

Modern diagnosis of pulmonary tuberculosis

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Abstract: In view of the need to maintain a high index of suspicion for tuberculosis (TB) in elderly patients and in patients with HIV infection, I would like to add to the reservations expressed about the guidelines for the management of adults lower respiratory tract infections. In modern conditions, when highly informative research methods have become available, the difficulties of diagnosing TL have not decreased at all. Now it is impossible to focus on the ideas of the recent past, which attribute only the discrepancy between clinical and pathomorphological diagnoses to errors in the diagnosis of tuberculosis. A serious omission is the late detection of TL, when the process has already acquired an irreversible form, and the patient has managed to infect many of the people around him. The role of such an exogenous infection in the development of tuberculosis in adults has been emphasized by recent studies, which have forced a revision of established ideas about the pathogenesis of tuberculosis.

Key words: modern diagnosis, tuberculosis, pathomorphological diagnosis.

Introduction. In the former context, “failure to respond to antimicrobial agents for common bacterial pneumonias should prompt concern that TB is a possible cause”, as was the case in a 25-year-old febrile patient who was referred for presumed pneumonia unresponsive to antibiotics, and in whom pulmonary TB proved to be the underlying cause of right lower lobe consolidation [3]. A high index of suspicion for *M. tuberculosis* as an alternative diagnosis should also prevail in the elderly [4], given the fact that there is an age-related increase in the prevalence of *M. tuberculosis*-related lower-lobe disease, and in view of the fact that “frequency of cavitation in the TB group showed a negative correlation with age” in a study [4]. The problem of correct and timely diagnosis of tuberculosis has become particularly relevant today due to the ongoing epidemic of this infection and significant changes in its clinical manifestations. And to the greatest extent this applies to pulmonary tuberculosis (TL), since it is patients with this localization of the process that occupy the main place in the entire chain of transmission and spread of the disease, which continues to be in the first place in importance among all infectious pathology. In modern conditions, when highly informative research methods have become available, the difficulties of diagnosing TL have not decreased at all. Now it is impossible to focus on the ideas of the recent past [1], which attribute only the discrepancy between clinical and pathomorphological diagnoses to errors in the diagnosis of tuberculosis. A serious omission is the late detection of TL, when the process has already acquired an irreversible form, and the patient has managed to infect many of the people around him. The role of such an exogenous infection in the development of tuberculosis in adults has been emphasized by recent studies, which have forced a revision of established ideas about the pathogenesis of tuberculosis. It has been established that, along with endogenous reactivation of latent tuberculosis infection (present in the absolute majority of the adult population of our country), exogenous infection with tuberculosis pathogens new to the patient is important [2]. These studies serve as additional evidence of the importance of the earliest possible diagnosis of TL. Methods of diagnosis of TL Instrumental and laboratory methods of diagnosis of TL have been

significantly improved recently, pushing clinical methods (anamnesis, physical examination) into the background as non-specific. However, underestimation of the latter serves as one of the prerequisites for diagnostic errors. At the same time, the most advanced of modern research methods are not always absolutely specific and accurate.

Method and material. Microbiological and histological methods remain the most informative (evidentiary) methods confirming the tuberculous nature of the process. Microbiological methods Bacterioscopy of stained smears of pathological material and sowing it on nutrient media are the most convincing and widespread methods of microbiological research.

Results. The advantages of direct bacterioscopy, developed in the time of R. Koch, are simplicity, accessibility and speed. However, this method is not sensitive enough, since even with careful implementation it mainly detects patients with massive bacterial excretion. Sputum culture on nutrient media is much more sensitive, but a long delay in its result (up to 2.5 months) significantly limits the possibility of early diagnosis. Accelerated methods of cultivation of mycobacteria (for example, automated growth accounting systems such as BACTEC) have not yet found mass application. The development of molecular biology has made it possible to detect mycobacterium DNA in biological material using polymerase chain reaction (PCR). The PCR method is many times more sensitive than seeding, but it is less informative due to frequent false positive responses - the detection of fragments of mycobacterium DNA in practically healthy individuals who are only infected with tuberculosis (latent tuberculosis infection). Modern and very numerous methods of molecular genetic studies make it possible to accurately identify individual strains of mycobacterium tuberculosis (MBT), quickly establish their drug sensitivity and trace the pathways of the pathogen transfer from a specific source of infection to others. However, in the differential diagnosis of tuberculosis with nonspecific pathology, the role of these methods is very limited. When evaluating the results of microbiological studies, one should keep in mind the very rare possibility of an "exit phenomenon". This phenomenon has to be encountered in cases when an old calcified tuberculous focus falls into the zone of destruction of lung tissue with pneumonia or lung cancer. MBT in this case, as a rule, are detected only during bacterioscopy and do not grow on nutrient media. The anamnesis of the disease and the usual methods of clinical examination make it possible to differentiate such cases from active TL. Histological method The histological method makes it possible to detect granulation tissue and caseous necrosis specific for tuberculosis in the biopsy material. This invasive method should be used immediately in the most difficult to diagnose cases. The informative value of histological examination is limited by the relative specificity of tuberculous granulations. Similar changes are noted, for example, in sarcoidosis and some rarer granulomatous processes. In addition, we have to take into account that in patients with congenital or acquired immunodeficiency (AIDS, hemoblastosis, immunosuppressive and cytostatic therapy), the formation of tuberculous granulations is disrupted, or they do not form at all. X-ray methods X-ray examination of the chest organs remains the primary method for diagnosing or at least suspecting TL. Its informative value has increased many times due to the widespread introduction of computed tomography (CT), replacing traditional X-ray methods. However, recently TL is increasingly manifested by an atypical X-ray picture. In addition, even with typical scialogical symptoms, the radiological diagnosis of this disease requires confirmation by clinical and laboratory methods. One of the old clinical methods is the method of establishing the diagnosis of TL based on the results of trial treatment (diagnosis ex juvantibus). At the same time, the doctor focuses on the dynamics of the clinical, laboratory and radiological picture. Thus, the diagnosis of TL requires a comprehensive assessment of the results of all available research methods. Focusing on the only, even the most evidence-based sign (for example, bacterial excretion), which diverges from the data of other studies, can cause serious diagnostic errors. Differential diagnosis of

individual forms of TL. The difficulties of differential diagnosis of TL are due to the variety and continuous pathomorphosis of its manifestations. In practical terms, among all this diversity, three most typical situations can be distinguished when differential diagnosis of TL with a different pulmonary pathology is required first of all. These are, firstly, infiltrative processes, in many respects resembling nonspecific pneumonia, secondly, disseminated lesions and, thirdly, rounded, more or less massive foci, often indistinguishable from tumors. Infiltrative TL. Infiltrative forms are the most frequent manifestations of TL and differ in diversity. Even in the periods of time that were successful for this disease, it was the infiltrative processes that were detected in more than half of all first-time cases. The difficulties of differential diagnosis are due to the fact that in its morphological essence, infiltrative TL is pneumonia with its characteristic predominance of exudative and necrotic components of the inflammatory reaction, but caused by MBT. Like nonspecific pneumonia, infiltrative forms of TL vary in prevalence (from bronchlobular forms to lobitis), often develop acutely and subacutely (for example, caseous pneumonia) and affect the basal parts of the lungs (especially in patients with diabetes mellitus and AIDS). Anamnesis of the disease makes it possible to establish important guidelines even in the most difficult to diagnose atypically occurring cases of infiltrative TL. Attention should be paid to contact with tuberculosis patients and risk factors (hyperinsolation). It is necessary to take into account the nature and severity of the concomitant pathology and the results of previous therapy (weak effect of broad-spectrum antibiotics, the appointment of glucocorticosteroids and physiotherapy). The old clinical rule, according to which with nonspecific pneumonia “much is heard, but little is seen,” and with tuberculosis, on the contrary, retains its significance in ordinary cases, but not with acutely progressive processes such as caseous pneumonia. The detection on radiographs of post-tuberculosis changes in the form of calcified foci or intra-thoracic lymph nodes, destructive changes characteristic of tuberculosis and foci of dropout is an important diagnostic sign of a specific process. Computed tomography is the best way to detect such changes. Finally, the detection of MBT, usually present in the sputum of patients, confirms the diagnosis of infiltrative TL. Targeted and repeated sputum examination on MBT should be carried out in all patients with acute and chronic pulmonary pathology. As a clinical example, we give the following observation. Patient U., 41 years old, became acutely ill shortly after excessive tanning. Treatment with broad-spectrum antibiotics for suspected pneumonia had no effect. CT showed extensive infiltrative changes in the lower lobe of the right lung, cavities formed, a moderate number of foci of contamination in the surrounding lung tissue and in the lower lobe on the left (Fig. 1). An abundant amount of MBT in sputum. Diagnosis: infiltrative tuberculosis of the lower lobe of the right lung, phase of decay and contamination, MBT+. Intensive anti-tuberculosis therapy contributed to the clinical cure. Disseminated TL. Disseminated forms of tuberculosis are incomparably less common than infiltrative ones – even in the pre-antibiotic era, they were observed in only 8-10% of all tuberculosis patients. But despite the rarity, most diagnostic errors are associated with them. Indeed, disseminated tuberculosis accounts for more than 80% of all cases of tuberculosis not diagnosed during life. The reasons for frequent errors in disseminated tuberculosis should be considered, firstly, the variety of clinical manifestations, secondly, the low information content of bacteriological research methods, and, thirdly, the delayed development of characteristic radiological changes. Sputum itself and MBT in it appear only in the late stages of the disease, when rapidly disintegrating infiltrates with thin-walled cavities appear against the background of a very long dissemination. In the earlier period of the disease, MBT is much more often detected by blood culture. Radiological changes in the lungs have to be differentiated with many (more than 150) other diseases manifested by pulmonary dissemination. Therefore, histological examination occupies a particularly important place among the methods of diagnosis of disseminated

tuberculosis, the material for which must be obtained immediately, including using very invasive methods – up to an open lung biopsy. One of the most insidious features of disseminated tuberculosis is the variety of clinical manifestations. More than 100 years ago, cases of so-called acute tuberculous sepsis (or "typhobacillosis Landuzi") were described. The clinical picture of this extremely rare disease resembles a severe form of typhoid fever, accompanied by severe intoxication, massive bacteremia and the absence of histological changes in tissues specific to tuberculosis. The disease usually ends fatally. Only in recent years have some casuistic observations been published, when patients were saved thanks to anti-tuberculosis therapy initiated for the diagnosis of *ex juvantibus* after the suspicion of other infections was rejected. The tuberculous etiology of the process in such patients was confirmed after their clinical recovery on the basis of positive results of blood culture. In everyday practice, we have to deal with other forms of disseminated tuberculosis, and above all with the increasingly common miliary tuberculosis, characterized by the severity and severity of the course. The course of other forms of disseminated tuberculosis can be subacute and even chronic, accompanied by limited or very widespread lung damage. A common feature of all such processes is the absence of a visible source of dispersion. X-ray examination remains the main method of detecting these forms of the disease, and the lack of specificity of its results is largely compensated by their comprehensive assessment in comparison with clinical and laboratory data. Clinical example: patient L., age – 31 years. At preschool age, she suffered tuberculosis of the thoracic spine. During the last 1.5 months, at first gradually, and then rapidly, the symptoms of general intoxication increased, the temperature rose to febrile, shortness of breath developed. A meager amount of MBT in saliva and sputum. Diagnosis: disseminated pulmonary tuberculosis, infiltration phase, MBT+. Antitubercular therapy gave a pronounced effect. Differential diagnosis of disseminated processes is described in detail in very extensive manuals, it cannot and should not be the subject of a short article. We emphasize only the importance of the earliest possible diagnosis of disseminated tuberculosis, since at any stage of its course, the development of tuberculous meningitis is possible – the most frequent and severe complication of this disease. Pulmonary tuberculomas Special difficulties arise in the differential diagnosis of tuberculosis – rounded foci in the lungs. Pulmonary tuberculomas occupy a modest place among other clinical forms of tuberculosis – 2-4.5%. The difficulty of clarifying their nature is due to the scarcity, and often the absence of clinical signs of the tuberculosis process. Anamnesis, physical examination, even a purposeful search for MBT in sputum and in the flushing waters of the bronchi in such patients most often give negative results. An important role in the diagnosis is played by the X-ray method, and especially CT. Signs such as the upper lobe localization of foci, the presence of calcified inclusions in them, focal and cicatricial changes in adjacent areas of the lung, as well as indications of tuberculosis in the anamnesis – all this inclines the diagnosis in favor of TL. Nevertheless, even the totality of these symptoms does not allow us to exclude peripheral lung cancer, with which a differential diagnosis is most often necessary. Cases of a combination of tuberculosis and lung cancer have become very frequent nowadays, when the prevalence of both these diseases has increased significantly. The possibilities of *ex juvantibus* diagnosis in such patients are very limited, since postponement of surgical intervention can have fatal consequences for the patient. That is why there is an urgent need to obtain material from pathological foci for histological (or at least cytological) examination. The methods of transbronchial and transthoracic puncture used for this purpose are increasingly giving way to limited thoracotomy. Such an operation is not so dangerous compared to the delay in diagnosis. Along with clarifying the diagnosis, in many cases it turns out to be a radical method of treatment, since it removes tuberculoma – the main focus of tuberculosis lesion.

Conclusion. Concluding a brief description of the problems of differential diagnosis of TL, as well

as ways to overcome these problems, it is necessary to note their continuing relevance. The increasing difficulties of differential diagnosis of pulmonary tuberculosis are associated not so much with increased requirements for its accuracy, but also with constant changes in the pathogenesis, clinical and radiological symptoms of this disease, especially in patients with concomitant pathology that significantly changes the classic manifestations of tuberculosis. In recent years, there has been a noticeable progress in the methods of instrumental research. This progress, as well as achievements in the field of tuberculosis immunology, molecular biology and genetics of tuberculosis mycobacteria [7], allow us to hope that their widespread introduction into practice will increase the effectiveness of differential diagnosis of tuberculosis.

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