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Tuberculous spondylitis – analysis of 22 cases

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Abstract

Tuberculous spondylitis (TS) frequently poses both diagnostic and therapeutic challenges. The clinical symptoms, radiological imaging studies and laboratory tests are quite often inconclusive in the early stages of the disease.

Goal: To identify early clinical symptoms, review results from radiological imaging studies and laboratory tests to establish their diagnostic value and determine the effect of conservative therapy in patients with early TS.

Results: Twenty two (22) patients with TS subjected to conservative therapy were studied. Medullary compression syndrome was found in 10 patients. The highest diagnostic value was established by Magnetic Resonance Imaging (MRI) data for discitis engaging two adjacent vertebrae and QuantiFERON TB Gold and T SPOT.TB tests. The effect of the disease on 12 patients, whose treatment had started before the collapse of the bodies of the vertebrae was non-occurrence of any residual deformity of the spinal column. The effect on 9 patients, whose therapy started at a later stage was a recovery of the neurological deficiency and deformity occurrence of various degrees.

Conclusion: Repetitive lateral plain radiographs, MRI and QuantiFERON TB Gold test have proven of highest diagnostic value at this stage of the disease in our patients. The presence of clinical data, accelerated ESR levels, plain radiography and MRI evidence of an inflammatory process preceding the occurrence of bone destruction and the formation of paravertebral soft tissue collection provide sufficient reasons to conduct QuantiFERON TB Gold or T SPOT.TB testing and start an anti-tuberculous therapy. In the frequent cases when the diagnosis cannot be sufficiently proven, we recommend empirical anti-tuberculous therapy.

Key words: Tuberculous spondylitis; diagnosis; treatment.

Introduction

Vertebrae and intervertebral discs are the most frequent location of skeletal tuberculosis – a condition known as tuberculous spondylitis (TS) (Macnab and McCulloch, 1990; Boachie and Squillante, 1996; Aggarwal, 2006). In the last decade, there has been an increase in disease incidence on a global scale (Muller, 2000; Sovetova *et al.*, 2001; Zaveckien and Keleras, 2002; Aggarwal, 2006).

Tuberculous spondylitis (TS) frequently poses both diagnostic and therapeutic challenges. For the first time, the English physician Sir Percival Pott (1779) described the clinical signs of TS by the triple combination – gibbus, cold abscessus, paraplegy, and the surgical draining of the abscessus (Macnab and McCulloch, 1990; Boachie and Squillante, 1996). Contemporary diagnostic methods and specific therapeutic and surgical treatment have reduced considerably the incidence of the severe forms of the disease *with paraplegia*, but late diagnosis and inadequate therapy have caused irreversible neurological complications and disability. In the early stages of the disease, the clinical symptoms, radiological imaging studies and laboratory tests are inconclusive, and the determination and confirmation of the diagnosis is extremely difficult.

The goal of this study is to identify early clinical symptoms, review results from radiological imaging studies and laboratory tests to establish their diagnostic value and determine the effect of conservative therapy in patients with early TS.

Materials and methods

The study group consisted of 22 patients diagnosed with TS (16 men and 6 women in ratio 2.7:1) treated conservatively in the period 1998-2008. The patients' average age was 59.3 (33-82 years, SD - 11.2). We have identified considerable increase in disease incidence since 2003 (8 patients before 2003 and 14 after 2003, $p < 0.05$).

Results

Clinical findings

Only 1 patient had a childhood history of tuberculosis, whereas another had developed TS on the background of active infiltrative-pneumonic pulmonary tuberculosis. The thoracic vertebrae were affected in 9 (40.9%) patients; the lumbar vertebrae in 6 (27.3%), and the cervical vertebrae in 4 (18.2%) cases. In 3 (13.6%) patients, the process was divided in two stages, and in 1 patient, more than two adjacent vertebrae were impaired. The patients' complaints were mainly of girdle pains (100%) with nocturnal predilection. In the early stage of the disease, no objective clinical, plain radiographic or computer tomography evidence was established. Later, the astheno-adynamy (11 patients, 50%) and consumption (8 patients, 36.4%) syndromes were manifested. Subfebrility was found in 12 (54.5%) of our patients. The average time elapsed from the occurrence of the symptoms to the making of the diagnosis was 46 days (24-115, SD - 25). In 10 (45.5%) of our patients, the diagnosis was determined at a late stage of the disease when ostheolysis had developed, and the vertebral bodies collapsed, forming a compressed medulla syndrome. The average duration of the symptoms of this compression from the onset of the complaints was 62 days (48-105, SD - 16). During that period the patients were immobilized by the pronounced vertebral syndrome and the severe spinal pains experienced by attempting physical mobility.

The changes in the white blood cell line had poor diagnostic value and were inconclusive. Five (22.7%) patients had mild leukocytosis (11.1-14.8 $\times$ 109/l), 7 (31.8%) had leukocyte shift to the left combined with lymphopenia in 3 of them, and one patient's lymphocytosis was up to 44%. Two of the patients with osteolysis had serum alkaline phosphatase near the upper reference margin (270 and 293 E/l). All patients had increased Erythrocyte Sedimentation Rate (ESR) levels – 101 mm/hour on average (75-115). The intradermal tuberculin Mantoux test had no diagnostic value as no patients gave a positive response. The Adenosine deaminase (ADA) and Quantitative polymerase chain reaction (QPCR) in serum were tested in 16 patients, and they were all within reference values. Surgical decompression was administered to 5 patients, and the histological examination revealed granulomatous inflammation with areas of caseous necrosis in 4 of them. One of the patients' histological results indicated a chronic non-specific inflammation. Inoculations of tissue samples from all operated patients were placed into Lowenstein-Jensen medium. The inoculations of 4 patients remained sterile; in 1 patient, the diagnosis was confirmed by positivisation of inoculations on the 52nd day. Immunological tests for rapid diagnosis of tuberculosis were done on 12 of the patients (QuantiFERON TB Gold tests on 9 patients and T-SPOT.TB tests on 3 patients). These tests detected the release of IFN-γ from lymphocytes of sensitized patients when their blood was incubated with peptide mixtures simulating two M. tuberculosis proteins called ESAT-6 and CFP-10. The QuantiFERON TB Gold test was positive on 8 of the tested patients, and the T-SPOT.TB test was positive on 2 of the patients.

The plain radiography of the lungs attested to calcificates in 4 patients; one had signs of infiltrative pulmonary tuberculosis and one of a pleural effusion. The most characteristic radiographic symptom of the disease in its early stages when the process is localized only in the intervertebral disc was the rapid lowering of the disc height revealed by repeated plain radiography every 7-10 days (Fig. 1). All patients in the early stage of the disease had this finding and the computed tomography did not establish any abnormalities. MRI established bone marrow edema in the adjacent vertebral bodies and a hyperintense (in T2) and hypointense (in T1) collections in the affected disc (Fig. 2). In the later stages of the disease, the radiological methods reveal various degrees of roughness on the disc surfaces of adjacent vertebrae, with bone structure scarcity, most pronounced ventrally, osteolysis and a collapse of the vertebral body (Fig. 4). The described lesions are associated with expressed paravertebral and epidural soft tissue collection increasing its denseness along the periphery after the introduction of contrast matter. A similar finding was observed in 12 patients. In 5 of them, the CT finding was interpreted as a tumor process or metastasis in the vertebral body.

Treatment outcome

The treatment we applied to patients with compression syndromes from the medulla or cauda equina was a combination of four tuberculostatics in the first 20 days (Streptomicin 1 g/24 h, Rifampicin 600 mg/24 h, Ethambutol 15 mg/kg/24 h, Rimicid 5 mg/kg/24 h), a triple combination by the 6th month and two drugs by the 9th or 12th month depending on the gravity and the evidence of the control MRI in the 9th month. Moderate corticosteroid doses were administered in the first month as additional treatment. The patients without signs of medulla compression followed the same therapeutic regimen, but without Streptomicin and corticosteroids. One of the patients had liver cirrhosis; therefore, he was

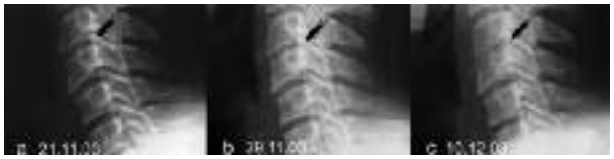

FIG. 1. — Plain radiography of a 57-year old man followed up dynamically on the 1st, 8th and 19th day. Pronounced narrowing of the disc space between C3 and C4 with formation of an osteolytic foci on the anterior disc surface of C4 is observed.

FIG. 2. — MRT of the same patient on the 24th day. The T2W images (a) show high signal changes in the bodies of C3 and C4 and the residue of the intervertebral disc, liquid collections under the anterior and posterior longitudinal ligaments along C2-C4. The TIRM images (c) (technique suppressing the signal of the fatty tissue and sensitive to presence of liquid) show high signal the bodies of the two vertebrae (marrow edema). No changes in the transversal dimensions, contours and signal intensity of the myelon are observed.

FIG. 3. — MRT of the same patient at the 9th month of the treatment. TIRM images do not reveal signs of signal amplification; no para-, pre-and epidural collections and changes in the myelon are seen. The disc between the two vertebrae, though substantially narrowed is preserved and there is no fusion and marked deformation. No signs of canal stenosis, changes in the myelon and process activity are established.

FIG. 4. — MRT of 67-year old patient at diagnosing. The sagittal T1W and T2W images (a and b) at level h5- h6 is seen high extent fusion of the two vertebral bodies. TIRM images (c and d) show that those vertebrae are high signal, similar zones are found also in the bodies of the adjacent Th4 and Th7 vertebrae. The same technique differentiates paravertebral, prevertebral and epidural high signal collections, the latter causing myelon compression and high signal changes in it.

FIG. 5. — MRT of the same patient at the 12th month of the treatment. TIRM images do not reveal signs of signal amplification, no para-, pre- and epidural collections as well as myelon changes are seen. The two vertebrae are fused with gibbus formation. No signs for stenosis of the canal, changes in the myelon and process activity are observed.

given a triple combination of reduced doses throughout a 14 month treatment. On the 5th month of discontinuation of the treatment, the overall condition of patients deteriorated, as observed by the clinical and MRI evidence. This called for additional 6 months of therapy. After the start of the additional treatment, the radicular pains submerged by the end of the first week. Patient mobility became possible after the 2nd/3rd week (depending on the extent of bone destruction) with the use of lumbostat, thoracal corset or a neck collar. Towards the end of the second week of anti-tuberculous therapy, ESR values decreased by 15%-25%, and by the end of the 4th week, they went down another 40%-50%. ESR normalization occurred between the 2nd and 4th month depending on the severity of the process at the onset of the treatment. In 12 of the patients where the therapy had started at the stage of discitis and osteolysis of the adjacent surfaces of vertebral bodies, the disease ended with the preservation of the disc space without fusion of adjacent vertebrae and residual deformity (Fig. 3). In 9 of the patients with compression syndrome and vertebral bodies collapse, the disease outcome was a recovered neurological deficiency (in two with residual pyramid signs), fusion of adjacent vertebrae with residual deformity of the spinal column (Fig. 5). One patient, after shown clinical improvement in the 5th week of the therapy, developed hemolytic anemia and liver insufficiency, possibly associated with the tuberculostatic therapy, and passed away.

Discussion

In our study, TS affected mainly the age group 50-75. The disease onset is vague and its course is chronic. Back pain is observed as the most common symptom. The unclear onset and the lack of plain radiography at the time of first complaints delay the diagnosis usually by 5-10 weeks. With the progress of the pathological process, pain consistently

intensifies, particularly during night-time (McLain and Isada, 2004). The clinical finding depends on the stage of the disease. Usually, the local pain is accompanied by radicular symptomatics, and in later stages also by symptoms of compression of the medulla or cauda equina. Pronounced vertebral syndrome, scoliosis, local palpatory and percutory pain are established. Other clinical symptoms are intermittent subfebrility, sweating, anorexia, easy fatigue and weight loss.

ESR level increase is always observed and is the most reliable test for tracking the activity of the disease and the effectiveness of the treatment (Macnab and McCulloch, 1990).

The plain radiography finding manifests itself 4 weeks or later after the clinical manifestation of the disease (Macnab and McCulloch, 1990). In all our patients, the process had started from the intervertebral disc next involving the two adjacent vertebrae. The earliest finding that we established, unlike other authors (Hershey *et al.*, 1999), was the rapid narrowing of the disc space followed by focal destruction of the disc surfaces and cuneiform collapse of the adjacent vertebral bodies. During the initial stages of observation the picture is similar to that of degenerative vertebral changes, which on their own can cause back pain, so there is a possibility of misinterpretation of the finding. This shows that there are no early specific X-ray signs enabling the differentiation between narrowing of disc space resulting from an infection and that associated with degenerative changes. The routine plain radiography is of greater importance for the location of the process rather than the tuberculosis diagnosis in the initial stage of the disease. Plain radiographs made each 7-10 days, we find, have high diagnostic value in the very early stages of the disease development. The established quick narrowing of the disc space is a reliable sign of an inflammatory process (Macnab and McCulloch, 1990).

CT has little diagnostic value in the early stages of the disease and in an advanced process with osteolysis, there could be difficulties in differentiating from neoplasms (the disc space with the latter is usually preserved) (Smith *et al.*, 1989; Macnab and McCulloch, 1990; Jinkins, 2002). The tuberculin test, ADA and QP R in serum did not have diagnostic value in our cases. In the early stages, MRI is a method of choice and can visualize the changes pointing to an infection much better – high signal intensity on T2-weighted and TIRM images from the involved disc and adjacent vertebrae (Smith *et al.*, 1989; Desai, 1994; Jinkins, 2002; Narlawar, 2002; Sinan *et al.*, 2004; Teo and Peh, 2004). However, there is no reliable MRI criteria to differentiate between pyogenic and tuberculous spondylitis (Smith *et al.*, 1989; Lindahl *et al.*, 1996). MRI is the method of choice to determine the efficiency and duration of the treatment.

The histological and microbiological examination after needle aspiration biopsy or surgical intervention is the most reliable method for determination of the diagnosis (Berk *et al.* 1996; Francis *et al.*, 1999), however, it is inapplicable in patients at an early stage of the disease. Although lacking 100% sensitivity, modern immunological methods have made it possible to diagnose the disease at the earliest stages in most of the patients. In 10 out of 12 patients, the diagnosis was confirmed with those tests. In 4 out of 5 patients subjected to surgical treatment, the diagnosis was confirmed with biopsy. To confirm the diagnosis, we used an empirical therapeutic test with tuberculostatics with the other 8 patients. All patients had experienced clinical and roentgenological aggravation on the background of parenteral treatment with broad-spectrum antibiotics. The effect of empirical treatment is evidenced in the first 2-3 weeks and results in decreased pain, asthenoadynamic syndrome and reduction of ESR values. In the absence of response to anti-tuberculous therapy in the first 30 days another pyogenic infection or bone metastases should be considered.

Conclusion

Regardless of the advancement of current immunological and radiological methods, the diagnosis of spinal tuberculosis is still a challenge to physicians, especially in the early stages of the disease. Repetitive lateral plain radiographs, MRI and QuantiFERON TB Gold test have proven of highest diagnostic value at this stage of the disease in our patients. The presence of clinical data, accelerated ESR levels, plain radiography and MRI evidence of an inflammatory process preceding the occurrence of bone destruction and the formation of paravertebral soft tissue collection provide sufficient reasons to conduct immunological tests and start an antituberculous therapy. In the cases when a TS diagnosis is likely but not proved, it is appropriate to start an empirical antituberculous therapy. Any delay of the treatment seeking confirmation of the diagnosis would cause permanent deformities, neurological deficiency or bad outcome and therefore would be unjustified. The precise diagnosis of the disease requires a correlation between the clinical signs and data from plain radiography, radiological imaging methods and laboratory tests (Smith *et al.*, 1989). In spite of the progress in diagnostic methods, positive response to empirical antituberculous therapy to

determine a reliable diagnosis is not always possible (Berk *et al.* 1996; Francis *et al.*, 1999; Jinkins, 2002; Golden and Vikram, 2005; Aggarwal, 2006).

The treatment of TS is usually conducted with medications although indications and surgical methods are still under discussion (Rezai *et al.*, 1995; Boachie and Squillante, 1996; Fukuta *et al.*, 2003; Wood, 2003). The results of our study enable us to recommend surgical treatment only for patients with signs of pronounced medulla compression and severe motion deficit. In the case of early diagnosing, a 9-12-month treatment course with a triple combination of antituberculous medications and lack of evidence for activity of the process from a control MRI is sufficient (Horsburgh *et al.*, 2000).

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