.