Modern View about Diagnosis of Spinal Tuberculosis

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A B S T R A C T

Tuberculosis (from the Latin tuberculum - tubercle) is an infectious disease caused by Mycobacterium tuberculosis [1, 16]. The problem of tuberculosis remains relevant, since most often (62.2%) people of working age from 18 to 44 years old suffer from tuberculosis [6, 132, 150]. For every 100 newly diagnosed patients, there are 6 patients with HIV infection [74]. Mortality among such patients is 2 times higher than mortality from all other causes among patients with active tuberculosis and averages 22.6% [46, 62]. Damage to the spine due to tuberculosis has been known since ancient times; mention of this disease is found in Hippocrates and Galen [1, 94, 135]. According to Galinskaya L.A. et al . (2013), numerous historical documents and medical research materials indicate the widespread distribution of this form of osteoarticular tuberculosis in the distant past. According to the observations of specialists, the first place in terms of localization of the lesion is the thoracic (60%) and the second is the lumbar (30%) spine. The cervical (5%) and sacral (5%) parts of the spine are affected to a lesser extent [9, 33, 46, 156]. It is worth noting that in adults, double and triple localization of lesions were previously rare; now their frequency is about 10%. The number of affected vertebral bodies varies widely. Damage to 2-3 vertebral bodies in newly diagnosed patients is most often detected (in 65% of cases), destruction of one vertebral body is detected in 1-3% of cases [1, 108, 99]. Many authors are of the opinion that the diagnosis of "tuberculous spondylitis" is based, first of all, on establishing the fact of contact with a patient with tuberculosis, the presence of trauma and other predisposing factors [6, 107]. However, the leading role in the diagnosis of bone destructive changes in tuberculous lesions of the spine is played by radiation examination methods [81, 92]

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Epidemiology. Tuberculosis (from the Latin tuberculum - tubercle) is an infectious disease caused by Mycobacterium tuberculosis [1, 16]. The problem of tuberculosis remains relevant, since most often (62.2%) people of working age from 18 to 44 years old suffer from tuberculosis [6, 132, 150]. Over the past decade, the Russian Federation has seen an improvement in epidemiological indicators for tuberculosis [38, 54]. In 2008, the incidence decreased by 26.0% (85.1 per 100,000 population). This trend continued in subsequent years; in 2013, compared to 2012, the decrease was 7.5% (from 68.1 to 63.0 per 100,000 population) [36]. But the highest rates of tuberculosis incidence are still recorded in three federal districts of the Russian Federation - in the Ural, Siberian and Far Eastern Federal Districts [38]. The population mortality rate from tuberculosis decreased by an average of 43.4% [58]. In the general structure of tuberculosis incidence, extrapulmonary forms range from 4 to 17% [46]. In recent years, due to an increase in the number of cases of tuberculosis in combination with HIV infection, a significantly more severe condition of hospitalized patients with extrapulmonary tuberculosis has been noted [3, 50, 59, 122, 133, 149]. For every 100 newly diagnosed patients, there are 6 patients with HIV infection [74]. Mortality among such patients is 2 times higher than mortality from all other causes among patients with active tuberculosis and averages 22.6% [46, 62]. In addition, there is currently an increase in multidrug-resistant 15 forms of pulmonary and extrapulmonary tuberculosis [15, 88]. Observations by N.A. Sovetova et al. (2014) show that primary drug resistance is found in every third patient with tuberculosis. This is due to the fact that primary infection or superinfection can be carried out by strains of Mycobacterium tuberculosis that are resistant to the main anti-tuberculosis drugs [51]. As a result of the above features of the modern tuberculosis process, the clinical picture has become more diverse, the duration of the disease has increased and the prognosis has changed [15]. The most typical localization of extrapulmonary tuberculosis is the osteoarticular form, which accounts for 10-26% of the total number of patients [6, 103]. Various parts of the skeleton are affected, but in 50-60% it is the spine [16, 32, 64, and 106].

Etiology and pathogenesis of tuberculous spondylitis. Damage to the spine due to tuberculosis has been known since ancient times; mention of this disease is found in Hippocrates and Galen [1, 94, and 135]. According to Galinskaya L.A. et al. (2013), numerous historical documents and medical research materials indicate the widespread distribution of this form of osteoarticular tuberculosis in the distant past. This hypothesis is confirmed by tuberculous changes discovered during excavations in the spine of Stone Age people. When examining burials of the Neolithic period in France, traces of bone tuberculosis pathology were identified in 3.5% of finds. Russian scientists Rokhlin D.G. and Maykova -Stroganova V.S. (1957) describe cases of spinal tuberculosis in adults, the skeletons of which were found on the territory of Russia in burials of the last centuries BC and the beginning of our era [6]. In 1779, the first detailed description of its main symptoms (hunchback and associated paralysis) was given by the English surgeon Perswell Pottom , by whose name the disease is called in English literature (Pott`s death). N.I. was also interested in tuberculous lesions of the spine and septic abscesses associated with them. Pirogov, who left behind the preparations he made, which are stored in the museum of the Department of Pathological Anatomy of the Military Medical Academy named after S.M. Kirov. N.I. Pirogov in the “Annals of the Surgical Clinic in Derp” (1837 and 1839) gives a description of clinical and especially pathological changes in spinal tuberculosis, the ways of spread of edematous abscesses, and changes in soft tissues along the abscess [14]. In 1848, Voskresensky A.E. in the monograph “Tuberculosis Disease of the Spinal Column” described in detail the clinical symptom complex of tuberculous spondylitis [1, 136, and 141]. Spinal tuberculosis, or tuberculous spondylitis, is an infectious disease caused by Micobacterium tuberculosis. Spinal tuberculosis is characterized by the formation of a specific granuloma and progressive bone destruction, which leads to pronounced organic and functional disorders of the affected part of the skeleton [50, 137]. According to the observations of specialists, the first place in terms of localization of the lesion is the thoracic (60%) and the second is the lumbar (30%) spine. The cervical (5%) and sacral (5%) parts of the spine are affected to a lesser extent [9, 33, 46, and 156]. It is worth noting that in adults, double and triple localization of lesions were previously rare; now their frequency is about 10%. The number of affected vertebral bodies varies widely. Damage to 2-3 vertebral bodies in newly diagnosed patients is most often detected (in 65% of cases), destruction of one vertebral body is detected in 1-3% of cases [1, 108, and 99]. As a rule, extensive destruction is characteristic of the thoracic spine. The incidence of tuberculous 17 spondylitis among men is higher than among women [67, 75]. Tuberculous inflammation develops in the vertebral bodies. The initial lesions arise in the marginal parts of the vertebral bodies near the intervertebral discs. It is believed that the tuberculosis process in bone structures develops from the primary glandular complex, since in the lymph nodes, despite the identity of the changes in them and the pulmonary focus, the process is delayed for a longer time [8]. Dyachenko V.A. (1958) emphasizes that in the bone, for the development of the tuberculosis process, a number of predisposing factors are required: firstly, the presence of infection, secondly, its penetration into the bone, thirdly, the presence of appropriate “local and general soil” in the bone and the body [8]. By “local soil” the authors mean the characteristics of the bone marrow, rich in blood vessels, and by “common soil” - the biological characteristics of the organism. In this regard, it must be remembered that mycobacteria can “nest” in the bone marrow, despite the fact that the bone tissue may not be changed in the anatomical and clinical sense [8; 113, 123]. Thus, tuberculous spondylitis occurs as a result of reactivation and transfer of the source of infection from the primary complex, which may be located in the lung or in some other organ. With seemingly completely cured old pulmonary tuberculosis processes, Mycobacterium tuberculosis can be detected in the bone marrow, and such foci of "dropouts" can remain latent for a long time [47]. In the skeletal system (including the spine), the onset of the local pathological process is expressed in the fact that a reactive inflammatory process begins around the pathogen and an infectious granuloma develops. As inflammation progresses, areas of necrosis appear. Outstanding Soviet radiologists (Dyachenko V.A. and Reinberg S.A.) indicate that this exudative- necrotic reaction is accompanied by an increase in intralesional pressure and leads to activation and proliferation of endosteal blast cells. As a result, the number of blood capillaries in the endosteum increases, and osteoclasts appear that resorb the bone substance of the trabeculae. Next, the connective tissue granulation elements spread directly to the bone beams, which leads to their partial or complete resorption, i.e. true destructive chronic tuberculous osteitis, or bone caries, begins [8, 47]. As a result, due to the fact that the tuberculous carious process begins with a specific inflammation, it is precisely those parts of the skeleton that are most rich in red hematopoietic (myeloid) bone marrow that are affected, i.e., primarily the spongy bone substance [152]. A tuberculous focus can develop in the central parts of the vertebral body - a central type of vertebral lesion with a slight involvement of the intervertebral discs; but more often the process is localized in areas of the vertebral bodies adjacent to each other and in the intervertebral cartilaginous disc - intervertebral type of tuberculous spondylitis. Tuberculous inflammation spreads to neighboring vertebrae in two ways: extradiscal and intradiscal [157]. The intradiscal path is characterized by the involvement in the process primarily of the intervertebral cartilaginous disc with a bordering hyaline plate. The border plate plays the role of a buffer, but in adults it is less powerful and homogeneous than in children, which promotes the germination of tuberculous granuloma from the primary focus, which can spread vertically. With such a subchondral spread of the process, the connection between bone and cartilage is disrupted, the nutrition of the plate is disrupted, which reduces its stability. As a result, degeneration of the cartilaginous plate occurs, elements of tubercular tissue grow through it and the process transfers to the nucleus pulposus , and through the latter to the second plate and to the adjacent vertebra. The observed decrease in the height of the intervertebral cartilage is one of the early signs of spondylitis and depends primarily on a decrease in the elasticity of all its elements, especially the nucleus pulposus, which, when the cartilaginous plate grows or perforates, finally loses its dense cover, spreads and softens. The narrowing of the intervertebral space is also facilitated by a reflex increase in muscle tone that occurs in connection with perifocal inflammation. Changes in the disc are predominantly necrotic, cheesy in nature [14]. In the extra-discal path from the primary focus, granuloma grows through the cortical layer of the vertebral body in its anterior, lateral or posterior sections. Most often, the primary focus is located closer to the anterior surface, which leads, on the one hand, to a weakening of the stability of the anterior part of the vertebral body and its wedge-shaped deformation, and on the other hand, to the spread of the process to the anterior or lateral surface of the body subperiosteally or through the periosteum with subsequent formation " strain ". When a granuloma emerges on the lateral surface of a vertebra, not covered by the anterior longitudinal ligament, a leaky abscess forms near the vertebrae - paravertebral , first under the periosteum, and then beyond it. In such cases, a leaky abscess (unilateral or bilateral) may remain in place, acquiring a spherical shape like a "swallow's nest" located on the side of the spinal column, which is observed mainly in the thoracic spine. In those anatomical zones where muscles are attached to the vertebral bodies, edema abscesses are able to spread through the intermuscular spaces and migrate [14]. The described changes lead to severe destruction of the vertebrae. The body of the affected vertebra in the anterior sections is compressed and takes on a wedge-shaped shape, forming a typical angular hump. According to pathological studies, a common finding on sections of the spinal column are numerous tuberculosis "nests", scattered in many parts of the spinal column and located at a considerable distance from each other [156]. The multiplicity of foci is due to hematogenous dissemination of Mycobacterium tuberculosis, as well as, to a lesser extent, the spread of infection under the ligamentous apparatus of the spine. During life, these fresh exudative-curdled foci of tuberculous spondylitis are not detected either clinically or radiologically [47].

Features of diagnosis of tuberculosis of the radial spine. Many authors are of the opinion that the diagnosis of "tuberculous spondylitis" is based, first of all, on establishing the fact of contact with a patient with tuberculosis, the presence of trauma and other predisposing factors [6, 107]. However, the leading role in the diagnosis of bone destructive changes in tuberculous lesions of the spine is played by radiation examination methods [81, 92]. The radiation picture of tuberculous spondylitis depends on the duration of the process. According to the classification of P. G. Kornev (1971), based on the pattern of development of the pathological process, 3 phases are distinguished: prespondylytic , spondylytic , post-spondylytic . The prespondylytic phase is characterized by the formation and development of primary tuberculous osteitis [46, 50]. Clinical symptoms at the onset of the disease are scanty and nonspecific. Patients complain of decreased appetite, sleep disturbances, low-grade fever, fatigue, and stiffness in the affected part of the spine after physical activity (for example, long walking or lifting weights) [1]. On X-ray examination, one of the early, most persistent signs of tuberculous spondylitis is a narrowing of the intervertebral space. The affected intervertebral disc loses its basic properties (elasticity and firmness) and gradually undergoes decay. At the onset of the disease, with slight narrowing of the intervertebral disc, the edges of the vertebrae may be smooth and unchanged [131]. Tuberculous spondylitis is diagnosed in the prespondylitis period in a small number of patients, since x-ray methods do not reflect the state of the bone marrow and areas of infiltration in it, which occur when there is no destruction of the bone beams noticeable on x-rays [9, 111]. With the advent of magnetic resonance imaging (MRI), it became possible to detect 22 trabecular edema in the affected vertebra, when the size of the destruction is still small and there is no significant decrease in the height of the intervertebral discs [28, 57, and 69]. Bone marrow edema is an early, but not specific sign of a pathological, including inflammatory, process in the bone. During an MR examination in the prespondylytic period, a tuberculous lesion in the vertebral body has a hyperintense MR signal in the T2, T2 FS mode and hypointense in the T1 mode, its contours are clear, the intervertebral disc and paravertebral tissues are not changed [66]. At the same time, using MRI it is impossible to assess the bone structure of the spine, which is a disadvantage of the method [56]. Spondylytic specific phase of spondylitis. With corresponds to Radiation progression, the diagnosis of spinal tuberculosis during this period, as a rule, begins with a survey radiography in two projections of the affected part of the spine, to identify the localization and extent of bone destructive changes [35]. On an x-ray in a direct projection, the height of the intervertebral disc is reduced unevenly; in a lateral projection, the disc is compressed in the front more than in the back, since the anterior sections of the cartilage are loaded and destroyed more than the posterior ones. When the cartilaginous disc is completely destroyed, the intervertebral space is not identified [9, 86, 141]. Computed tomography (CT) can be used to assess the condition of intervertebral discs, but this must be justified because a large scanning area increases examination time and radiation exposure to the patient. Also, in cases of severe spinal deformity in the absence of a multi-slice tomograph, step-by-step CT does not allow one to obtain a complete picture of the pathological changes. Mitusova G.M. (2002) emphasizes that in such cases, the use of traditional radiography of the spine in two projections is preferable [28]. Subsequently, with tuberculous spondylitis, 23 the involvement of the adjacent vertebra in the inflammatory process and the formation of destruction of adjacent end plates occurs. X-rays and computed tomography reveal a focus of destruction with unclear contours in the vertebral body. This path occurs as a result of the spread of tuberculous granuloma subglottically (under the anterior or posterior longitudinal ligament) from the primary destroyed vertebra to the adjacent one or through the disc in the area of the nucleus pulposus with subsequent destruction of the entire intervertebral disc [47]. A typical sign of tuberculous spondylitis is deep, often subtotal contact destruction of the endplates, which is an important differential diagnostic criterion. The classification of G. M. Mitusova (2002) provides for several options for destruction in the vertebrae during tuberculosis on CT: focal, total, according to the type of caries. With focal lesions, the author describes one or several rounded areas of destruction of bone beams with clear sclerotic contours and dense sequestra inside the lesion. The area of sclerosis around the lesion can vary from a narrow rim to compaction of the entire remainder of the vertebral body. With total destruction, the vertebral body is destroyed to a significant extent and is presented in the form of a large number of chaotically located dense bone fragments, some of which can migrate into the lumen of the spinal canal and adjacent soft tissues. The peripheral parts of the vertebral body are "eaten away" during caries-type destruction without the formation of sequesters [28]. The affected vertebral body is wedged into the body of the adjacent one, with the formation of an angular bend in the spinal axis, directed with the apex posteriorly (hump), which leads to irreversible deformation of the spine. The tuberculous process can be localized in the spinous processes or, less commonly, in the arches and facet joints. Destruction of elements of the posterior spinal column in tuberculosis is quite rare. The transition of the process to the vertebral arches is observed in 15% of cases [8]. 24 The post-spondylytic phase is characterized by temporary or sustained elimination of the tuberculous process with preservation of spinal deformity. When examining patients in the post-spondylytic phase, the affected vertebrae have clear, uneven, sclerotic contours. Defects in the vertebral bodies are partially filled with newly formed bone trabeculae. Characteristic is irreversible deformation of the spine and pronounced degenerative changes in bone tissue. These signs are better visualized with traditional radiography and CT. During the process of regeneration, a coarser and more powerful, compared to the norm, structural network of bone beams is formed. In a common process, a fixed fusion of two vertebrae (bone block) is formed and a hump is formed [21]. The ligamentous apparatus also ossifies, and the images show asymmetrical brackets that constrain the edges of the adjacent affected vertebrae [9]. As a rule, tuberculous changes in the spine can be detected with traditional radiography only several months after the development of the infectious process. Early changes in the spine, when the bone beams are slightly destroyed by granulation tissue, go unnoticed on the images, which is a disadvantage of this method. Diagnostic difficulties on radiographs in up to 20% of cases are also caused by isolated tuberculous osteitis, especially when localized in the processes and arches of the vertebrae. In such cases, CT is preferable [57]. Computed tomography significantly improves the diagnosis of tuberculous spondylitis and allows one to assess the depth of contact destruction of the vertebrae, the condition of the spinal canal, and the spread of the process to adjacent vertebrae. The use of CT can be difficult in cases of severe spinal deformities and also in cases of tuberculous lesions of the spine over a large area, however, with the advent of the latest generation multislice computed tomographs, this limitation is being removed [65]. CT examination allows early detection of bone destruction, including in areas of the suboccipital , cervicothoracic, and sacral areas that are difficult for x-ray examination [56, 142, 148]. It is worth noting that tuberculosis of the suboccipital region stands apart. The peculiarities of the radiation picture of tuberculous lesions in the suboccipital region are associated with the fact that in these areas there is a relatively small amount of cancellous bone substance [18, 19]. The tuberculous process of this localization is accompanied by superficial destruction of articulating bones, destruction of the articular-ligamentous apparatus, which leads to disruption of the relationships of the vertebral bodies and their pathological displacement [56, 61, 68]. In addition to a decrease in the height of the intervertebral disc and the presence of a focus of destruction in the vertebra, a valuable diagnostic criterion for spinal tuberculosis is the presence of a sequestrum, which is formed in 89% of cases [57]. Sequestrum in tuberculosis has a round shape, small size and looks like a "melting piece of sugar". In the picture, the sequester has a heterogeneous structure: in the center there is a darker area of necrotic bone substance, surrounded by a lighter border of granulation or decay. This radiological picture is due to the fact that in the sequestrum itself the central mass of the bone substance is not destroyed and only its peripheral parts are resorbed due to the activity of granulations, at the same time the adjacent bone walls are resorbed and are increasingly replaced by connective tissue and decay [47]. With standard radiography, there are certain difficulties in visualizing small-sized sequesters, as well as due to unfavorable technical conditions of the study. For example, summation of intestinal loops when performing 26 x-rays of the lumbar spine. These disadvantages are leveled out when performing computed tomography, which makes it possible to more accurately determine the presence, position, shape and size of sequesters [101]. Attempts to avoid the summation of shadows in an x-ray and to obtain images of individual organs and sections have been made as long ago as radiology appeared. To achieve a high-quality tomographic image of the spine or layer on an x-ray, synchronous movement of two of the three components is necessary: the tube, the object of study, the cassette. Tomographic examination makes it possible to determine the nature, localization and extent of the pathological process in the spinal column [48]. When performing linear (planar) tomography, it is necessary to take into account many parameters: the choice of layer and its thickness, the direction of the swing angle, study projections, etc. The most optimal conditions for spinal tomography are achieved with a swing angle of 30°-60°, a layer thickness from 2 to 6 mm and in steps from 0.5 to 2 cm (depending on the size of the pathological focus). During a tomographic study, in order to obtain high-quality images, it is necessary to accurately get into the desired layer [2]. In search of a more informative tomographic technique in 1931, Z. des Plantes proposed zonography, which consists of a layer-by-layer study with the selection of a thick tomographic layer. The increase in information content during zonography is due to the acquisition of an isolated zone of interest in the image, which includes the spine, intervertebral discs, ligamentous apparatus and paravertebral tissues [49]. On zonograms, the image approaches three-dimensional, including elements of an x-ray and tomogram while simultaneously enhancing the contrast and sharpness of the highlighted layer. The method is quite simple in technical execution. The swing angle is 7°-10°, the thickness of the isolated layer is 3 cm with the X-ray beam centered on the 27th section of the spine being studied [48]. The depth of the area of interest is measured with a ruler in a horizontal position of the patient on the tomography table before the start of the study. Calculate the distance from the table to the approximate location of the spinous processes, to which 6 cm is added. The obtained data are set on the tomograph scale and a breath-hold photograph is taken. To perform zonography of the spine, it is necessary to securely fix the patient in the most comfortable position on the table. The image depends on the correct choice of the depth of the area of interest. Unreliable data may arise when the patient's subcutaneous fat and muscle layer are pronounced [49]. With the further evolution of the technical base, it became possible to conduct high-resolution X-ray examinations, which eliminate almost all the disadvantages characteristic of standard radiography and planar tomography [55]. This method is digital multi-slice linear X-ray tomography (tomosynthesis). The term " tomosynthesis " was first published in the work of Grant DG in 1972 and comes from the Greek (" tomos " - section; " synthesis " - placing together) [77]. With tomosynthesis , one "pass" of the tube produces a series of low-dose exposures (up to 70-75 sections) [82-84]. In this way, a large anatomical region, such as the entire thickness of the spinal column, can be analyzed. This is achieved due to the fact that during tomosynthesis , a number of small doses of exposure are produced during one swing with a moving sensor and a tube moving in a limited range of angles [22, 23, 73]. The resulting images are divided into parts that convey anatomical structures at different depths and from different angles [129]. The result is multiple projections and reconstructions of slices of varying depths parallel to the detector surface. Spatial ambiguity is removed and it becomes possible to see whether a given characteristic is real [55, 154]. Thus, a distinctive feature of multi-slice linear X-ray tomography is the high quality of images and the possibility of post- processing images (with a slice thickness of up to 1 mm) without additional radiation exposure. Digital multi-slice linear X-ray tomography in world practice is usually used to study the mammary glands and lungs [2, 93, 114, 138, 146]. However, we did not find any works devoted to the detection of spinal tuberculosis using this technique.

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