Central Asian Journal of Medicine

CLINICAL AND LABORATORY MANIFESTATIONS OF TUBERCULOUS SPONDYLITIS

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ABSTRACT

The **purpose** of our study was to characterize the clinical and laboratory features of tuberculous spondylitis at the level of the general medical network.

Materials and methods. Comprehensive examination of 110 patients with tuberculous spondylitis was conducted in the department of tuberculosis of bones and joints of the Republican Specialized Scientific and Practical Medical Center of Phthisiology and Pulmonology.

Results. The study results showed decrease of blood hemoglobin levels and erythrocytes count in patients with tuberculous spondylitis. Blood acute-phase proteins were increased several times in patients with tuberculous spondylitis. Blood coagulation biochemical markers analyses showed an increased level of fibrinogen and D-dimers.

Conclusion. Clinical and laboratory manifestations of tuberculous spondylitis in modern conditions are characterized by mild anemia, an increase in the blood of acute-phase proteins, fibrinogen, D dimers, reactive hepatitis and decrease of the blood fibrinolytic activity.

Key words: tuberculous spondylitis, laboratory tests, clinical symptoms.

INTRODUCTION

Fifty percent of all extrapulmonary tuberculosis lesions localized in bones and joints [10], which makes osteoarticular tuberculosis one of the leading problems in phthisiology. Most frequently osteoarticular tuberculosis affects spinal column and ranges from 40 to 82.4% [5].

Increased morbidity of the extrapulmonary tuberculosis in recent years is associated with the problem of drug resistance of Mycobacterium tuberculosis [14].

Late verification of the diagnosis leads to a high percentage of complications due to compression of the spinal cord by abscesses and bone fragments as a result of pathological fractures of the vertebral bodies [4,7,13].

In modern conditions, the clinical manifestations of spinal tuberculosis depend on the location, duration of the pathological process, virulence of mycobacteria, the degree of functional immune disorder of the human body and the presence of concomitant diseases [1].

The largest number of patients with tuberculous spondylitis belong to the age group of 16–30 years. Spinal tuberculosis can have varied presentations and long duration of history before complications. Back pain is the most common symptom in tuberculous spondylitis, and is the only complaint in 61% of patients. Fever, malaise, loss of appetite, and loss of weight are infrequent in spinal tuberculosis (20%–30%). Before onset of complications imaging features are not typical [8].

The purpose of our study was to characterize the clinical and laboratory features of tuberculous spondylitis at the level of the general medical network.

MATERIALS AND RESEARCH METHODS

Comprehensive examination of patients with tuberculous spondylitis was conducted in the department of tuberculosis of bones and joints of the Republican Specialized Scientific and Practical Medical Center of Phthisiology and Pulmonology.

Total number of patients was equal to 110, 65(59.1±4.7%) male and 45(40.9±4.7%) female patients. The age of the patients ranged from 20 to 81 years, the average age was 50 years.

Medical examination included the collection of data on the main, concomitant and past diseases and injuries, as well as general, orthopedic and neurological condition.

Laboratory tests. Hemoglobin, erythrocyte count, color index, leukocyte count and leukocyte formula, as well as erythrocyte sedimentation rate were tested in all patients. The liver function was evaluated by the level of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) according to the Reitman-Frenkel method, total bilirubin according to Yendrashik. The kidney function was evaluated by the level of urea and creatinine in the blood serum. Diabetes mellitus was confirmed by the level of fasting and postprandial serum sugar, as well as glycated hemoglobin percentage. Blood electrolytes, such as magnesium, potassium, calcium were determined according to indications.

Hemostasis status was clarified by blood hematocrit percentage, thrombotest, prothrombin index, plasma fibrinogen rate, plasma re-calcification time, percentage of blood clot retraction. Fibrinolytic activity was evaluated by Kotovshchikova M.A. and Kuznik B.L. method. The method is based on the fact that normally, under the influence of natural lysis of the clot, the formed elements of blood precipitate. With an increase or decrease in lysis, the volume of fallen formed elements increases or decreases accordingly.

Urine was analyzed by determination of color, transparency, PH, protein content and microscopy of the urine sediment with the determination of the cellular composition, salts, bacteria, fungi and cylinders.

Cardiac electrical activity assessed by electrocardiography on BTL-08 SD device.

External respiration function diagnosed on “Valenta” (Saint Petersburg, Russia) device.

Internal organs organic disorders confirmed with ultrasound technique on Siemens (Berlin, Germany) device.

A radiologist's and/or a histological report, and/or a positive result of a bacteriological examination confirmed Tuberculous spondylitis diagnosis.

X-ray examinations included: magnetic resonance imaging (MRI) (MRI SIGNA HD/e, 1.5 Tesla, General Electric, USA), which was performed in most patients because of its better informativeness. Computed tomography (CT) (Siemens, Germany), which was performed in patients with steel implants, when MRI was not possible. Both research methods applied in differential diagnostic cases. Radiological signs of tuberculous spondylitis were one or more of the following: a focus of bone destruction with unclear edges and the presence of a bone sequester inside; presence of abscess with calcification; abscess with subperiosteal extension.

Tissue samples collected from surgical procedures was fixed with formalin, stained with hematoxylin-eosin, and cut with a microtome, than examined under a microscope. Central necrosis, surrounded by epithelioid and Pirogov-Langhans cells confirmed tuberculous inflammation.

Pathologic tissues and fluids collected from surgeries, punctures, fistulas excretions and sputum were studied bacteriologically. Molecular genetic methods were GeneXpert® MTB/Rif (Sunnyvale, California, U.S.A) and GenoType MTBDRplus (Hain Lifescience GmbH, Nehren, Germany). Cultures of mycobacteria growing studied in BACTEC MGIT 960 (Becton Dickinson India Pvt. Ltd., Gurgaon, India) and inoculation of solid Lowenstein-Jensen medium.

STATISTICAL ANALYSIS.

Statistical analysis of the study was carried out using modern computer systems such as IBM/PQ of the latest generation using a package of standard Excel programs.

RESEARCH RESULTS

Tuberculous spondylitis began with pain in the affected part of the spine in 99 (90±2,9%) patients. Fever had 21 (19.1 ± 3.7%) of patients, 14 (12.7±3.2%) of them had loss of appetite and loss of weight, 7 (6.4±2.3%) complained of sweating. The main provoking factors for the onset of the disease were trauma, physical activity and previous colds in 20 (18.2 ± 3.7%), 21 (19.1 ± 3.7%) and 21 (19.1 ± 3.7%) cases, respectively. No provoking factors has 48 (43.6 ± 4.7%) of the patients. Before admission to the RSSPMC of Phthisiology and Pulmonology, patients received various treatments without or with temporary improvement. Six (5.5 ± 2.2%) patients indicated contact with a tuberculous patient. The duration of symptoms was several months, average 15.9 months.

Decreased hemoglobin is a sign of blood loss or malnutrition. Our study results showed decreased blood hemoglobin levels and erythrocytes count in patients with tuberculous spondylitis to the level of 118±9.04 g/l and $3.6\pm0.31*10^{12}$ accordingly, that is corresponds to the mild anemia. Quantitative indicators of the leukocyte formula remained within normal limits: leukocytes - $6.7\pm1.1*10^{9}$, band cells - 1.3±0.9%, segmented cells - 64.2±5.1%, eosinophils - 1.6±0,8%, lymphocytes – 27.2±4.1%, monocytes – 5.5±1.9%. The correlation between hemoglobin and ESR was r = -0.32, a weak negative correlation. Thus, chronic intoxication of tuberculous infection leads to loss of appetite and mild anemia.

Nephropathy in patients with tuberculous spondylitis was characterized by: hyperproteinuria in 29% of patients, multiple epithelial cells in urine sediment were observed in 6.5% of patients, leukocyturia was detected in 25.8% of patients, erythrocyturia detected in 16.1% of patients, and in 16.1% of the patients had various casts in urine. Elevated levels of urea and creatinine in the blood were detected in 6.5% of patients without changes in the renal parenchyma due to neurogenic urinary retention. Ultrasound examination showed salts and kidney stones in 9.7% of patients, while signs of inflammation were observed in 3.2% of patients.

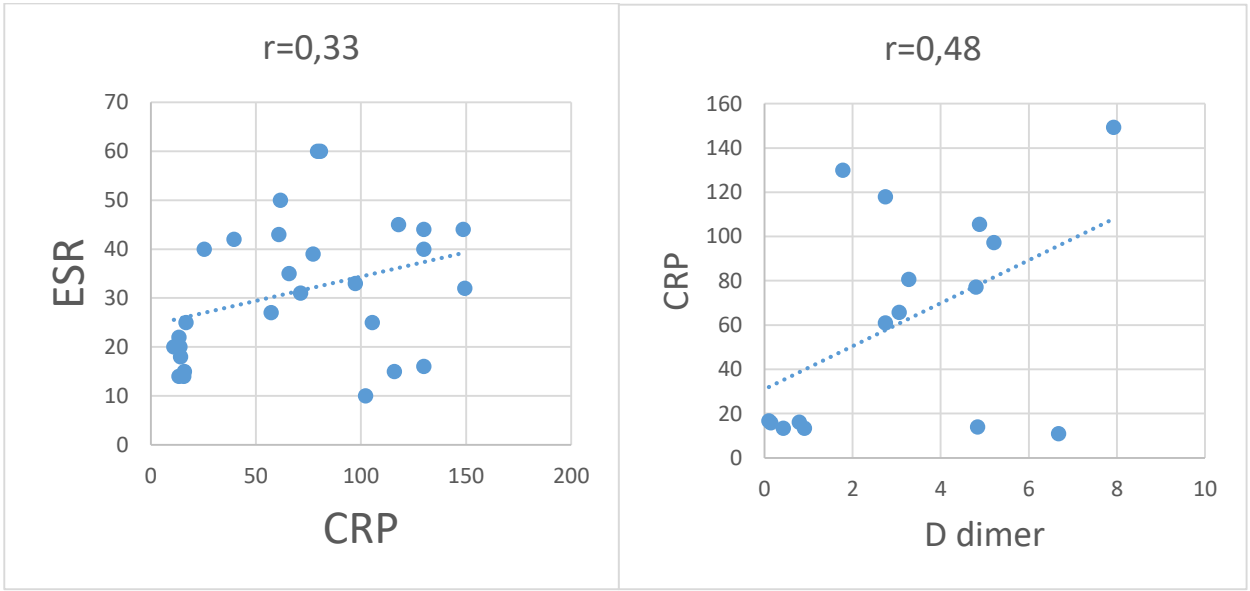
According to ECG data, 32.3±8.4% tuberculous spondylitis patients had sinus tachycardia and 9.7±5.3% of patients had arrhythmia, as a manifestation of tuberculous intoxication, since the dynamics of the ECG showed normal values. Left ventricular hypertrophy as a manifestation of hypertension was detected in

19.4±7.1% of patients. Myocardial ischemia was detected in 9.7±5.3% patients. Dystrophic changes in the myocardium were noted in 60-75 years old patients in 19.4±7.1% of cases.

Secondary hepatitis can be caused by various bacterial, viral infections and intoxication. The liver size enlargement detected in 86.6% of tuberculous spondylitis patients without any focal parenchymal changes. However, alanine aminotransferase and aspartateaminotransferase levels were within the normal limits, 0.56±0.4 mmol/l and 0.46±0.4 mmol/l accordingly.

Blood acute-phase proteins were increased several times in patients with tuberculous spondylitis. “C” reactive protein was 65.3±50.7 mg/ml, erythrocyte sedimentation rate was 30.5±18.4 mm/h. Although the correlation between the increase in ESR and CRP was weak r = 0.33.

Blood coagulation biochemical markers analyses showed an increased level of fibrinogen and D-dimers, 7.75±3.8 g/l and 2.2±2.1 mcg/ml respectively, in patients with tuberculous spondylitis. We also found increased platelet count up to 337.5±109.9, that positively correlated with the blood fibrinogen levels, r=0.35. Nevertheless, fibrinolytic activity of the blood in in patients with tuberculous spondylitis showed decreased levels, 8.98±5.3%. At the same time, there was an inverse correlation between the increase in fibrinogen and fibrinolytic activity, r = -0.4 and no correlation between fibrinolytic activity and the level of blood D-dimers. The D-dimers blood levels were mostly influenced by the degree of inflammation according to CRP, r = 0.5, although there was no correlation between the level of blood D-dimers and ESR (Figure 1).



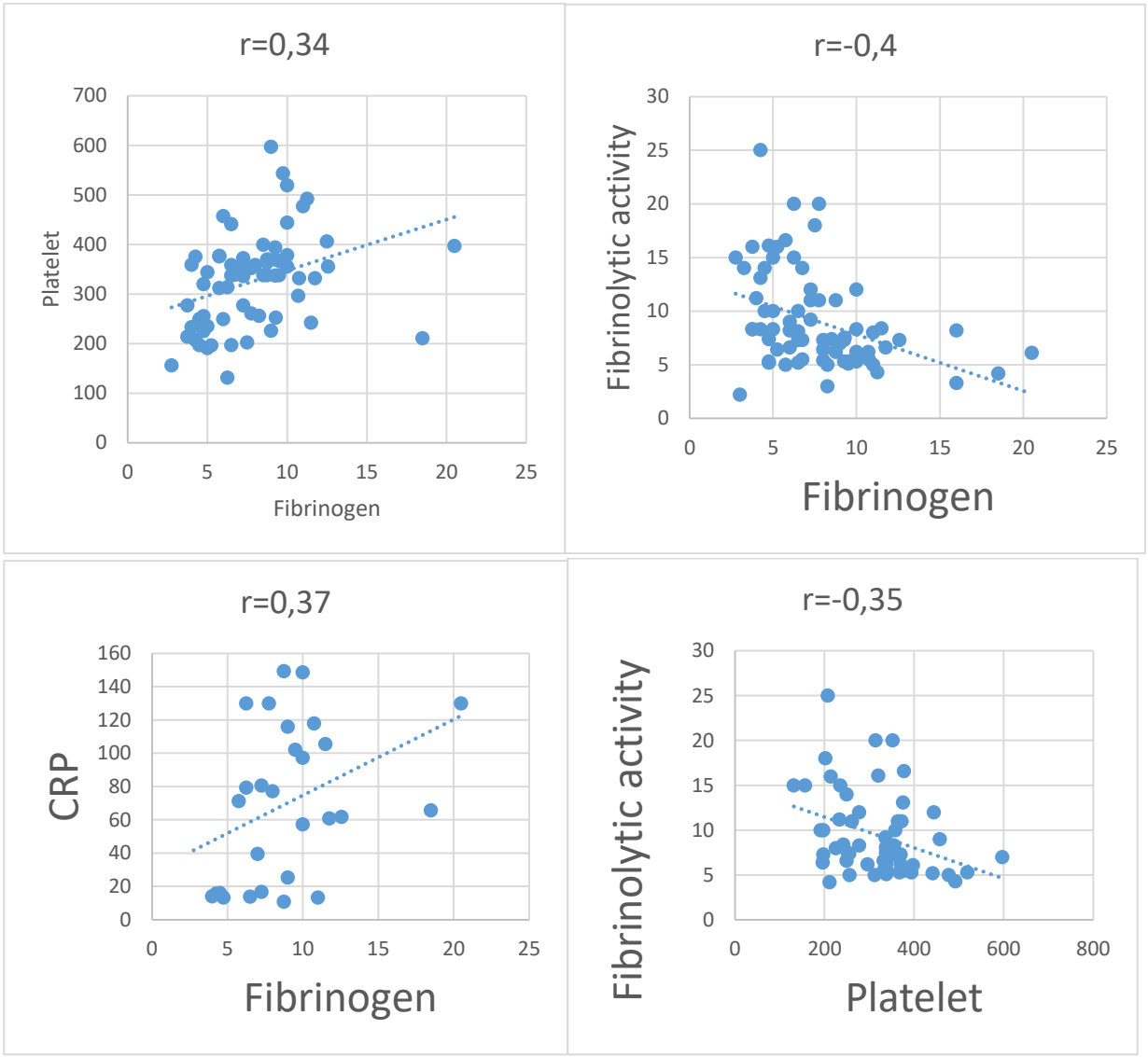


Figure 1.

DISCUSSION

According to the literature, pulmonary tuberculosis causes an increase in fibrinogen and D dimers in the blood. Eteudo A.N. et al., 2017 examination results of 180 tuberculosis and 90 non-tuberculosis subjects (control) showed higher prothrombin time, activated partial thromboplastin time and platelet count values than the control group [6].

Min W et al, 2017 detected the serum D-dimer levels of 192 patients with pulmonary TB and 110 patients with community acquired pneumonia. The results showed significantly higher serum D-dimer levels in patients with pulmonary [9]. Our study results showed an increase in blood fibrinogen levels up to 7.75±3.8 g/l and D dimers up to 2.2±2.1 mcg/ml in patients with tuberculous spondylitis.

Ahmed Abdalla Agab Eldour et al, 2014 assessed the blood coagulation changes in patients with Pulmonary Tuberculosis and concluded prolongation of PT, APTT, thrombocytosis, anemia and elevated ESR [2]. Similarly, decrease of

hemoglobin and erythrocytes, 118±9.04 g/l and 3.6±0.31*10^{12} accordingly, SRP increase up to 65.3±50.7 mg/ml and ESR increase up to 30.5±18.4 mm/h we observed in patients with tuberculous spondylitis. Moreover, the D-dimers blood levels positively correlated with CRP, r = 0.5. Thus, tuberculous inflammation causes increase of blood fibrinogen and D dimers levels despite the localization of the lesion.

Suryakusumah L et al., 2021 study showed higher levels of prothrombin time, aPTT and D-dimer in far advanced pulmonary tuberculosis cases, and decrease of that markers after intensive phase treatment. Author concluded, that pulmonary tuberculosis infection is associated with hypercoagulability [12].

Akpan PA et al, 2017 studied data of 120 TB patients and 120 apparently healthy subjects/ The study results showed significantly higher fibrinogen concentration, fibrin degradation product, interferon gamma as well as interleukin 10 levels of active TB patients versus control subjects indicating the presence of infection-induced inflammatory response which mediates acute phase reaction as well as increase fibrinolytic activity [3].

Our patients' data showed decreased percentage of fibrinolytic activity to 8.98±5.3% measured by Kotovshchikova M.A. and Kuznik B.L. method. Accordingly, high fibrinogen and D dimer serum levels, but low blood fibrinolytic activity suggest that fibrinolysis taking place at the tuberculous inflammation focus. Y. Shen et al., 2017 compared D-dimer levels in pleural effusion of 32 patients with tuberculous pleurisy and 55 patients with non tuberculous pleurisy and concluded that pleural D-dimer levels are higher in tuberculous pleurisy than other causes of pleural effusions [11].

The liver size enlargement detected in 86.6% of our tuberculous spondylitis patients can be explained with enhanced liver synthesis of acute-phase proteins, because transaminase levels was normal.

CONCLUSION

Clinical and laboratory manifestations of tuberculous spondylitis in modern conditions are characterized by mild anemia, an increase in the blood of acute-phase proteins, fibrinogen, D dimers, reactive hepatitis and decrease of the blood fibrinolytic activity.

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