Capabilities of Combined Application of Multislice Linear Digital X-Ray Tomography and Ultrasound Examination in Diagnosing Spinal Tuberculous Lesion

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The aim of the investigation was to assess the capabilities of combined application of multislice linear digital X-ray tomography (tomosynthesis) and ultrasound examination in diagnosing spinal tuberculous lesion.

Materials and Methods. 117 patients with tuberculous spondylitis (n=46) and hematogenous vertebral osteomyelitis (n=71), treated from 2010 to 2015 in the Research Institute of Phthisiopulmonology affiliated to I.M. Sechenov First Moscow State Medical University, were included into the study.

Results. The main radiation signs of tuberculous spondylitis and hematogenous vertebral osteomyelitis using multislice linear X-ray tomography have been specified. The following is characteristic of tuberculous spondylitis: mixed lytic destruction of vertebral bodies (p=0.04), anterior wedge-shaped deformation of the 2/3 and more of the vertebral body height (p=0.04), a rare damage of the arches, transverse and/or spinous processes (p=0.05). A diagnostic efficacy of the standard roentgenography, CT, tomosynthesis and a combination of tomosynthesis and US examination in revealing inflammatory changes in paravertebral tissues in patients with spinal tuberculosis has been determined. The sensitivity of the methods was 71.6, 90.2, 80.0 and 88.5% respectively, specificity amounted to 79.2, 93.1, 84.0 and 81.8%, respectively. The analysis of the diagnostic significance of the radiation techniques in differential diagnosis of tuberculosis and spinal osteomyelitis estimated the best values of sensitivity in CT (89.7%) and multislice linear digital X-ray tomography (84.6%) compared to the standard roentgenography (82.2%). Specificity was equal to 84.0, 79.3 and 76.1%, respectively.

Conclusion. The combination of multislice linear digital X-ray tomography and US examination enables a significant reduction of radiation dose during examination of patients suspected of tuberculous spondylitis.

Key words: spinal tuberculosis; tuberculous spondylitis; vertebral osteomyelitis; radiation diagnosis; tomography; tomosynthesis.

In recent years, significant aggravation of hospitalized patient condition has been observed in connection with the increasing number of tuberculosis cases combined with HIV-infection and diabetes mellitus, including extrapulmonary tuberculosis [1–4].

Osteoarticular localization is the most typical for extrapulmonary tuberculosis, amounting to 10–26% of the total number of patients [5–8]. Various parts of the skeleton are affected but the spine is involved in 50–60% of cases [9–14].

The diagnosis of "spinal tuberculosis" is commonly based on a complex assessment of clinical manifestations, laboratory findings and the results of examination by radiation techniques. Nevertheless, even the availability of hi-tech diagnostic methods allows specialists to reveal tuberculous spondylitis only in 40% of cases at the late stages, while common and complicated forms occur in 70% of the adult patients [6].

Radiological methods play a leading role in the diagnosis of spinal tuberculosis [15, 16]. CT application undoubtedly improves spinal tuberculosis diagnosis, allowing one to find alterations not visualized by traditional roentgenography. However, such factors as a high radiation dose (especially in diagnosing several spinal

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segments), a high examination cost relative to a classical roentgenography, do not allow frequent CT application, for example in dynamic observation of patients in the process of treatment. Today, traditional roentgenography continues to be the most disposable method of detecting bone destruction in the spinal column, though it fails to visualize pathological changes at the early stages of infectious process development. This situation demands the search for novel methods, which enable leveling actually all disadvantages typical to standard roentgenography and tomography [17]. Multislice linear digital X-ray tomography (tomosynthesis) is believed to be such a method. But the works devoted to detecting spinal tuberculosis by means of tomosynthesis have not been found by us.

An optional method of diagnosing alterations in paravertebral tissues in tuberculous spondylitis is ultrasound (US) examination. It helps detect the length of the inflammatory process in the muscles, to clarify its extension and connection with the surrounding organs, making it possible to choose a correct access and extent of intervention [18]. The place of US examination in a phthisiological practice, especially for patients with changes in the spine, has not been defined up to the end.

The assessment of the combined application of these methods in diagnosing tuberculous spondylitis will make it possible to reveal timely and qualitatively alterations in the spinal column and adjacent tissues in tuberculous process.

The aim of the investigation was to assess the capabilities of the combined application of multislice linear digital X-ray tomography (tomosynthesis) and ultrasound examination in the diagnosis of spine tuberculous lesion.

Materials and Methods. 117 patients with specific and nonspecific spondylitis, treated from 2010 to 2015 in the Research Institute of Phthisiopulmonology affiliated to I.M. Sechenov First Moscow State Medical University, were included into the study. Morphological confirmation of the diagnosis was performed in all observations.

Patients were divided into two groups to be analyzed. Group 1 included 46 patients (28 men, 18 women) having spinal tuberculosis, median age 48.1±2.2 years. Group 2 comprised 71 (46 men, 25 women) patients with hematogenous vertebral osteomyelitis, median age 50.8±1.6 years. The study complies with the Declaration of Helsinki (the Declaration was passed in Helsinki, Finland, June, 1964, and revised in October, 2000, Edinburg, Scotland) and was performed following approval by the Ethic Committee of I.M. Sechenov First Moscow State Medical University. Written informed consent was obtained from every patient.

In group 1 the spine was the primary localization of tuberculous process in 21 patients (45.7%). In other observations granulomatous inflammation in the spine was developing concurrently with tuberculosis of the lungs and other organs (Figure 1).

Mean time from pain appearance in the affected section of the spine till a visit to a doctor was 6.02±0.66 months.

In group 2 with vertebral osteomyelitis inflammatory diseases and operative interventions were noted in the history of 31 patients (43.7%) (Figure 2). After the operation, pain in the spine started in 1–15 months, 4.8±1.2 months on average. The case history of pulmonary tuberculosis was aggravated in 4 patients, in all observations pulmonary tuberculosis being presented by a focal form without clinical, laboratory and roentgenological evidence of activity.

In patients with vertebral osteomyelitis, mean time from pain appearance in the affected section of the spine till a visit to a doctor was 1.9±0.2 months.

All 117 patients underwent standard roentgenological examination using KARS-BKS apparatus (MEDTECH,

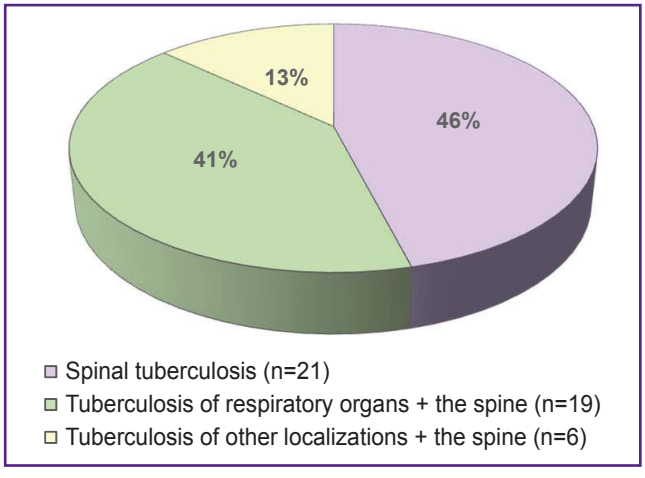

Figure 1. Distribution of patients in the group with tuberculous spondylitis depending on the primary localization of the tuberculous process

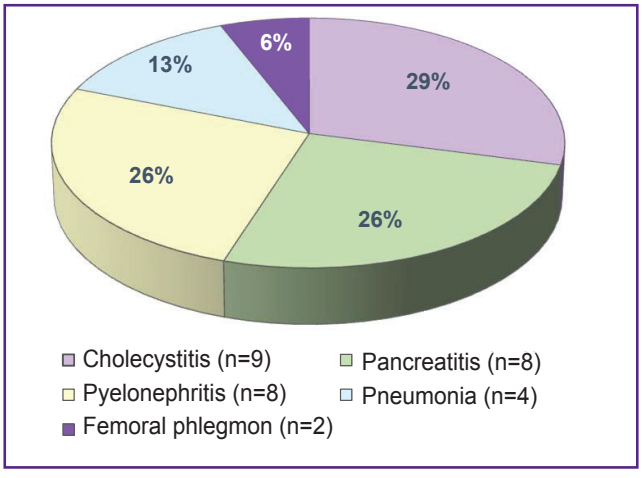

Figure 2. Concomitant diseases in patients with hematogenous vertebral osteomyelitis

Russia). X-ray computed tomography was performed to 80 patients using 64-slice SCENARIA spiral computed tomography system (Hitachi, Japan).

Multislice linear digital X-ray tomography (tomosynthesis) was carried out by SONIALVISION SAFIRE 17 R/F roentgenodiagnostic complex (Shimadzu, Japan). The spinal column was examined in two projections in a tomosynthesis mode using 55 observations. Frontal projection was performed according to the standard protocol. The slice thickness was 2 mm in the cervical and lumbar sections and 3 mm in the thoracic part. Some diagnostic difficulties appeared during the tomosynthesis of the lumbar spine in the lateral projection: with the standard settings of the system we failed to visualize vertebrae to a full width and tissues surrounding the spine. In this case, we additionally measured the height and width of the scanning zone on the images of the lumbar spine in the frontal projection. Thus, examining the lumbar spine a personified approach, considering a lordosis height of every patient, was used.

Comparison of the effective radiation doses during examination of the cervical, thoracic or lumbar part of the spine by different techniques showed, that it was the least in standard roentgenography (Table 1).

Ultrasound examination of the paravertebral tissues was performed to 37 patients using US Preirus HI Vision device (Hitachi, Japan) using a 4 MHz radiation frequency sector probe and 5–10 MHz linear probe. A patient was in a ventricumbent position with the head supported by the forearms bent in the elbow joints. US examination was carried out in horizontal, sagittal and parasagittal planes with the assessment of the blood flow in adjacent tissues and abscesses in a color Doppler mapping mode.

The material was statistically processes by means of Statistica, Release 10.0 program package. Frequency differences were evaluated using nonparametric criterion χ^2, and for small samples Fisher's exact test was applied. To verify the hypothesis of statistical significance of differences in the groups, the method of paired comparison with the application of Student's test ($p<0.05$) and 95% confidence interval in all cases were used. Assessment of sensitivity, specificity and accuracy, prognostic value of positive and negative results of the radiation methods was done using standard formulas.

Table 1

Effective radiation doses in various X-ray examination methods (mSv)

The area of spine examination	Standard roentgenography	Tomosynthesis	CT
Cervical spine:			
FP	0.033	0.074	
LP	0.09	0.31	0.5–0.7
∑	0.123	0.384	
Thoracic spine:			
FP	0.232	0.185	
LP	0.154	0.185	
∑	0.386	0.37	4.2–5.2
Lumbar spine:			
FP	0.347	0.97	
LP	0.191	2.35	5.6–8.2
∑	0.538	3.32	

N o t e s. FP: frontal projection; LP: lateral projection; ∑: total dose.

Results. 105 affected vertebrae and 63 intervertebral disks in 46 patients with spinal tuberculosis and 158 affected vertebrae and 96 intervertebral disks in 71 patients with hematogenous vertebral osteomyelitis have been analyzed.

In tuberculous spondylitis the pathological process involved two adjacent vertebrae in one spinal segment or at the border of the spinal parts in 42 (91.3%) of cases. In 2 observations tuberculous solitary lesion of L1 vertebra was found, and confirmed by morphological investigations as well. In 2 patients tuberculous spondylitis was localized in different segments of the vertebral column (thoracic and lumbar) without involvement of the vertebrae at the level of thoracic-lumbar transition. Thoracic (37.5%) and lumbar (33.3%) parts of the spine were affected most frequently and, actually, to an equal extent. In 7 observations multilevel localization with the damage of two segments and involvement from three to five vertebrae was noted.

Statistically significant differences in the number of the damaged vertebrae in both groups of patients found with the help of X-ray methods (standard roentgenography, CT, tomosynthesis) were not established.

Three types of the vertebral body destruction were distinguished based on the results of the assessment by the given method (Figure 3): 1) subchondral destruction (planar, involving mainly two adjacent arch laminae); 2) focal (areas of rounded or oval form); 3) mixed (combination of the two former types).

Statistically significant differences of values in the examined groups were observed in the type of destruction and involvement of posterior parts of the vertebral column in the inflammatory process according to the results of the three methods. Mixed destruction ($p=0.04$) was encountered significantly more often in tuberculosis, the development of subchondral lytic destruction was typical for osteomyelitis ($p=0.03$) and damage of posterior parts of the vertebrae ($p=0.05$).

Sequestration in spine tuberculosis was observed more often than in osteomyelitis; it was detected by standard roentgenography in 12.7% of vertebrae (7 of 55), CT in 34.8% (24 of 69), tomosynthesis in 20% (11 of 55). Hence, tomosynthesis surpasses standard roentgenography in sequester visualization, but is inferior to CT. For integrity of the study, the assessment of this parameter was performed in the equal groups: in standard roentgenography — 55 damaged vertebrae, CT — 69, tomosynthesis — 55. For this purpose, patients for whom tomosynthesis was not used, were excluded from the

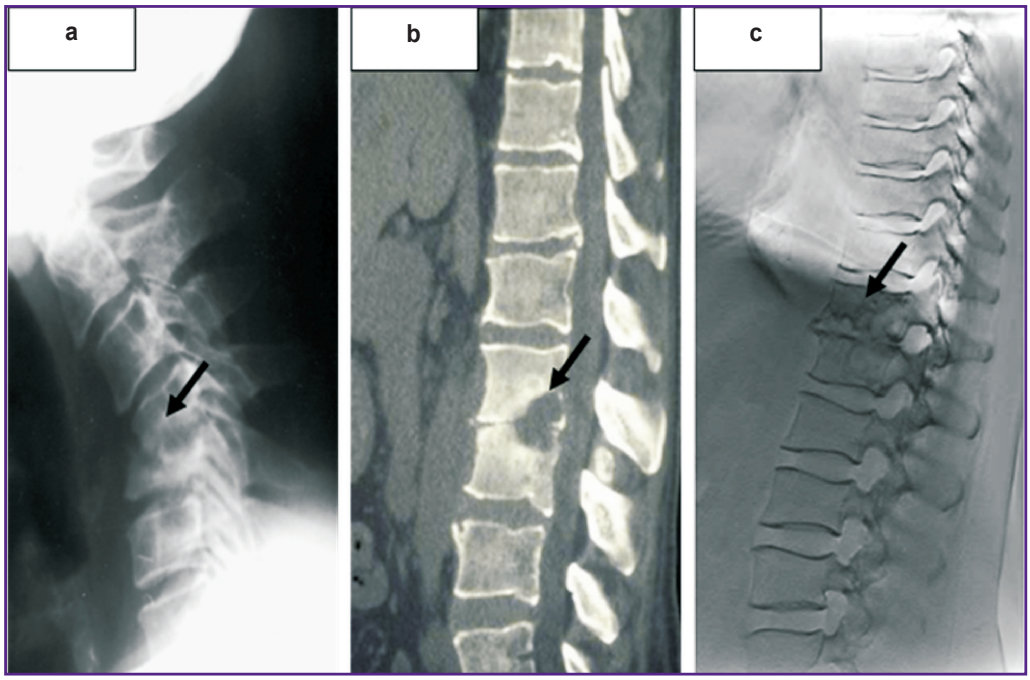

Figure 3. Types of vertebral body lytic destruction in tuberculous spondylitis detected by the three methods: (a) roentgenography (lateral projection, subchondral destruction of the vertebrae C4, C5; arrow); (b) CT (reconstruction in sagittal projection, focal destruction in the posterior parts of vertebrae L3, L4; arrow); (c) tomosynthesis (lateral projection, mixed destruction of vertebrae Th11, Th12; arrow)

group (n=46, 105 damaged vertebrae) of patients who underwent standard roentgenography.

Background rarefaction in the bodies of the damaged vertebrae was found in 23.1% of patients with spine tuberculosis, and in 23.4% with hematogenous vertebral osteomyelitis. Osteosclerosis was noted in 42.1% of patients with spine tuberculosis, and in 34.2% with hematogenous osteomyelitis. Statistically significant differences in the assessment of these characteristics in the bodies of the damaged vertebrae by the three roentgenologic methods were not found. In all cases osteosclerosis was revealed in patients with a long-term course of the disease ($p<0.05$). Thus, comparing two groups it has been estimated, that the characteristic signs of osteomyelitis relative to tuberculous spondylitis were as follows: a shorter term of becoming ill ($p=0.01$), reduction of the vertebra height by 1/3 of the body and less ($p=0.04$), and rarer development of the anterior wedge-shaped deformity of the vertebra bodies ($p=0.05$). It is most likely to be connected with the fact, that patients with osteomyelitis seek a medical aid at the early stage due to a pain syndrome, and according to their complaints a targeted X-ray examination of the spine is carried out. This helps to prevent the irreversible deformation of the vertebral column.

Comparison of the roentgenological findings with morphological diagnosis was performed to assess the capabilities of the radiation diagnostic methods (Figure 4).

Values of sensitivity were calculated for the three methods (i.e. the probability of a positive finding in a patient, characterizing the ability of a method to detect tuberculous lesion in those cases, when it actually takes place), as well as specificity (the ability of a method to detect the group without spinal tuberculous lesion). The greatest values of sensitivity in detecting spine tuberculosis were obtained in CT application (89.7%) (Table 2). The sensitivity in tomosynthesis was 84.6%, in standard roentgeography 82.2%.

Extension of inflammation to the paravertebral tissues and intercurrent destructive alterations are typical for spondylitis. In the frames of our investigation, the analysis of US data in 15 of 46 patients with tuberculous spondylitis, and in 22 of 71 with hematogenous vertebral osteomyelitis has been conducted. Comparative evaluation of alterations in paravertebral soft tissues of the dorsum in spinal tuberculosis and osteomyelitis has been performed. In 20 patients (54.1%) there were detected two variants of inflammatory reaction in the soft tissues in spinal tuberculosis and osteomyelitis: abscess (n=15; 75%) and infiltration (n=5; 35%).

The assessment of the US signs of abscesses and infiltrates in B-mode, i.e. contours, structures, echogenicity, showed no statistically significant differences in patients of both groups. In color Doppler mapping mode, the zone of inflammation in the paravertebral area in osteomyelitis may have small regions of intensive blood flow around or in the capsule of the formations. In tuberculous inflammatory congestive

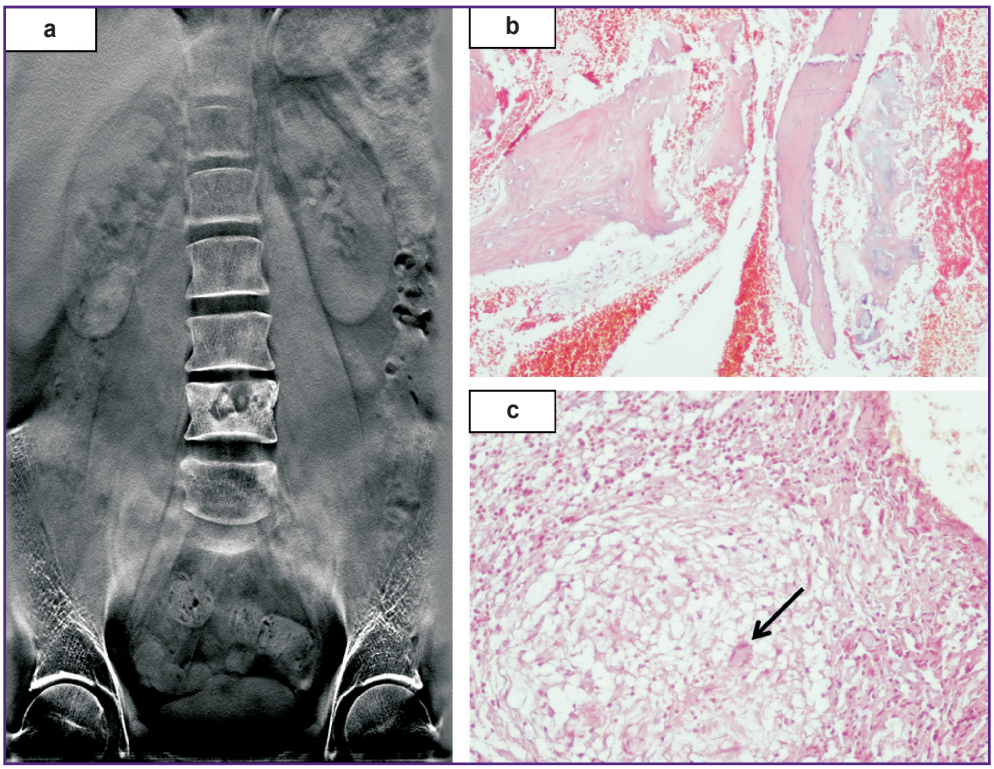

Figure 4. Examination of the lumbar part of the spine in a patient with spondylitis: (a) tomosynthesis; destruction of vertebral body L4 with sequester formation; (b) a fragment of bone tissue with the signs of destruction, hyperemia; (c) connective tissue with tuberculous granuloma containing giant polynuclear Pirogov–Langerhans cell (arrow); hematoxylin and eosin staining, ×200

Table 2

Capabilities of various radiation diagnostic methods in detecting tuberculous spondylitis (%)

Parameters	Roentgenography (n=117)	CT (n=80)	Tomosynthesis (n=55)
Sensitivity	82.2	89.7	84.6
Specificity	76.1	84.0	79.3
Accuracy	78.4	85.0	81.8

abscesses, regions of intensive blood flow are not usually found, corresponding to the concept of “a cold abscess” (Figure 5).

US in two groups failed in some cases to visualize the signs of paravertebral inflammatory process. In 6 observations tissues near the vertebrae were asymmetrically thickened, with oblong inclusions of reduced echogenicity along the muscular fibers, without the evidence of increased blood flow in color Doppler mapping mode, which was not estimated to be an inflammation (false-negative results). In 1 case there was a false-negative result during localization in the thoracic spine due to the limited resolution of the method. False-positive results in 2 patients were connected with visualization of asymmetrically diffusely thickened iliolumbar muscle, with small echogenic inclusions in the depth of the muscular fibers and sharp-fuzzy borders, that was taken for infiltration. Ribs, pronounced subcutaneous fat, lipid involution of muscles limited the capability of US method in diagnosing paravertebral abscesses.

Changes in paravertebral tissues were suspected in 28 cases of 46 (60.9%) on roentgenograms in frontal and lateral projections, and in 17 cases of 26 (65.4%) using tomosynthesis. In 14 patients (30.4%) abscess was not calcified. Abscess calcification was noted in 9 cases (19.6%) in patients with the disease lasting over 8 months, the contours being sharp. Infiltrates without calcification were diagnosed in 5 patients. Visualization of alterations in paravertebral region in standard roentgenography and multislice linear digital X-ray tomography was hindered due to a relatively low resolution of these techniques. False-positive results in standard roentgenography and tomosynthesis appeared in localizing tuberculous abscess in the sacrum spine (at the level of S3–S4), and also in diffuse thickening of the iliolumbar muscle. False-negative results were obtained in case of small dimensions (up to 2–3 cm) of prevertebral abscess in the cervical and thoracic parts that was most likely to be connected with the density

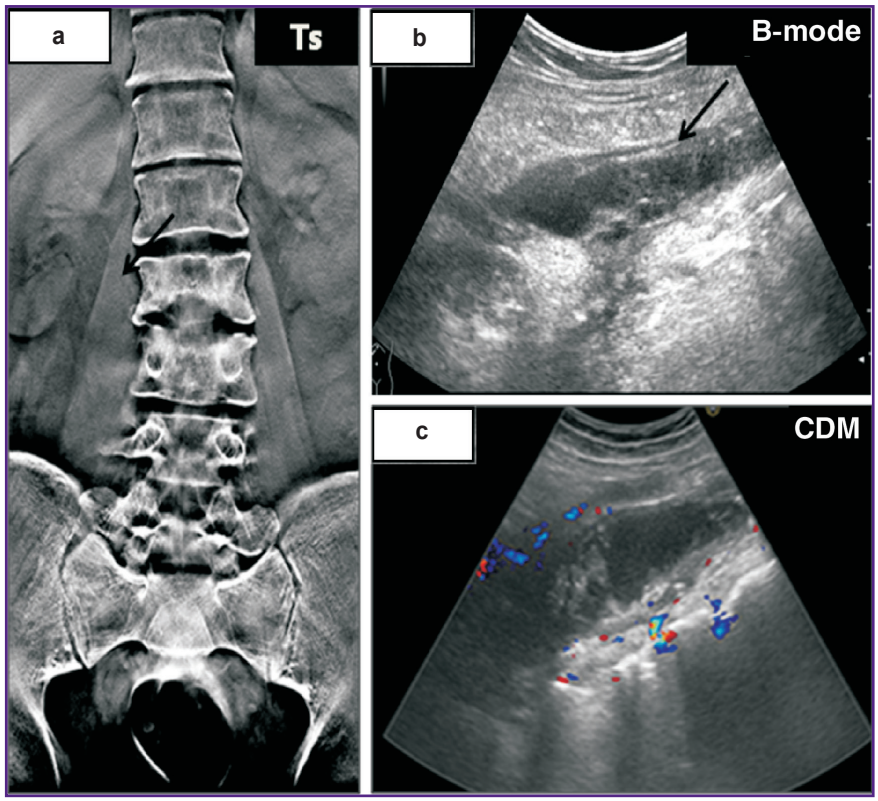

Figure 5. Examination of the patient with spinal tuberculosis: (a) tomosynthesis of the lumbar spine in anterior-posterior projection; destruction of adjacent body surfaces of vertebrae L3–L4; asymmetry of iliolumbar muscles, no clear radiological evidence of abscess; (b) US image in B-mode and (c) in the mode of color Doppler mapping of psoas abscess in spinal tuberculosis; cavity formation of reduced echogenicity with heterogenous inclusions, with sharp contours along the whole length (arrow); US signs of increased blood flow in the depth of the abscess were not detected. Ts: tomosynthesis; CDM: color Doppler mapping

of congestive abscesses and summation of the shadows. In 10% of cases abscesses not revealed by these methods were found by CT.

In the assessment of the efficacy of radiation methods for diagnosis of abscess or infiltration in the paravertebral tissues, sensitivity means the probability of a positive result, and characterizes the ability of the method to detect inflammation in paravertebral region in those cases, when it actually exists, and specificity is an ability of the method to determine absence of inflammatory changes in the paravertebral muscles and tissues. To assess the efficacy of detecting paravertebral abscesses and infiltrates (Table 3) in the group of patients with spinal tuberculosis and osteomyelitis, the results obtained by radiation methods, were confirmed by the findings of intraoperative and morphological changes in the paravertebral tissues. Since we failed to find statistically significant differences in the occurrences of congestive abscesses in spinal tuberculosis and osteomyelitis, we calculated the efficacy of the methods in two groups considering the results of roentgenography in 117 patients, CT in 80, and tomosynthesis in 55, US + tomosynthesis in 37 patients. CT appeared to be the most effective method of detecting alterations in the paravertebral area. The complex "tomosynthesis + US" is more informative than conventional roentgenography, but is inferior to CT.

Table 3

Diagnostic efficacy of the radiation methods in detecting the evidence of inflammatory alterations in paravertebral tissues (%)

Parameters	Roentgenography (n=117)	CT (n=80)	Tomosynthesis (n=55)	Tomosynthesis + US (n=37)
Sensitivity	71.6	90.2	80.0	88.5
Specificity	79.2	93.1	84.0	81.8
Accuracy	72.6	91.3	81.6	86.5

Specificity reduction in the given combination of methods is associated with hyperdiagnosis of the inflammatory changes.

An accurate diagnosis of inflammation in paravertebral tissues in tuberculous spondylitis and vertebral osteomyelitis enables phthisiatricians to specify the process extension and to readjust the treatment tactics.

Discussion. Classification of the destruction types in our study is somewhat different from the one presented by Mitusova et al. [18]. The author describes destruction of the vertebral bodies as focal, total and contact (caries-type) in tuberculous spondylitis. In total destruction the body of the vertebra is significantly destroyed and presented in the form of a large number of randomly arranged dense bone fragments, the part of which can migrate into the lumen of the spinal canal and adjacent soft tissues. In caries-type destruction vertebral arch laminae are "cankered" without sequester formation. From our point of view, the term "subchondral type of lytic

destruction" instead of "contact" is more acceptable, since spinal tuberculosis can affect only one vertebra without transition on the adjacent arch lamina of the subjacent or superposed vertebra. This type of destruction may be considered as a synonym of "epiphyseal destruction" [16]. We also consider inexpedient to distinguish the total destruction as a separate variant. Such destruction, according to our data, is caused by compression of the vertebral bodies and may develop in any type of destruction, reflecting the aggressiveness of tuberculous process and its duration. Frequently, trauma in patients with spinal tuberculosis results in the total destruction, as vertebral bodies have already been altered.

A characteristic sign of tuberculous spondylosis is the involvement of two contact vertebrae and intervertebral discs between them into the pathological process [19]. Standard roentgenography detected specific granulomatous inflammation in 100% in the vertebral bodies or significantly rarer (4.8%) in the form of combination of destruction in the bodies, arches and/or transverse spinous processes. The results obtained agree with the data of a number of investigations where it is indicated, that the tuberculous process rarely extends to the arches or processes of vertebrae (2–10%) [19, 20]. In our two cases the involvement of posterior parts of the spine in the process were not diagnosed on the roentgenograms, but were revealed by CT.

Application of CT is certain to improve the diagnosis of tuberculous spondylitis, enabling detection and assessment of the destruction depth in the regions difficult for roentgenological examination — in the bodies, arches and transverse processes [20]. Multislice linear digital X-ray tomography allows one to perform a more "delicate" diagnosis in contrast to standard roentgenography [15, 21]: the data on osteo-destructive alterations in the spine, obtained by this method, coincided in the majority of cases with CT findings.

When assessing such a sign in tuberculosis as sequestration, we noted a divergence of our findings with the occurrence of this sign in the studies of other authors [22]. It may be connected with the fact, that the presence of sequestration was evaluated by us only in case of visualization of the classical radiological signs described by Reinberg [23]. A typical tuberculous sequester is characterized by a rounded form, small dimensions and is similar to a melting piece of sugar. In the central parts, therefore, a denser region of the necrotized bone is located, surrounded by a zone of rarefaction (granulation). Chaotically arranged bone fragments in the spinal canal lumen or in the destruction cavity were classified by us as a fragmentation of vertebrae without sequestration. In Reinberg's opinion, formation of a sequester is not a sign of unfavorable or severe course. In tuberculosis of the spine a sequester may be entirely replaced by the connective tissue with restoration of the normal bone structure in contrast to osteomyelitis sequester [23]. Consequently, vertebra fragmentation may be considered as a prognostically worst sign compared to sequestration. Notably, that multislice linear digital X-ray tomography also surpasses standard roentgenography in visualization of sequesters, but is inferior to CT to some extent.

Formation of paravertebral abscess, whose visualization by standard roentgenography is difficult due to a low resolution of this method in visualization of soft tissues, is typical for tuberculous spondylitis running concurrently with destructive alterations [24]. Two variants of inflammatory process development in the paravertebrate tissues in spinal tuberculosis were distinguished by us: abscess and infiltrate. A limited accumulation of pus with sharp contours was referred by us to abscesses. Infiltrates did not have sharp borders with muscles or tissues. In Kornev's opinion [25], infiltration is one of the stages of forming a true abscess. Infiltration into the adjacent tissues and significant fusion of the external wall of the congestive abscess is observed in the period of granuloma growth at the site of its invasion. Then the external wall of the infiltrate consolidates and transforms into a fibrous tissue. In "old" abscesses the inner layer may become much thicker and dense due to the connective overgrowth and lime salt deposits [25].

Thus, any of the discussed radiation methods has its strong and weak points in the assessment of alterations in the spine and paravertebral area during detection of tuberculous spondylitis and differential diagnosis of this disease. Searching for precise, timely and accessible method of revealing tuberculous process in the spine will promote prevention of the irreversible changes and selection of the proper treatment tactics.

Conclusion. A complex application of tomosynthesis for the assessment of bone destructive changes in the spine and US examination for diagnosis of paravertebral abscesses allows phthisiatricians to reduce a radiation dose in examining patients with spinal tuberculosis, to timely begin a targeted treatment, and therefore to decrease significantly a period of preoperative diagnosis and improve the prognosis of the disease.

Within the frames of our investigation for the first time in the Russian Federation and the world practice, radiation signs of tuberculous spondylitis and hematogenous vertebral osteomyelitis were defined using multislice linear digital X-ray tomography. Indices of efficacy (sensitivity, specificity, accuracy) were obtained for various X-ray methods in the diagnosis of these diseases.

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