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A rare case of disseminated tuberculosis; multiple intracranial and intramedullary tuberculomas with concurrent tuberculous spondylitis and meningitis

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ABSTRACT

Concomitant presentation of intracranial and intramedullary tuberculomas is a rare entity. We report a 38-year-old immunocompetent woman with intramedullary and intracranial tuberculomas with concurrent tuberculous spondylitis and meningitis, who presented with paraparesis and back pain. Despite initial antituberculous therapy, the patient's neurologic status deteriorated with the development of paraplegia. Following surgical intervention, the patient gradually recovered muscle strength and bladder function.

1. Introduction

Mycobacterium tuberculosis (TB) remains a major public health concern, particularly in developing countries [1–10]. Extrapulmonary tuberculosis as a result of hematogenous spread, rarely involves the central nervous system (CNS) accounting for 0.5–2% of all tuberculosis cases [3–11]. First described by Abercombie in 1828, intramedullary tuberculoma (IMT), an extremely rare manifestation of TB, constitutes only 2/1000 of CNS tuberculomas [5–10]. The concurrent presence of IMT and intracranial tuberculoma is also extremely rare [8–11]. IMT presents with subtle symptoms of progressive myelopathy which is difficult to distinguish from benign or malignant spinal space-occupying lesions (SOLs) [6]. Magnetic resonance imaging (MRI) is a sensitive tool in differentiating tuberculoma from other SOLs [6,7]. The first MRI description of tuberculoma was given by Rhoton et al. in 1988 [1]. The evolving nature of the TB granulomatous lesion leads to its changing appearance in MRI. Tuberculoma has been described as a low-intensity lesion on T2 weighted images (T2W). Central hyperintensity depends on the amount of caseous necrosis. It is also hypointense to isointense on T1 weighted images (T1W). Chronic granulomatous inflammation breaks down the blood-cord barrier and causes homogenous enhancement. With evolving caseous material, the lesion will present with ring enhancement and classical "target sign" [10–15]. We report a 38-years-old woman with the coexistence of IMT, multiple intracranial tuberculomas, and multilevel thoracolumbar TB spondylitis that was treated with anti-tuberculosis therapy (ATT). Due to progressive deterioration of motor function she underwent spinal cord decompression surgery with subsequent improvement.

2. Case Report

2.1. Clinical presentation:

A 38-year-old woman initially presented with headache, nausea, fever, chills, and back pain. Cerebrospinal fluid (CSF) noted glucose levels 20 mg/dL, protein 110 mg/dL and 90 lymphocytes/mm^3. CSF *M. tuberculosis* Polymerase chain reaction (PCR), bacterial, and mycobacterial CSF cultures were negative. The chest X-ray was normal. Lumbar spine MRI demonstrated L2-L3 vertebral body destruction, inflammatory changes, and relative spinal canal narrowing. The spinal cord signal and shape were normal. An L2 vertebral bone biopsy demonstrated vascular proliferation, increased marrow fibrosis, and new bone formation without evidence of malignancy or granulomatous inflammation. She received antibiotics for presumed bacterial meningitis with clinical improvement.

Five months after the initial presentation she was readmitted with back pain and weight loss (13 kg in two months). Repeat lumbar spine MRI noted a left psoas muscle abscess (Fig. 1). CT guided biopsy of the

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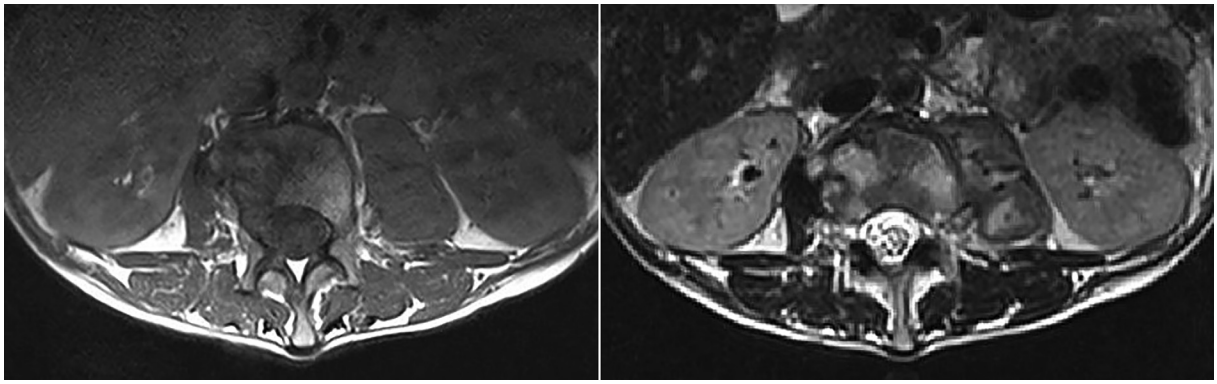

Fig. 1. T1W (Left) and T2W (Right) axial lumbar MR images showing left psoas muscle abscess.

left psoas muscle was performed; the aspirated fluid was positive for TB by PCR testing with growth of *M. tuberculosis* in cultures at 15 days.

Lumbar spine and brain MRI were normal on admission. On day 3 of admission, she developed fever and loss of consciousness. Repeat CSF evaluation noted glucose levels 28 mg/dL, protein 117 mg/dL and 160 lymphocytes/mm^3, positive acid-fast smear and TB CSF PCR. A Mantoux test on admission had been negative and she was also negative for HIV. Chest CT revealed no pulmonary involvement. She was started on ATT with isoniazid 300 mg daily, rifampin 600 mg daily, pyrazinamide 1.5 mg daily, and ethambutol 800 mg daily via directly observed therapy (DOT) for 2 months. Following completion of the intensive phase of ATT, she was continued on isoniazid 300 mg daily and rifampin 600 mg daily.

Three months after initiation of ATT she represented with back pain, mild bilateral lower extremity weakness, and paresthesia. Right lower extremity strength was intact, while the left lower extremity strength was reduced. Brain MRI showed multiple diffuse small, well-circumscribed, ring-enhancing lesions with surrounding edema mostly in the frontoparietal lobes (Fig. 2). Thoracic spine MRI showed a T5-T6 intradural intramedullary enhancing lesion, isointense in T1W, and hypointense in T2W (Fig. 3). CSF analysis noted glucose 40 mg/dL, protein 63 mg/dL and white blood cells 10/mm^3. CSF TB PCR was negative. An HIV antibody/antigen screen was negative. Due to symptomatic improvement and the result of previously performed susceptibility testing that has shown susceptibility to the aforementioned drug combination, she was continued on ATT without regimen changes.

Five months after starting ATT she was readmitted with progressive bilateral lower extremity weakness, right lower extremity anesthesia, truncal anesthesia below T6 level, and urinary incontinence. Muscle forces of both lower limbs were 0 with hyperactive deep tendon reflexes, ill-sustained clonus, and positive Babinski's sign. No evidence of upper extremity motor or sensory deficit was observed.

Thoracic spine MRI showed a destructive hypointense lesion on T1W and isointense on T2W with anterior wedging at the sixth thoracic vertebral body (T6). An intradural intramedullary enhancing lesion, isointense on T1W, and hypointense on T2W was reported at the level of T5-T6 with no significant alteration in size compared to previous MRI (Fig. 4).

2.2. Surgical management:

The patient underwent open surgical resection of the intramedullary lesion, T4-T5 total laminectomy, and T6 semi-laminectomy. After dural opening, a firm mass of purulent material was excised.

2.3. Histopathologic findings

Histopathological study of the surgical specimen revealed chronic caseating granulomatous inflammation. Vertebral body lesion biopsy showed normal bony tissue.

2.4. Follow-up

Over the next five months, there was a gradual improvement of sensorimotor neurologic status and bladder function. ATT was stopped after 12 months.

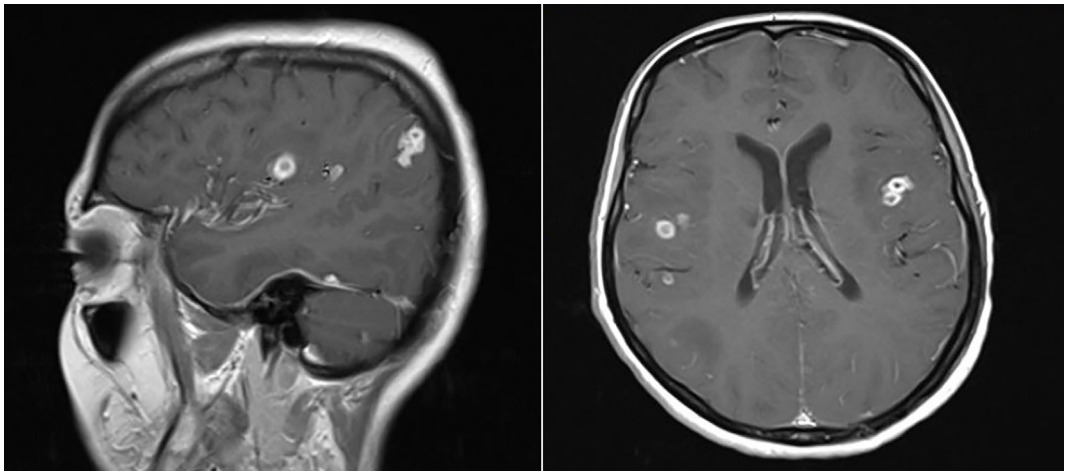

Fig. 2. Post-gadolinium sagittal (Left) and axial (Right) brain MR images.

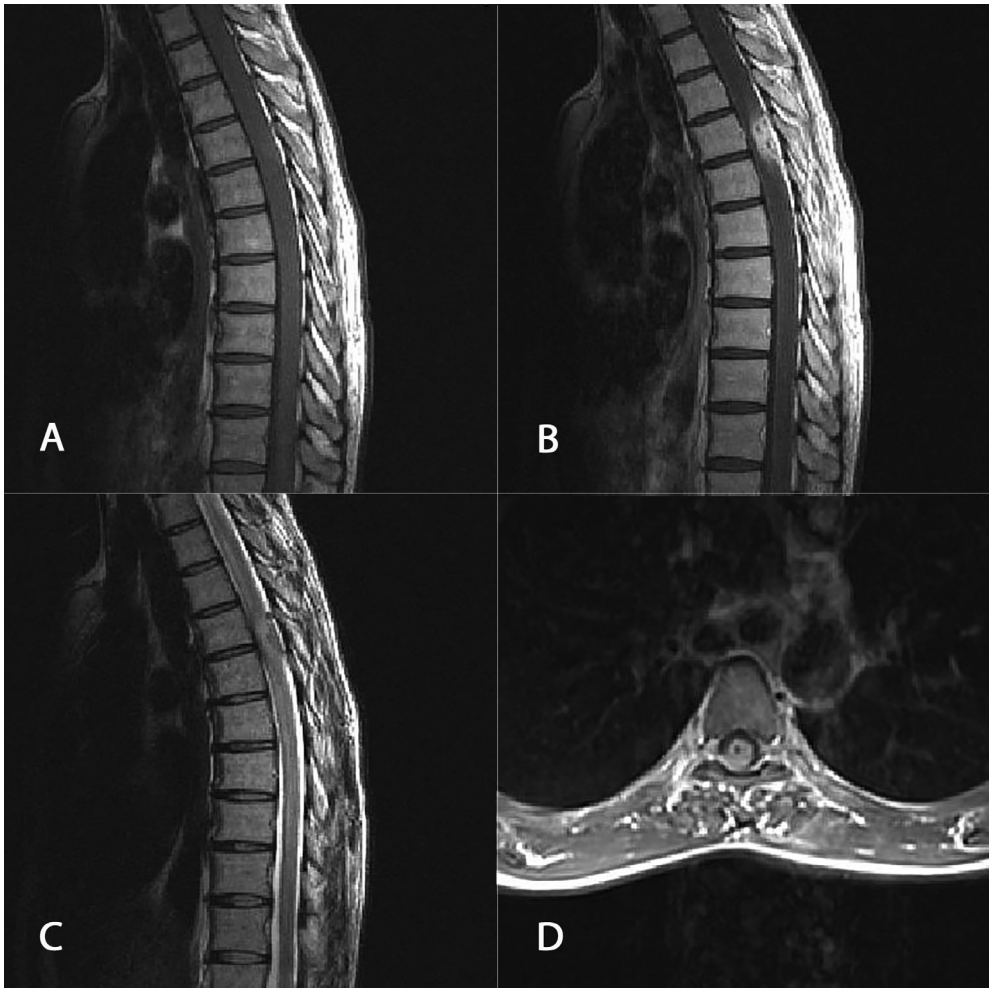

Fig. 3. Pre-gadolinium T1W (A), Post-gadolinium T1W (B) and T2W (C) sagittal MR images; Post gadolinium T1W axial MR image (D).

3. Discussion

3.1. Epidemiology

Tuberculosis, characterized by caseous granuloma formation, is common in many developing countries [12]. Extrapulmonary TB rarely involves CNS [11]. Tuberculoma is the second frequent manifestation of neuro-tuberculosis after meningitis [6–9,16]. Intramedullary tuberculosis (IMT), an extremely rare entity, is reported in only 2/100000 of all tuberculosis patients and 2/1000 of neuro-tuberculosis patients. The spinal cord to the cerebral tuberculosis ratio has been estimated at 1:42. IMT is more frequent in younger age and developing countries [12]. Ghane et al [10] and Krishnan et al [2] reported a 5-years-old and a 12-years-old patient respectively, with coexisting IMT and intracranial tuberculoma. However, many of the cases described in the literature were adults like our patient.

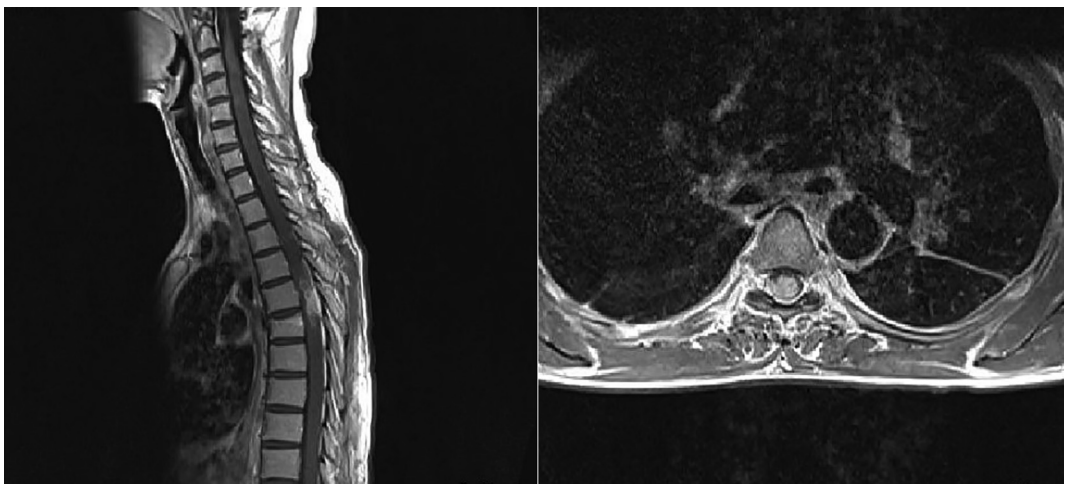

Fig. 4. Post-gadolinium sagittal (Left) and axial (Right) thoracic MR images.

3.2. Etiology

Lim et al [12] and Park et al [6] reported patients with multiple intracranial tuberculomas and IMT who were previously treated for pulmonary tuberculosis. IMT is always secondary to tuberculosis involvement in other organs and more often pulmonary tuberculosis [5]. Even so, in our patient, a pulmonary CT scan did not show any involvement of the lungs.

3.3. Clinical presentation

Usually, IMT presents with insidious symptoms of myelopathy. Tilva et al [5] reported a 55-years-old patient with progressive weakness of both lower limbs from four months ago; however, Thirunavukarasu et al [13] reported a 23-years-old patient with rapid onset of progressive weakness during five days, which is relatively similar to our case. Clinical features of IMT usually consist of spinal cord compression signs. McDonnell et al [15] and Lim et al [12], both reported patients with lower limb weakness, paresthesia, urinary retention, and low back pain, which is similar to our case, although overflow urine incontinence was noted in our patient.

3.4. Diagnosis

IMT should be regarded as an important differential diagnosis in patients with space-occupying lesions of the spinal cord, especially those with tuberculosis elsewhere [3–15]. IMT is hard to distinguish from other SOLs; therefore other causes of masses such as sarcoidosis, histiocytosis, brucellosis, and malignant metastatic lesions should be considered in the differential diagnosis [5]. IMT may involve any level of the spinal cord, but the dorso-lumbar area is more frequently infected due to regional blood flow, which is 45% of the total blood supply compared to 34% for cervical cord [2,5,12]. MRI is the standard method for IMT evaluation and the evolving nature of tuberculoma leads to varying morphologies of the lesion in MRI [2–7]. IMT is described as a hypointense to isointense lesion in T1W images and hypointense to hyperintense lesion in T2W images [7,16]. The classical target sign is the result of growing caseous material in the central part of granuloma [5,7,12]. In our case, MRI features of the lesion are identical to the literature. The lesion was isointense in T1WI and hypointense in T2WI.

3.5. Management

Treatment of choice for IMT is controversial [8–10]; however, ATT as the first measure is frequently Administered [1–4]. Tanwar et al [14] reported a 28-years-old patient with multiple intracranial and intramedullary tuberculomas that recovered completely with ATT without any demand for a surgical operation. Kemaloglu et al [9] reported a 32-years-old patient with pulmonary tuberculosis deteriorating on ATT with progressive neurological symptoms who finally needed surgical intervention due to IMT of the conus medullaris. Similar to our patient, Park et al [6] presented a case of multiple tuberculomas of the brain and spinal cord with progressive motor weakness despite adequate medical therapy, who underwent surgical treatment. A surgical procedure is indicated if there is lack of response to ATT, uncertain diagnosis, or deterioration of neurological status [9–14,16].

4. Conclusion

Intracranial and intramedullary TB, although rare, can be seen without previous tuberculous involvement of lung or other organs as a primary manifestation of TB. A high degree of clinical suspicion is needed as CNS TB is often paucibacillary; CSF culture, CSF TBPCR, and even histopathologic examination of biopsy specimens may be negative. Antituberculous therapy is recommended, however progressive neurological deficits may happen while on ATT necessitating surgical intervention.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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