

CASE REPORT

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Hybrid PET/MRI findings in a case of pulmonary and extra-pulmonary tuberculosis associated with motor-neuron disease-like illness—a coincidence or a causation?: a case report

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Abstract

Background: The association of tuberculosis and motor neuron disease-like illness has not been described previously. We present a case of co-existent pulmonary and extra-pulmonary tuberculosis in a young man whose clinical presentation was suggestive of a motor neuron disease-like illness and was subsequently diagnosed with tubercular infection. This case provokes our thought as to whether the association between tuberculosis and motor neuron dysfunction was just a co-incidence, given the high prevalence of tuberculosis in our set-up, or does it point towards a possible causative role of infection in motor neuron disease.

Case presentation: A 31-year-old man presented with progressive thinning of bilateral upper and lower limbs with associated pain and twitching sensation in upper and lower limb muscles. He had a history of loss of appetite and unintentional weight loss. On clinical examination, there was evidence of fasciculations in bilateral quadriceps, bilateral biceps, and paraspinal muscles which was further confirmed with electrophysiology. The work-up for underlying autoimmune, toxic and metabolic aetiology, and paraneoplastic aetiology was found to be negative. CT scan of the chest was suggestive of consolidations in bilateral upper lobes with multiple tree-in-bud nodules in both the lungs. Hybrid 18-Flourine-fluorodeoxyglucose positron emission tomography and magnetic resonance imaging (F-18-FDG PET/MRI) imaging was also suggestive of pulmonary and extra-pulmonary tuberculosis. Imaging of the brain revealed atrophy along bilateral motor cortices with reduced tracer uptake. Diagnosis of tubercular infection was confirmed with nucleic acid amplification test and the patient was put on anti-tubercular therapy. On follow-up after 6 months, the patient reported improvement in the symptoms and the muscle power in bilateral upper and lower limbs.

Conclusion: We have described a very rare association of pulmonary and extra-pulmonary tuberculosis with motor neuron-like illness. It may be debated that such an association may just be co-incidental; however, given the improvement in the symptoms and signs of the motor neuron disease-like illness on follow-up while the patient was on anti-tubercular therapy, it may point towards a causative relationship between tubercular infection and motor neuron dysfunction. Further epidemiological studies should be sought for in order to reach a conclusive answer.

Keywords: Motor neuron disease, Tuberculosis, Positron emission tomography, Magnetic resonance imaging

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Background

Tuberculosis (TB) is a chronic granulomatous infection usually caused by an acid fast bacillus named *Mycobacterium tuberculosis*. It is one of the oldest infectious diseases known to affect humans [1]. India has the highest burden of disease in the world with an incidence of 28,00,000 new cases reported in the year 2017 according to the Global TB report 2017 which accounts for about a quarter of the total cases reported globally [2]. The problem is further complicated by multidrug-resistant tuberculosis (MDR-TB) and emergence of extensively drug-resistant tuberculosis (XDR-TB) which have become a major global public health concern [3]. Tuberculosis can occur in any individual irrespective of age and gender; however, immunocompromised individuals, e.g., patients with HIV-AIDS are at a higher risk [4]. Pulmonary tuberculosis is the commonest form of tuberculosis in humans. Extrapulmonary tuberculosis accounts for 45% of cases of tuberculosis in the Indian subcontinent with lymph nodes and bones and joints tuberculosis accounting for about 60% of these cases [1].

Motor neuron disease is a group of neurodegenerative disorders which have varied clinical presentations including weakness, falls, foot drop, dysarthria, dysphagia, cognitive abnormalities, respiratory abnormalities, etc. [5]. Among the various subtypes of motor neuron disease, amyotrophic lateral sclerosis is the most common subtype [5]. The disease is known to occur most commonly in the age group of 60–70 years [5]. Among the various proposed aetiologies of motor neuron disease, infection is thought to be one of the underlying causes of motor neuron disease [6].

We present a unique case of co-existent pulmonary and extra-pulmonary tuberculosis whose clinical presentation was suggestive of motor neuron disease-like illness. This case is thought provoking as to whether the co-existence of motor neuron dysfunction and tubercular infection was just of co-incidence or whether tuberculosis can trigger a motor neuron dysfunction. Improvement in the symptoms on follow-up after anti-tubercular therapy points to a possibility of motor neuron dysfunction caused by tubercular infection since work-up for other aetiologies was negative.

Case presentation

A 31-year-old male patient presented with complaints of pain in upper and lower limbs accompanied by gradual thinning of upper and lower limbs over a period of 1.5 years. Initially, dull aching type of pain used to occur in the thighs and calves of bilateral lower limbs which was aggravated by exertion. After 1 month of onset, he began having pain in bilateral upper limbs, mainly in the arms. He also noticed gradually progressive thinning of both the upper and lower limbs. He had an unintentional

weight loss of approximately 8 kg over a period of 1.5 years and also had intermittent cough and low grade fever. He also felt twitching of his thigh muscles which began about 6 months after onset of symptoms. He had a past history of occasional alcohol intake. He did not have any history of dysarthria or dysphagia. There was no history of bowel and bladder involvement.

On examination, he was conscious, co-operative, and well oriented to time, place, and person. His vitals were stable. There was diffuse atrophy of the muscles in both upper and lower limbs bilaterally. Fasciculations were noted in bilateral biceps, paraspinal muscles, and thigh muscles. Deep tendon reflexes were exaggerated in bilateral upper limbs but normal in lower limbs. His plantar response was flexor. The Medical Research Council (MRC) grading of muscle power was suggestive of muscle power of 3/5 in bilateral upper and lower limb muscle groups. Visual acuity and fundus examination were normal.

His laboratory investigations revealed anemia with hemoglobin level of 11.1 g/dl. His liver function test revealed hypoalbuminemia with elevated globulin levels. Work-up for autoimmune pathology and para-neoplastic antibodies was negative. Electromyogram (EMG) confirmed the fasciculation potentials in bilateral biceps, quadriceps, and paraspinal muscles. Computed tomography (CT) scan of chest was done which showed evidence of multiple cavitary consolidations predominantly involving bilateral upper lobes with multiple tree-in-bud nodules in both the lungs (Fig. 1).

Considering a possibility of an underlying paraneoplastic aetiology, the patient was referred for 18-F-FDG PET-MR examination. Whole body images (skull top to mid-thigh) in all five bed positions were acquired followed by dedicated brain MRI in 3D mode 60 min after IV injection of 307.1 MBq of 18-F-FDG using a simultaneous Siemens mMR Biograph scanner. 18-F-FDG PET-MR images of chest revealed multiple patches of abnormal FDG uptake in bilateral upper lobes, right middle lobe, and apical segment of left lower lobe (Fig. 2) with multiple FDG avid sub centimetric mediastinal lymph nodes. PET-MR images of the abdomen revealed eccentric thickening of the ileocecal junction with the thickness of 1.5 cm for a length of 5.6 cm with abnormal FDG uptake with SUV_{max} of 13.6 (Fig. 3). Multifocal thickening with abnormal FDG uptake was noted in the ileal loops in right iliac fossa with associated mesenteric fat stranding and mesenteric lymphadenopathy (Fig. 4). MRI of brain was suggestive of atrophy of bilateral precentral gyri with moderately decreased uptake of FDG in the corresponding areas (Fig. 5).

Considering the clinical picture and findings on CT chest and whole body 18-F-PET-MR, a diagnosis of motor neuron disease-like illness associated with pulmonary and abdominal tuberculosis was considered. The patient

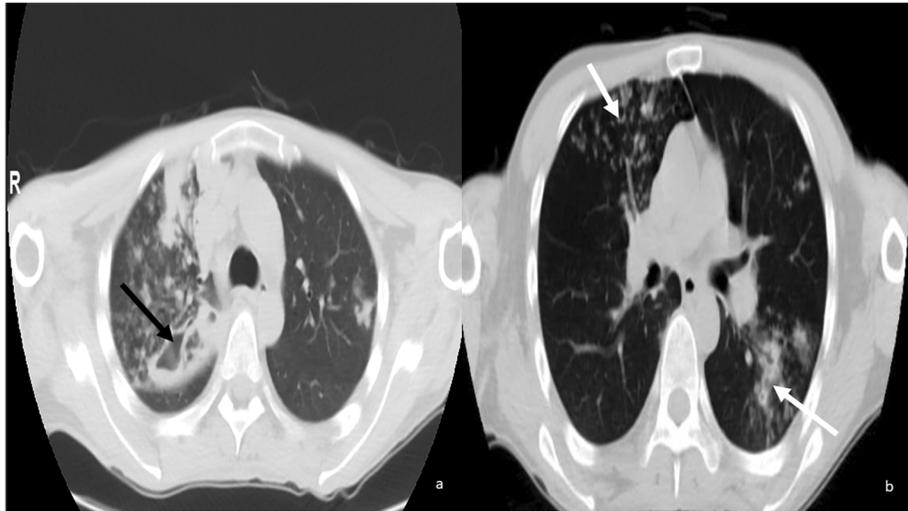


Fig. 1 CT scan of the chest. **a** Cavitory consolidation is noted in right upper lobe (black arrow). **b** Multiple tree-in-bud nodules are noted in bilateral lungs (white arrow)

subsequently underwent nucleic acid amplification test of sputum sample, which showed positivity for *Mycobacterium tuberculosis*. After confirmation of diagnosis of tuberculosis, the patient was started on anti-tubercular medication. The anti-tubercular treatment consisted of two phases, an initiation phase and a continuation phase. During the initiation phase of 2 months, an oral fixed dose combination of Isoniazid (75 mg), Rifampicin (150 mg), Pyrazinamide (400 mg), and Ethambutol (275 mg) was administered as 3 tablets per day. Following this, oral fixed dose combination of Isoniazid (75 mg), Rifampicin (150 mg), and Ethambutol (275 mg) was given as 3 tablets per day for 4 months. The patient tolerated the anti-

tubercular medication and did not have any adverse effects during the course of the treatment.

On last follow up, which was 6 months after starting anti-tubercular regimen, the patient reported improvement in muscle power in upper as well as lower limbs to MRC grade 4. However, he still felt pain in bilateral lower limbs and occasional twitching of lower limb muscles. The patient had returned to his job and had gained about 3 kg of weight and did not complain of fever and cough.

Discussion

Motor neuron disease (MND) is a devastating disease characterized by loss of upper motor neurons as well as

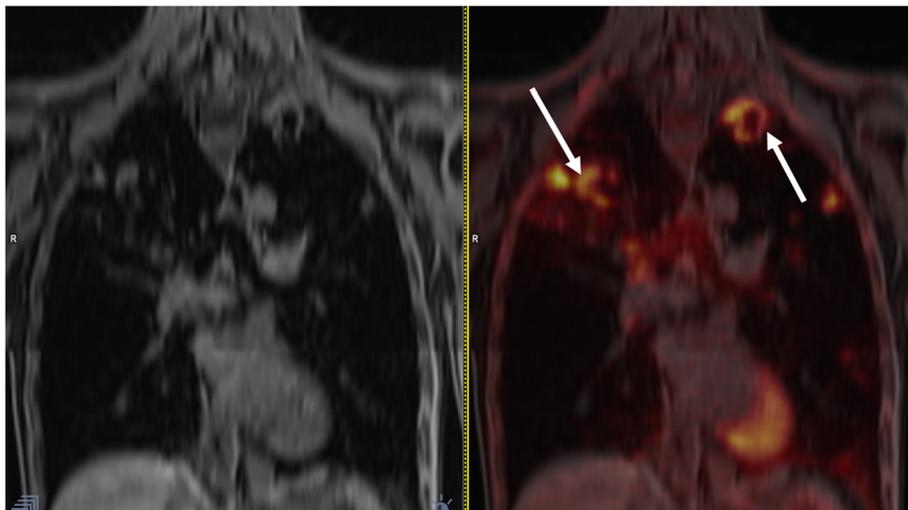


Fig. 2 Hybrid PET/MRI imaging of the chest. Images of chest revealed multiple patches of abnormal FDG uptake in bilateral upper lobes, right middle lobe, and apical segment of left lower lobe (white arrows)

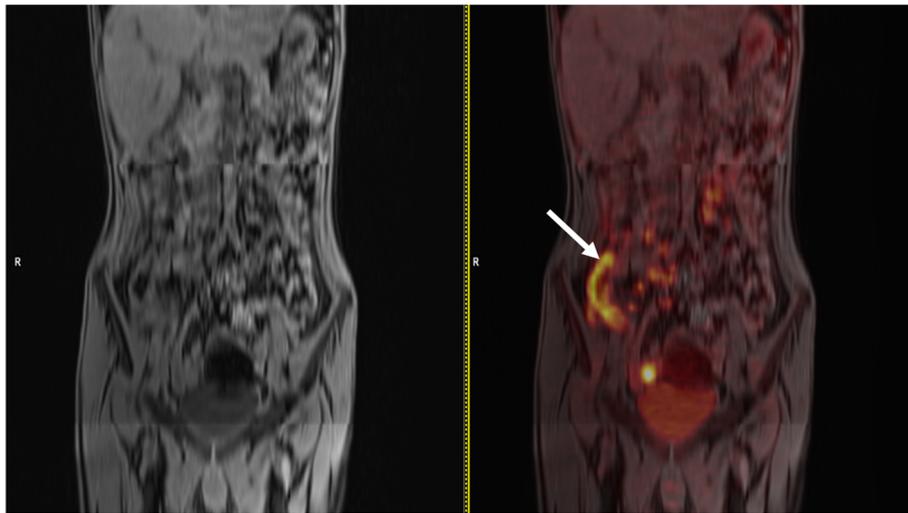


Fig. 3 Hybrid PET/MRI imaging of the abdomen. Eccentric thickening of the ileocecal junction is noted with FDG tracer uptake (white arrow)

lower motor neurons [7]. The characteristic clinical feature of MND is loss of motor function without sensory loss [8]. The diagnosis of MND is based on identifying the clinical features with associated diagnostic tests including electromyogram (EMG) [8]. Among the various diagnostic criteria, the modified El Escorial criteria and the Awaji criteria are among the most commonly used in clinical practice [9, 10]. Radiologically, MND cases may show various signs on MRI such as atrophy of the precentral gyrus, “motor dark line” on T2-weighted images and hyperintense signal involving the corticospinal tracts [11–13]. Molecular imaging studies using positron emission tomography (PET) and

single photon emission tomography (SPECT) have shown hypoperfusion and hypometabolism in motor cortex in patients with MND [14]. The exact underlying aetiology of motor neuron disease is not known; however, role of genetic factors, oxidative stress, inflammatory, and infective causes have been proposed. Pathologic links between *Schistosomiasis* and MND has been reported [6]. It has also been suggested that exposure of outdoor sports persons to dirt, soil, and dust contaminated with *Mycobacterium avium* subspecies *paratuberculosis* predisposes them to increased risk of MND [15]. Association of ankylosing spondylitis with MND has also been reported [16].

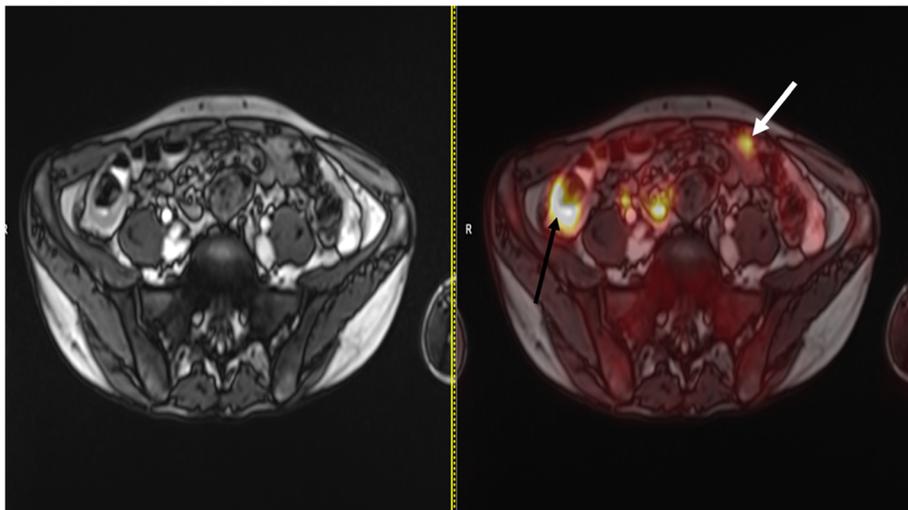
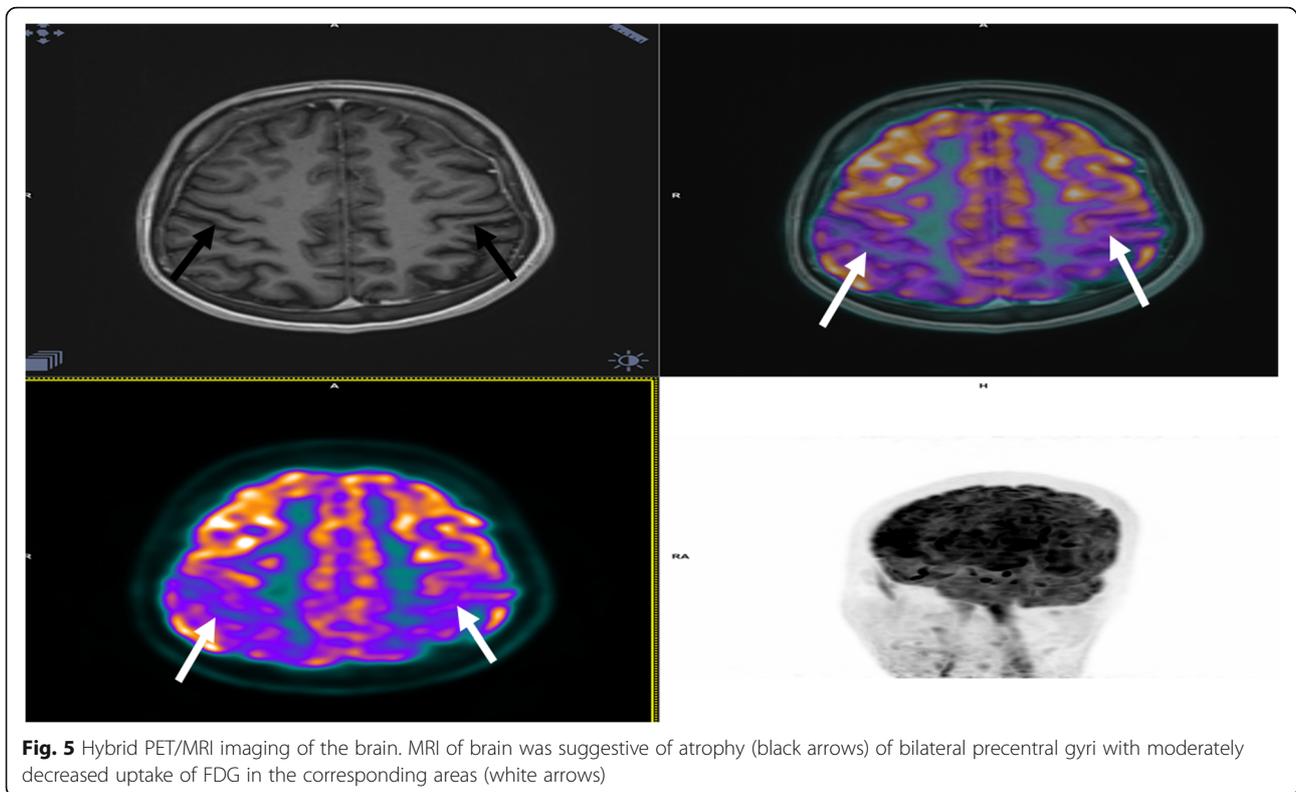


Fig. 4 Hybrid PET/MRI imaging of the abdomen. Multifocal thickening with abnormal FDG uptake noted in the ileal loops in right iliac fossa (black arrows) with associated mesenteric fat stranding and mesenteric lymphadenopathy (white arrow)



Our case description is the first in the literature describing the hybrid PET/MR findings in a case of pulmonary and extra-pulmonary tuberculosis with associated motor neuron-like illness. We hypothesize that infection with *Mycobacterium tuberculosis* could have triggered an immune response which would have manifested as motor neuron dysfunction and subsequent improvement could be explained by the response to anti-tubercular therapy. However, it would be difficult to establish causation on the basis of a single case report, and this could be considered as a limitation of this case report. Also, we do not intend to describe the clinical presentation as the motor neuron disease or amyotrophic lateral sclerosis but rather as motor neuron disease-like illness, since the patient's symptoms improved subsequently which does not fit in the classic description of motor neuron disease. However, reversible motor neuron disease has also been described in the literature [17].

Conclusion

We have described a very rare association of co-existent pulmonary and abdominal tuberculosis with motor neuron disease-like illness. Characteristic findings were demonstrated on chest CT and whole body PET-MR scan. It is not known whether the association between tuberculosis and motor neuron disease is causative or not. The role of immune response to tubercular antigens,

immunomodulation in chronic infection, and direct role of *Mycobacterium tuberculosis* in causation of motor neuron disease needs to be further investigated. We propose further studies exploring the possible causative role of *Mycobacterium tuberculosis* in motor neuron disease.

Abbreviations

AIDS: Acquired Immunodeficiency syndrome; EMG: Electromyogram; 18-F-FDG: 18-Fluorine-Fluorodeoxyglucose; HIV: Human immunodeficiency virus; MDR-TB: Multidrug-resistant tuberculosis; MND: Motor neuron disease; MRC: Medical Research Council; MRI: Magnetic Resonance Imaging; PET: Positron emission tomography; SPECT: Single photon emission tomography; SUV_{max} : Maximum standardized uptake value; TB: Tuberculosis; XDR-TB: Extensively drug resistant tuberculosis

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None

Authors' contributions

SP gave substantial contributions to having drafted the paper, analysis of data, and interpretation. SM gave substantial contributions to the conception provided and helped in revision. CN gave substantial contributions to the conception provided, design of work, interpretation of data, and substantively revised it. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The need for ethical approval for this case report was waived off by the Ethical Committee, National Institute of Mental Health and Neurosciences,

Bangalore, Karnataka, India. The patient included in this study gave written informed consent to participate in this research.

Consent for publication

The patient included in this research gave written informed consent to publish the data contained within this study.

Competing interests

The authors declare that they have no competing interests

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