MULTIPLE DRUG-RESISTANT LUMBOSACRAL TUBERCULOUS SPONDYLITIS IN A FOREIGN-BORN IMMUNOCOMPETENT YOUNG ADULT- A CASE REPORT

Jui-Teng Chien, Kun-Huei Lin

The emergence of multiple drug-resistant strains of tuberculosis (MDR-TB) should be suspected if treatment failure occurs because globally its incidence is increasing. A 25-year-old Tibetan lama presented with a 2-month history of fistula formation over his low back and left thigh. He underwent wound debridement at another hospital with the diagnosis of cellulitis and osteomyelitis of the spine. On presentation, he was ambulatory with moderate back pain. MRI revealed lumbosacral spondylodiscitis, presacral abscess, and psoas abscess. With no clinical improvement after two weeks°¶ 4-drug anti-TB chemotherapy, he underwent anterior corpectomy and fusion. Wound dehiscence developed one week postoperatively and debridement was repeated for three times. Profuse caseous discharge persisted in the following eight weeks despite the continued anti-TB regimen. Susceptibility tests performed during the last debridement proved to be mycobacterium tuberculosis resistant to INH and RIF. After shifting to second-line anti-TB drugs, both flank and thigh wounds healed rapidly.

With the increasing prevalence of MDR-TB, the treatment of TB spondylitis must take into account the possibility of drug resistance especially in immigrants from TB-endemic countries and in patients having a history of anti-TB drug use or TB-related surgical procedures.

Keywords: lumbosacral spondylitis, multiple drug-resistance tuberculosis
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INTRODUCTION

Spinal tuberculosis (TB) is a dangerous form of skeletal TB because of its ability to cause bone destruction, deformity, and paraplegia. The emergence of multiple drug-resistant strains (MDR-TB) should be suspected if treatment failure occurs, either medically or surgically, because its global incidence is increasing[3,4]. Patients with MDR-TB are more difficult to treat, remain infectious for longer period of time, and may pose a

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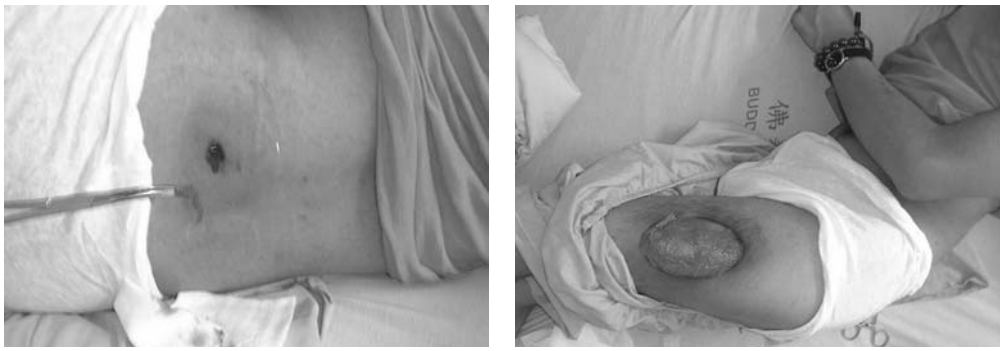


(a) (b)

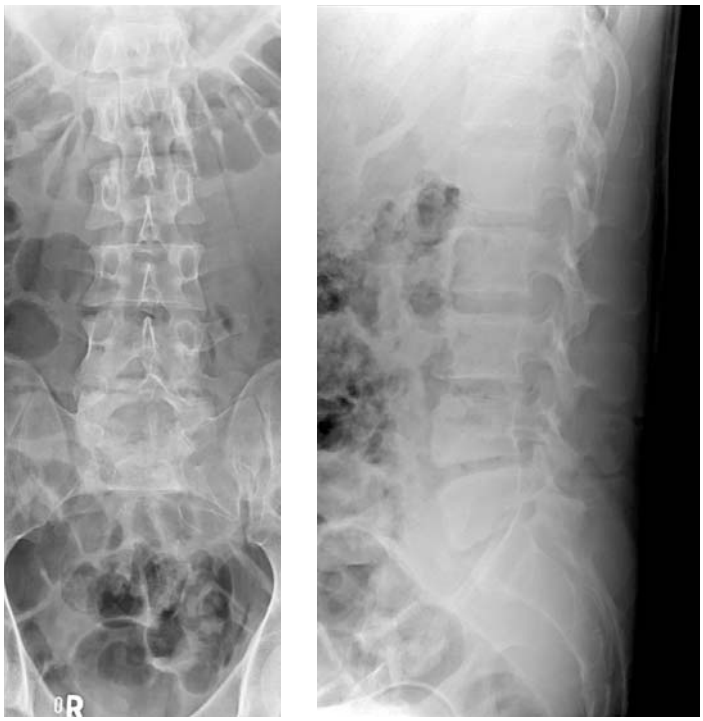
Fig. 1:
Fistula formation over the back (upper) and left thigh (lower).

public health hazard[5]. Increased migration, international travel, along with the vast number of foreign workers has hastened the spread of TB from highly endemic regions to Taiwan. We report a case of lumbosacral spondylitis caused by MDR-TB presenting with back and thigh fistula in a young Tibetan lama.

CASE REPORT

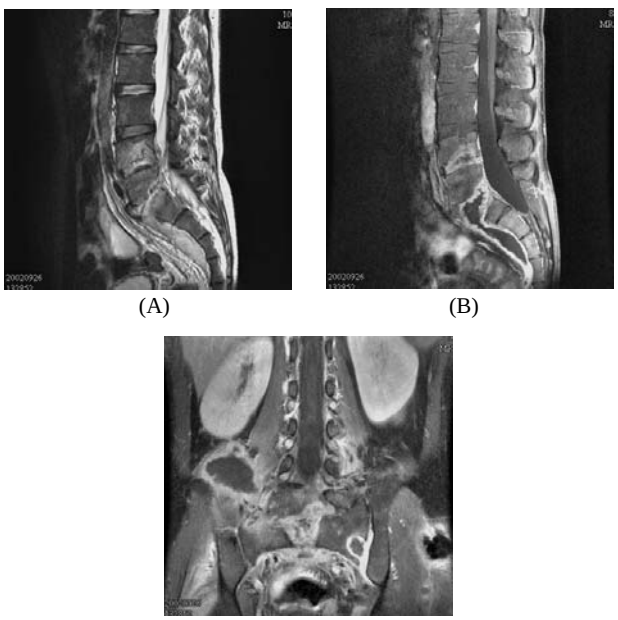
A 25-year-old man, a Tibetan lama born in Nepal, was referred to our hospital in September 2002 with a 2-month history of fistula formation over his low back and left thigh. As he recalled, a back mass developed in January 2002 when he was still in India, the country where he lived for the most of his life before he came to Taiwan. Incision/drainage was performed there and anti-TB medication was prescribed for a few weeks. Soon after he arrived at Taiwan in July 2002, severe back pain, spiking high fever, and left thigh fistula developed. He was sent to a local hospital where he underwent local wound debridement and was given parenteral first-generation cephalosporin under the impression of cellulitis of the thigh and osteomyelitis of the spine, without mentioning any diagnosis related to tuberculosis. Back pain and fistula persisted postoperatively, so he was transferred to us after 5 weeks' hospitalization.

On examination, he looked well-nutritioned and was ambulatory. He was afebrile and had no coughing. The only complaints were wound pain and moderate lower back pain after walking for longer distance. No motor or sensory deficits or sphincter dysfunction were detected. The fistula over his lower back and the left thigh were deep and were discharging profusely (Figure 1). Laboratory tests were unremarkable except for the elevated sedimentation rate and the C-reactive protein. The chest radiograph was normal with no detectable scarring or cavitary lesions. The lateral radiograph of the lumbar spine revealed endplate erosion and decreased disc height over L4/5 and L5/S1 (Figure 2-A). The anteroposterior view showed slight bulging of the right psoas muscle (Figure 2-B). Magnetic resonance imaging (MRI) demonstrated L4/5 and L5/S1 spondylodiscal destruction and a presacral, well-demarcated abscess that exhibited high signal intensity on T2-weighted sequence (Figure 3-A) and strongly enhanced peripheral ring after injection of gadolinium (Figure 3-B). The coronal MRI revealed a well-encapsulated abscess formation over both the right psoas muscle and the left inguinal area (Figure 3-C). Under the impression of TB lumbosacral spondylits with presacral/psoas abscess and fistula formation, empirical anti-TB regimen with Rifater (Rifampicin 120mg、Isoniazid 80mg、Pyrazinamide 250mg) and ethambutol (EMB) was initiated as suggested by the chest medicine internist. Two weeks later, no obvious clinical response was seen. Therefore, he underwent abscess evacuation, anterior debridement with partial corpectomy of L5, fusion with humeral allograft from L4 to S1, which was supplemented with posterior instrumentation under the same anesthesia (Figure 4). Unfortunately, left flank wound erupted one week postoperatively. Vigorous debridement was repeated for 3 times. However, profuse caseous fluid discharge persisted in the following 8 weeks



(a) (b)

Fig. 2.: (A) Lateral X ray showing L4/5 and L5/S1 disc space narrowing with end plate erosion (B) AP view showing mild bulging of right psoas muscle.



(A) (B) (C)

Fig. 3.: (A) T2-weighted sagittal MRI revealing extensive L4/5 and L5/S1 spondylodiscal destruction and (B) strongly enhanced peripheral ring after injection of gadolinium of the well-demarcated presacral abscess. (C) Coronal MRI revealed abscess formation over right psoas muscle, left sacroiliac joint and left thigh.

despite the continued use of the anti-TB regimen and bedside wound care. In the last debridement done in November 2002, pus culture was repeated and drug susceptibility tests were performed. Strains of *mycobacterium tuberculosis* resistant to both isoniazid (INH) and rifampin (RIF) but sensitive to EMB were identified. After switching to second-line anti-TB drugs (para-aminosalicylic acid, Prothionamide, EMB, PZA), the patient showed significant clinical response with decreased discharge in just 4 weeks. The flank and thigh wounds healed uneventfully after another minor wound debridement. The same anti-TB medication was continued for 6 months until May 2003 when he returned to India. Via telephone interview in September 2004, he stated that he was doing well with only mild soreness over his lower back after longtime standing or walking.

DISCUSSION

Despite the many advances of modern medicine, tuberculosis (TB) remains one of the world°¶s leading infectious causes of death. Drug resistant tuberculosis has

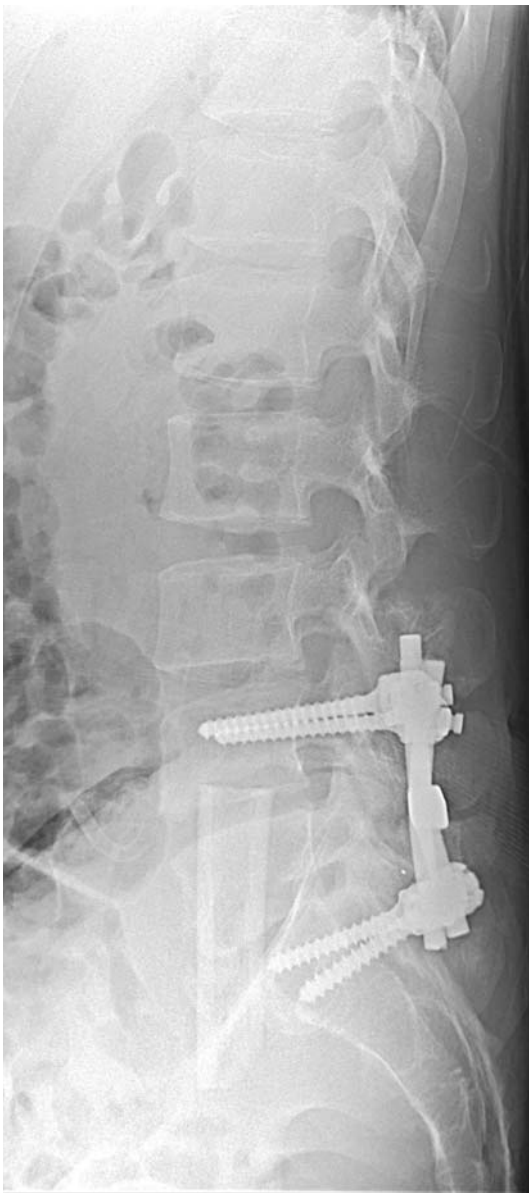


Fig. 4.: Seven months after L5 partial corpectomy, L4-S1 interbody support with humeral allograft, and posterior instrumentation from L4 to S1.

been recognized since chemotherapy first became available in the 1950s. Multiple drug-resistant tuberculosis (MDR-TB), defined as resistance of *Mycobacterium tuberculosis* to at least isoniazid and rifampin, emerged recently and has become a worldwide problem with increasing prevalence even in the industrialized countries[4]. In a recent survey of 35 countries, 12.6% of *Mycobacterium tuberculosis* isolates were resistant to at least one drug, and 2.2% were resistant to both INH and RIF[12]. Several recent surveys reported that the prevalence of MDR-TB ranged from 3.9% to 10% in different areas of Taiwan[8,10,18]. In some highly endemic countries such as Nepal and northern India, the rates of MDR-TB were reported to be 48% and 33.8% respectively[3,17].

Spinal TB is the most common form of skeletal TB, accounting for about 50% of all skeletal TB, which itself contributes 15% of the extrapulmonary TB[13]. It can affect all levels of the spine, most commonly the thoracic but relatively uncommon the lower lumbar vertebrae (10-15%) and the lumbosacral region (2-3%)[14,15].

Chemotherapy is the mainstay treatment for most tuberculosis patients. However, surgical treatment for spinal tuberculosis has the following advantages: earlier cure by extirpation of the infected focus, histological confirmation of diagnosis, shortening the duration of chemotherapy, correction/prevention of deformity, and early effective neurological recovery[1,2,11].

The reasons of initial treatment failure in this patient were multiple. Surgical debridement and bone fusion were helpful in evacuation of the abscess, reduction of the bacterial load, and restoration of the spinal stability. In the presence of severe back pain, marked bony destruction, and massive lumbosacral abscess, a delay of two weeks for the empirical use of anti-TB chemotherapy was probably unnecessary although there were no neurological involvements as commonly seen in cervical or thoracic tuberculosis. Our failure in earlier detection of the emergence of MDR-TB, which had more aggressive virulence and infectivity than the drug-susceptible strains[5,20], further compromised the treatment outcome. Despite the profuse discharge and poor wound healing persisting for several weeks postoperatively, we had never thought of the possibility of drug resistance until the last debridement when the pus was re-cultured and drug susceptibility test was performed for the first time. Drug susceptibility tests allow the treatment to be modified but it may take several weeks due to its slow growth. In recent years, polymerase chain reaction (PCR) has been helpful for earlier and more rapid detection of *M. tuberculosis* bacilli than the conventional phenotypic

assays. Because PCRs do not rely on *in vitro* growth, these genotypic methods can potentially reduce the diagnostic time for resistant strains from weeks to days[16].

Controversies still exist in terms of the duration of chemotherapy. To eradicate tuberculosis and to prevent recurrence, a four-drug regimen (INH, RIF, EMB, and PZA) given for at least 12 months is advocated to treat spinal tuberculosis[11]. For MDR-TB, the second-line drugs should be continued for at least 18 months even after surgery[21]. The reported patient received only 6 months of second-line anti-TB chemotherapy because his visa expired before a full course could be completed. Fortunately, he had excellent response to the second-line drugs with good wound healing and relief of back pain. By the time he left Taiwan, negative conversion of the pus culture was confirmed. On telephone interview about two years after the initial surgical treatment at our institute, the patient reported only minor symptoms although some dislodgement of the humeral allograft was seen on the last radiograph taken about 7 months postoperatively. Further dislodgement or even pseudarthrosis might have actually occurred but the remaining anterior structures supported by the posterior instrumentation and fusion could be attributable to the good result.

There were several predisposing factors for this patient to develop MDR-TB. As a lama born in Nepal but raised in India, the patient spent most of his life in northern India where TB had been highly endemic and MDR-TB was prevalent[13,17]. Additionally, he stated that he had contracted TB before he came to Taiwan and had been treated with local debridement over his back mass and medication which presumably was either inadequate or incomplete. According to Iseman and Madsen[6], the most powerful predictor of the presence of MDR-TB is a history with previous treatment for TB. Patients from countries with endemic MDR-TB populations have an increased risk for harboring MDR-TB, either through primary infection with a resistant strain or resistance development through inadequate or incomplete anti-TB treatment[7].

The initial unhappy experience in the management of this patient highlights several important concerns in face of MDR-TB. First, the prevalence of MDR-TB is increasing globally even in developed countries such as Taiwan[8,10,18]. Therefore, MDR-TB should be strongly suspected if unusual treatment failures occur not only in foreign-born patients but also in local cases. Second, patients infected with MDR strains are more difficult to cure and more likely to remain sources of infection for a longer period of time[9,19]. If not detected and treated properly, the close contact between the preaching lama and the followers in the auditorium or temple may pose great risks of disease transmission. Third, the threat of TB and MDR-TB transcends borders because travels back and forth from TB-endemic areas also bring the disease into Taiwan. Similar potential threat also exists in the vast number of foreign workers and immigrants, most of them from southeastern Asia or China where MDT-TB is highly prevalent[3,17].

CONCLUSION

Although MDR-TB patients are an epidemiological threat to the community, it is not so difficult to detect if the clinicians, especially the orthopedic surgeons, have a high index of suspicion in certain groups of patients with predisposing factors. The treatment of MDR-TB depends on prompt diagnosis, the availability of drug susceptibility testing, timely surgical debridement, and an uninterrupted supply of second-line anti-TB medications.

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