

Results of complex examination of bone mineral density in patients with tuberculous spondylitis

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Introduction Osteoporosis is one of the most common and important symptoms of tuberculous involvement along with the classic symptomatology. **Aim** To evaluate bone tissue mineral density and microstructure in patients with tuberculous spondylitis. **Materials and Methods** The results of studying 75 patients with active tuberculous spondylitis admitted to the Department of Bone and Joint Tuberculosis of Republican Specialized Scientific and Practical Medical Center of Phthisiology and Pulmonology in 2015 formed the basis of the present work according to the intended purpose. Complex examination of the patients included their case history, clinical and laboratory data, and orthopedic status evaluation. Radiological examination consisted of performing sagittal and frontal radiographic views, CT, and/or MRI of the involved segments. Both tomographic examinations (CT and MRI) were performed, if indicated, for differential diagnosis to identify the pathological process. **Results** Male patients of working age prevailed in the group of patients with normal bone mineral density. The number of patients with decreased bone mineral density was twice more as compared with those with normal bone mineral density. One-third of the patients were over 50 years of age. The value of bone tissue resorption exceeded the normal rate by two-fold. The values of bone tissue formation in middle-aged patients were increased irrespective of gender but remained within the limits of the two-fold increase. **Conclusion** Tuberculous spondylitis causes general changes in the bone metabolism values in 90 % of the patients. Intensive bone resorption takes place in tuberculous spondylitis that exceeds twice the rate of bone tissue formation.

Keywords Tuberculous spondylitis, bone tissue, bone mineral density

Tuberculosis most commonly affects the cancellous bone such as the epiphyses of the long bones and the short bones of the skeleton [1]. The lesion in cancellous bone is typically isolated and solitary. Tubercular foci primarily occur in cancellous bone and are most frequently seen in the vertebral bodies and epimetaphyseal areas. Along with the classic symptoms (spinal deformity, abscesses, and spinal disorders), osteoporosis is one of the most common and important symptoms of tuberculous spinal lesions. The etiology and course of osteoporosis with bone tuberculosis have not been studied. The presence of local or regional osteoporosis is important in the diagnosis of tuberculous lesions [2], particularly when other infectious bone lesions, including those that are nonspecific in nature, are part of the differential diagnosis. In other infectious lesions, both

local and systemic osteoporosis are observed.

The diagnosis of osteoporosis is multifaceted and usually starts with routine diagnosis based on X-rays and continues with advanced examinations such as ultrasound or X-ray densitometry [3].

Other methods for the diagnosis of osteoporosis include blood and urine chemistry and histomorphometry of the bone tissue [3].

Despite the large number of methods reported in the literature, data on comprehensive studies are limited. The literature data on comprehensive studies of bone tissue status in tuberculous lesions are very scarce.

Aim of the study: to conduct a comprehensive evaluation of the microstructure and bone mineral density (BMD) in patients with tuberculous spondylitis.

MATERIALS AND METHODS

Examination results of 75 patients with active tuberculous spondylitis admitted to the Department on Tuberculosis of Bones and Joints in RSSPMCPPhP in 2015 were analysed. The age of the patients ranged from 24 years to 81 years; 54 were males (72 %) and 21 were females (28 %). The distribution of patients according to sex and age is presented in **Table 1**.

The duration of the disease was more than 1 year in 18 (24 %) patients and less than 1 year in the remaining 57 (76 %) patients. The mean duration of the disease was 4 months.

The subjects were predominantly male patients aged 40–49 years. Lesions of 2 vertebrae were prevalent

and occurred in 73 (97.3 %) patients, while lesions of 3 vertebrae occurred in 2 patients (2.7 %), with the L4 and L5 vertebrae being the most frequently involved (**Table 2**).

Table 1

Distribution of patients according to sex and age

Age (years)	Males	Females
19–29	12	0
30–39	5	9
40–49	21	0
50–59	10	6
60 and older	6	6
Total	54	21

Table 2

Specific process localization in spine

Level of lesion	Number of affected vertebrae
C5	4
C6	7
C7	4
Th3	4
Th4	4
Th5	4
Th6	4
Th9	7
Th10	7
Th11	7
Th12	7
L1	10
L2	10
L3	7
L4	31
L5	31
S1	4

During the complex examination of the patients, their medical history and clinical and laboratory data were studied and their orthopedic and neurological status was evaluated. Radiological examination included X-rays in the sagittal and frontal views and magnetic resonance imaging (MRI) of the affected segment. Both imaging studies (CT and MRI) were performed when indicated for the differential diagnosis of the pathological process. The studies were conducted using MRI SIGNA HD/e with a capacity of 1.5 Tesla and MSCT (32 slice) (General Electric, USA). MRI was performed in T1 and T2 modes. MSCT and MRI studies were conducted in the sagittal, frontal, and axial

views, with the thickness of the tomographic slices ranging from 2 mm to 5 mm.

All the patients underwent dual-energy X-ray absorptiometry using LUNAR DXF. BMD of the lumbar vertebral bodies and proximal femur (i.e., femoral neck, greater trochanter, and Ward's triangle) was assessed, and evaluation was performed according to the "Total body" program. Patients were divided into 2 groups: one with reduced BMD and another with normal BMD. The evaluation was conducted in accordance with the WHO recommendations, i.e., when T score is < -1.0 , BMD is reduced.

Bone metabolism was studied by determining the bone resorption marker Beta-CrossLaps (collagen degradation products) and bone formation marker PINP (N-terminal telopeptide) in serum using the automated electrochemiluminescence immunoanalyzer Cobas e 411 (Roche Diagnostics, Switzerland).

Histomorphometry was performed on 50 fragments of vertebral bodies obtained during surgery from the specific inflammation focus area. Bone samples from patients aged 30–40 years were used, and the diagnosis of tuberculous spondylitis was confirmed. Histomorphometry was conducted in the pathological laboratory of RSSPMCPPhP. Quantitative analysis of bone parameters and morphometry were performed using a light microscope, digital video camera, and computer.

All the patients received therapy for tuberculosis. The duration of the therapy prior to surgery ranged from 3 weeks to 2 months, with an average period of 1.5 months.

All 75 patients underwent curative reparative surgery with a histological and bacteriological confirmation of the diagnosis.

RESULTS

The diagnosis of tuberculosis was confirmed histologically and/or bacteriologically (Gene Expert, HAIN test, MGIT) in all 75 (100 %) patients with spondylitis.

When tomograms and radiographs were analyzed, special attention was paid to the localization and number of affected vertebrae, nature of the process, depth of vertebral body destruction, contents of the cavity, borders of destruction, and bone surrounding the focus. When the destruction focus had a 1–2 cm border, it was considered to be sclerous and when it had a border of up to 1 mm with no visual lines indicating the blurring of boundaries, it was considered to be clear. The bone structure around the destruction focus was assessed as being sclerous, unchanged, and fenestrated. Signs of bone osteoporosis in the deformed regions included a glomerular pattern of cancellous bone due to resorption of the separate bone trabeculae, thinning of the cortical layer, osteoporotic cortical bone, increased definition of the cortical layer due to increasing porosity of the vertebrae, and blurring of the boundaries of the destruction focus. In addition, MRI took into account the study mode, plane of the sections, condition of the intervertebral discs, anterior and posterior longitudinal ligaments, presence of abscesses

as well as their contours and signal, localization of the abscesses, and abnormal signals from the affected vertebrae.

In 38 patients, MRI findings revealed an early and significant manifestation of a spondylolytic phase with a reduced signal from the destruction area, the remaining vertebral body, and the destroyed endplate with infiltration of paravertebral soft tissue in T1 mode and a high signal from the destruction area (homogeneous or heterogeneous), the remaining vertebral body, and the involved disc in T2 mode. Radiographs of these patients showed that the border of the destruction focus was fuzzy and that the bone tissue surrounding the destruction focus was porous.

A decline in spondylolytic process was observed in 37 patients; this was manifested by a heterogeneous low signal from the destruction focus and reduced signal from the remaining vertebral body as well as abscess formation in T1 mode and a frequently reduced heterogeneous signal from the destructive cavity and unchanged or increased signal from the vertebral bodies in T2 mode. Defined destruction focus boundaries were evident on radiographs. However, the bone tissue surrounding the destruction focus remained porous or became glomerular in pattern.

BMD in patients with tuberculous spondylitis was studied by X-ray densitometry, and the results are listed according to the 2 patient groups mentioned previously (**Table 3**).

As shown in Table 3, males of working age prevailed in the group with normal BMD. The number of patients with reduced BMD, i.e., with generalized osteoporosis and osteopenia, was almost 2 times higher in this group (including patients older than 50 years in whom senile osteoporosis cannot be excluded). However, in the group with osteopenia and osteoporosis, the number of males of working age in whom comorbidities did not reduce BMD was higher. All 18 (24 %) patients with a disease duration of more than 1 year were included in the group with reduced BMD.

BMD is the result of bone turnover that is directly dependent on the processes of bone resorption and formation. In this study the serum markers of bone resorption and formation were evaluated. In our study, 4

(5.3 %) patients had bone turnover markers that remained within the normal range, while the remaining 71 (94.7 %) patients reported changes in serum bone turnover parameters (**Table 4**).

The results presented in **Table 4** indicate that in patients with tuberculous spondylitis, the values of bone resorption were 2–3 times higher than the normal range; the mean values of bone formation remained at the upper limit of normal. However, there was a correlation between age and reduced values of bone formation in patients older than 50 years.

We compared the results of histomorphometry (**Table 5**) with the results obtained by Petrenko (2002) [3] and with those obtained by Rehman (1994) [4] who performed histomorphometry on samples obtained from healthy men and women of different ages in England. The results of histomorphometry obtained in the present study are listed in **Table 5**.

Table 3

Results of dual-energy X-ray densitometry

	Mean BMD					
	Normal			Osteopenia and osteoporosis		
	M	F	Over 50 years	M	F	Over 50 years
Number of patients	19	9	0	28	19	19
Total	28	47				

Table 4

Bone turnover markers

Parameter		Mean value			
		M	F	Over 50 years	Younger than 50 years
P1NP	N-terminal telopeptide, ng/ml	62.8 ± 25.3	51.0 ± 26.6	52.2 ± 21.0	63.1 ± 21.0
Beta-CrossLaps	Collagen degradation products, ng/ml	0.0871 ± 0.53	0.592 ± 0.38	0.821 ± 0.49	0.719 ± 0.54
Normal					
P1NP	N-terminal telopeptide, ng/ml	< 58.59			
Beta-CrossLaps	Collagen degradation products, ng/ml	< 0.394	< 0.0299	< 0.556	Female, < 0.299 Male, < 0.394

Table 5

Histomorphometric data obtained in the present study (50 samples of bone tissue from specific inflammation focus area)

Parameter	Diameter of trabeculae, μm	Number of osteoclasts/mm ²	Number of osteoblasts/mm ²
Mean value	152.47 ± 65.79	4.4 ± 0.46	253.8 ± 8.49
Range	62.4–308.1	0–40	0–820

DISCUSSION

Petrenko (2002) [3] who studied histomorphometric bone parameters in patients with vertebral fractures previously divided them into 3 groups: those with normal BMD, those with osteopenia, and those with osteoporosis. According to X-ray densitometry results, the mean thickness of the bone trabeculae in the vertebral body in group with osteoporosis was reported to be 83.7 μm in women and 93.3 μm in males, that in the group with osteopenia was reported to be 164.57 μm in women and 148.6 μm in men, and that in the group with normal BMD was reported to be 202.3 μm in women and 242.83 μm in men.

Rehman et al. (1994) [4] studied normal histomorphometric bone parameters in men and women of different ages living in Anguilla and determined the normal number of osteoclasts (NOC) in trabecular bone tissue (4.8–6.8/mm²).

Comparative analysis of our own data (**Table 5**) with those obtained previously revealed that patients with tuberculous spondylitis had thinning of bone trabeculae corresponding to osteopenia without changes in the number of bone cells surrounding specific inflammation foci.

CONCLUSIONS

Tuberculous spondylitis causes general changes in bone turnover parameters in 94.7 % of cases. as high as bone formation. Enhanced resorption, in turn, can lead to a loss of the accumulated bone mass if In tuberculous spondylitis, bone resorption is twice antituberculosis and osteotropic therapies are not provided.

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