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Primary Multidrug Resistant Tuberculosis Involving Unique Extra Pulmonary Site

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Abstract
Prevalence of MDR among patients of extra pulmonary tuberculosis is less than 3% in Indian population. Isolated primary MDR tuberculosis of knee is rarely reported. We report a case of isolated primary MDR tuberculosis of the left knee in a 24 year old previously fit Indian male. This case emphasizes the need to exclude drug resistance in primary extra pulmonary tuberculosis cases and to keep tuberculosis among differential diagnosis for diseases involving any organ system of the body.

Introduction

Tuberculosis (TB) is an ancient disease known to exist since millennia. It is the leading cause of death from a single infectious agent, ranking above HIV/AIDS.[1] Burden of tuberculosis in India remains high with large number of deaths attributable to tuberculosis. Emergence of multidrug resistant tuberculosis (MDR-TB) has threatened global efforts to end TB. As a matter of major public health concern, in 2016, 47% of MDR-TB cases were from India, China and the Russian Federation.[1]

Pulmonary MDR-TB is widely reported but extra pulmonary MDR-TB has been described sparsely in literature. Primary extra pulmonary MDR-TB is described very sporadically and majority of them have been described involving lymph node,[2] sternum[3] and pleural cavity.[4] We report a case of primary extra pulmonary MDR-TB presenting as left knee joint effusion.

Case Report

A 24 year old active male presented with complaints of left knee swelling, fever, productive cough and weight loss from 20 days. There was no history of any trauma. There was no history of contact with person having tuberculosis. He had no history of tuberculosis in past. He was a non smoker and did not consume alcohol. He had no clinical signs on chest examination.

Patient had a pitting swelling above left knee joint, that was warm and non-tender with no redness of skin over it (figure-1). He was HIV seronegative.

Figure-1 patient photograph showing swelling above left knee joint)

Chest x-ray and high resolution computed tomography (HRCT) thorax showed no parenchymal lung lesions (figure-2a, 2b). However mantoux test was strongly positive (induration of 16mm). X-rays of knee showed no obvious lesion (figure-3).

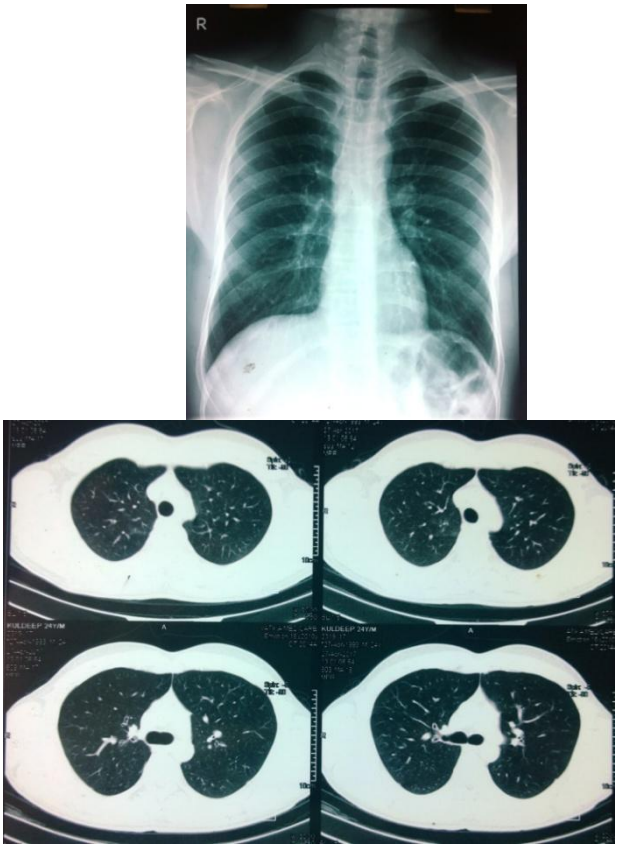

Figure-2a, 2b - Chest x-ray and high resolution computed tomography (HRCT) thorax showing no parenchymal lung lesions.

Figure-3- X-rays of left knee AP and Lateral view showing no obvious lesion.

Synovial fluid aspiration was done and aspirated fluid was sent for microbiological examination including pyogenic culture sensitivity, Ziehl-Neelsen (ZN) staining for acid fast bacilli (AFB) and cartridge based nucleic acid amplification test (CBNAAT). The pus showed no AFB and pyogenic culture was also sterile, however CBNAAT detected rifampicin resistant mycobacterium tuberculosis DNA.

Patient was put on standard treatment regimen for MDR-TB, including kanamycin, levofloxacin, ethambutol, pyrazinamide, ethionamide, cycloserine and a repeat sample of pus was sent for CBNAAT and line probe assay (LPA). Repeat sample of pus for CBNAAT detected rifampicin resistant mycobacterium tuberculosis DNA and LPA also confirmed presence of rifampicin and high level isoniazid resistance. At present patient is on treatment for MDR-TB from last one and a half months and has been symptomless during the treatment period.

Discussion

Drug-resistant TB was first recognized as a major public health concern in early 1990s and since then it is a continuing threat to end TB strategy of World Health Organization. There were 490,000 cases of MDR-TB and 110,000 cases of rifampicin resistant tuberculosis (RR-TB), which emerged in 2016.[1] Estimated incidence of MDR/RR-TB in 2016 for India was 2-3.5% for new cases and 10-13% for retreatment cases.[1] The data mentioned is mainly for pulmonary TB.

There is limited information available about the drug resistance patterns in extrapulmonary tuberculosis (EPTB). In one study, the prevalence of MDR in extrapulmonary TB was found to be 19% (37 out of 189).[5]

Globally use of rapid molecular tests is increasing as they are sensitive and quick methods of diagnosis. According to Technical and Operational Guidelines for TB Control in India, CBNAAT is the investigation of choice for diagnosis of EPTB.[6] Sensitivity of CBNAAT is high in FNAC/Biopsy specimen from lymph node, other tissue and CSF. Sensitivity is lower in pericardial, ascitic and synovial fluid samples.

CBNAAT detects DNA of Mycobacterium tuberculosis and also leads to simultaneous identification of a majority of the mutations that confer rifampicin resistance (which is highly predictive of MDR-TB). If CBNAAT shows rifampicin resistance treatment for MDR-TB is started and a second sample is sent for liquid culture drug sensitivity testing. Standard treatment regimen is, 6-9 month of intensive phase with kanamycin, levofloxacin, ethambutol, pyrazinamide, ethionamide, cycloserine and 18 month of continuation phase with levofloxacin, ethambutol, ethionamide, and cycloserine which is same as for pulmonary MDR-TB. These drugs are distributed widely in body and have good penetration into bodily fluids. Prognosis is better for extrapulmonary MDR-TB as compared to pulmonary MDR-TB and most of the patients who completed the treatment have survived.[6]

Patients with extrapulmonary TB need specialized investigations for collecting specimen for microbiological confirmation. In many cases, specimen for microbiological confirmation is not available and the diagnosis is made on clinical, radiographic or histopathological findings. Similarly difficulty also arises in obtaining the specimen for drug susceptibility testing. Therefore, there are only few case reports of extrapulmonary MDR-TB involving lymph node,[6] peritoneum,[7] meninges,[8] ribs[9] and spine.[10] Primary extrapulmonary MDR-TB is a rare entity. Primary extrapulmonary MDR-TB presenting as knee effusion is even rarer. Hence, there is an urgent need to have high degree of suspicion by physicians and surgeons to diagnose such cases. Drug resistant TB should be suspected if a patient is not improving on standard regimen.

With the growing numbers of TB cases, especially in an endemic country like ours a greater degree of suspicion is required to diagnose the primary MDR-TB cases and due heed should be given to the primary extrapulmonary cases. Every effort should be made a prompt diagnosis and start the treatment as early as possible. The present case will broaden our understanding of these rare presentations of a common disease and will also serve as a tool for early diagnosis and management of primary extrapulmonary MDR-TB in the future. Explicit guidelines like Index-TB guidelines should have separate section for extrapulmonary MDR-TB. A meta-analysis may provide much needed evidence based informations regarding drug resistance in extrapulmonary cases.

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