Advanced Multifocal Tuberculous Spondylitis without Disk Involvement and with Multidrug-Resistant Bacilli

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In this brief report, we describe a 23-year-old immunocompetent Nigerian patient with extensive multifocal tuberculous spondylitis without disk involvement. Cultures of sputum samples and biopsy samples from the L4 vertebra were positive for tuberculosis; drug-susceptibility testing of the isolates revealed multidrug resistance. Treatment with second-line drugs resulted in an excellent interim outcome after 6 months, without the need for surgical intervention.

A 23-year-old Nigerian man was admitted to the Asklepios Professional Clinic München-Gauting (Gauting, Germany) because of suspected tuberculosis (TB) of the right upper lobe at the end of May 2006. Tuberculin skin test results were highly positive. The patient had a history of weight loss and reported intermittent backache, which was absent at physical examination. No other symptoms had been observed. The results of routine laboratory tests were within normal limits, except for a C-reactive protein level of 94.4 mg/L. HIV test results were negative.

A standard antituberculosis treatment regimen, consisting of isoniazid, rifampicin, pyrazinamide, and ethambutol, was started. The diagnosis of pulmonary TB was confirmed by laboratory culture result. The patient was discharged from the hospital by the middle of July 2006.

Two weeks later, drug-susceptibility testing performed on the patient’s isolate revealed multidrug-resistant TB (MDR-TB), with resistance to isoniazid, rifampicin, pyrazinamide, streptomycin, and pyrazinamide, and susceptibility to ethambutol, cycloserine, moxifloxacin, ciprofloxacin, amikacin, linezolid, capreomycin, and paraaminosalicylic acid.

At approximately the same time, the patient was admitted to another hospital with severe backache and fever (temperature, up to 38.8°C). Cervical, thoracic, and lumbal radiographs showed no osseous abnormality, and a bone scan was without pathological findings. However, MRI and CT of the vertebrae showed a massive and multifocal destruction of 15 vertebral bodies.

CT revealed osseous destructions of all displayed vertebral bodies from Th9 continuously to S2 and S4 in the anterior, central, and posterior elements, but not of the end plates (figure 1). CT further demonstrated small paravertebral abscess formation at the left side of Th9 and Th10, with a small pleural effusion and a small abscess formation in the adjacent muscles of the back (not shown).

MRI was performed with sagittal T1- and T2-weighted spin echo sequences showing increased signal intensities within the vertebral bodies Th4–6, Th9, Th10, Th12, L1, L2, L4, L5, S1, and S2, as well as a right paravertebral abscess formation along Th3–5 (not shown). No intraspinal or disk enhancement was seen (figure 2). Chest radiography showed a basal pleural opacity on the left side, consistent with a dissemination of the paravertebral abscess per continuitatem, and a small-sized swell paravertebral on the right side (figure 3).

Because CT and MRI findings did not allow for a final diagnosis, a surgical biopsy of L4 was performed. The histopathologic examination of the sample showed necrotizing epitheloid cellular granuloma. The culture sample was positive for TB, and drug-susceptibility testing of the isolate resulted in a drug-resistance pattern identical to that of the isolate obtained from the sputum culture.

The patient was transferred to the Asklepios Professional Clinic München-Gauting for further antituberculosis treatment. At readmission to the hospital, the patient’s C-reactive protein level was 141.4 mg/L, and the patient’s γ-glutamyl transferase level was 151 U/L. On physical examination, the patient had diffuse back pain without neurologic deficits. Because the patient had infection due to proven MDR-TB, we administered a second-line treatment with linezolid (600 mg once daily), moxifloxacin (400 mg once daily), cycloserine (500 mg morning dose and 250 mg evening dose), ethambutol (1.6 g once daily), and amikacin (a 1-g dose administered 3 times
Figure 1. Two different layers of a sagittal reconstructed spiral CT of the lower thoracal, lumbal, and sacral vertebra showing extensive osseous destruction of Th9, Th10, L1, L4, L5, S1, and S4. More discrete involvement is seen in Th11, Th12, L2, L3, S2, S3, and S5 (seen in other layers). The margin of osseous destruction shows sclerotic reaction. Neither collapse of a vertebral body nor end plate or disk involvement are present.

Figure 2. A, Midsagittal T1-weighted spin echo image (400/7.8 milliseconds) of the cervicothoracic spine, demonstrating increased signal intensity in Th4, Th5, and Th6 with paraspinal abscesses in Th3–5. B, Midsagittal T2-weighted spin echo image (3500/100 milliseconds) showing increased signal intensity in Th4–6, Th9–12, L1, L2, L4, L5, and S1. Abscess formation is present in Th4, Th5, Th9, Th10, L1, L4, L5, and S1. No epidural or intraspinal involvement is seen. Because the MRI was obtained later in the course of disease, the signal intensity is similar for the T1- and T2-weighted spin echo images.

per week). Strict bed rest was not prescribed; however, a corset was worn during the first 3 months after treatment to prevent fracture. The routine surgical approach to the treatment of spondylodesis (i.e., debridement, grafting, and fixateur interne) was not recommended because of the multifocal destruction of the vertebral bodies.

The treatment was well tolerated. Moderate leukopenia (WBC count, >3.1 cells/μL) did not require a modification of therapy. The symptoms of backache disappeared completely within 3 months. After 6 months of inpatient treatment, MRI and CT findings demonstrated an excellent interim outcome, without any collapse of a vertebral body or residual abscess formations (figure 4). Directly observed outpatient treatment with linezolid, moxifloxacin, and ethambutol was prescribed for an additional 18 months. To date, the patient is highly compliant with therapy, has received regular outpatient treatment for 5 months, and is in excellent clinical condition.

Discussion. Of >500 patients with cases of tuberculous spondylitis without disk involvement (SPwD) or tuberculous spondylodiscitis (SPD) in our tertiary care center since 1981, this is the first patient to present with such extensive disease. The singularity of this case consists of the following findings: the magnitude of having 15 affected vertebral bodies, with involvement of anterior, central, and posterior elements; the lack of involvement of any vertebral disk or vertebral end plate without vertebral collapse, despite extensive disease; the relatively small paravertebral abscess formations; the lack of intraspinal involvement; the lack of neurological symptoms, despite involvement of the posterior parts of the vertebral bodies Th10, L1, L4, L5, S1, and S4; the lack of predisposing factors, such as HIV infection, drug addiction, alcoholism, diabetes, debilitation, previous tuberculous disease, detention, or residence in a refugee camp; and the presence of MDR-TB in a Nigerian citizen (insofar as Nigeria is not a country with a high prevalence of MDR-TB), diagnosed by culture of a sputum sample and a spine biopsy specimen.
Two distinct patterns of spinal TB can be identified on the basis of findings from plain radiographs, CT, and MRI: SPD and SPwD [1, 2]. SPD is characterized by destruction of ≥2 adjacent vertebrae and by opposed end plates, disk infection, and frequently paravertebral abscesses. In a retrospective French study involving 103 patients in whom spinal TB was diagnosed, 51 had SPD, and 52 had SPwD. Patients with SPwD were younger, were more likely to be immigrants (especially from sub-Saharan Africa), and were more likely to have TB foci at multiple spinal sites and at extraspinal skeletal sites [1].

The typical MRI pattern shows a decreased signal intensity in T1-weighted images of affected vertebral bodies and disks and an increased signal intensity in T2-weighted images of osseous and soft-tissue changes. In patients with late chronic vertebral TB, signal intensity is variable [2], as demonstrated in our case by a similar signal intensity in T1- and T2-weighted spin echoes.

Further atypical patterns of tuberculous involvement of the spine consist of infection of a single vertebra [3, 4] or multiple nonadjacent vertebrae (“skip lesions”) [5]. In the rare cases in which there is involvement of the posterior parts of the vertebral body or the neural arch, intraspinal abscesses are common [4].

In patients with SPwD, a lack of pathological findings on the conventional radiographs of the spine and the bone scan is described in 9% and 8% of patients, respectively [1]. Because of this, it is more than noteworthy that our patient not only had an atypical clinical presentation, with only mild symptoms, but also did not have imaging findings indicating any osseous abnormalities.

MRI has not demonstrated a statistically significant advantage, compared with CT, in detecting disease in individuals with chronic TB. Although CT and MRI are reliable in helping to differentiate spinal infections from one another or from neoplasm, biopsy or CT-guided fine-needle aspiration are still essential for diagnosis and adequate treatment.

In the literature, very few cases of SPwD or SPD comparable to our case can be found. Only 1 patient received a diagnosis after several percutaneous vertebroplasties with a similar extensive disease, with involvement of vertebral bodies Th10, Th11, L3, L4, L5, and S1 [6], and 3 patients received diagnoses with cervical, thoracic, and lumbar involvement but without disk involvement [1].

Because of the extent of the disease, the main differential diagnosis in such a case is metastatic neoplasia. The common form of pyogenic spondylitis is usually confined to a few vertebrae. Viral, fungal, and parasitic lesions or primary tumors are not very extensive. The very rare spinal echinococcosis,
which is endemic in the Middle East and India, often involves soft tissue and the epidural space [7]. Therefore, this atypical case could be referred to as a “metastatic” form of tuberculous spondylitis. Because our patient presented with such widely disseminated disease, it is noteworthy that deformities such as gibbus or consecutive neurological disorders could be prevented without the need for surgical intervention. Even more remarkable is the fact that, despite the diagnosis of MDR-TB infection, an excellent interim outcome was achieved with adequate second-line therapy.

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References