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Co-Existence of Extensively Drug Resistant Tuberculosis (XDR-TB) and Sarcoidosis in a Patient: A Case Report

P Prasanth*, N C Kajal, K T Nithin, Vikas Kumar and Ritu Dadra

Department of Chest and Tuberculosis, Government Medical College, Punjab, India

Abstract

Tuberculosis (TB) and sarcoidosis are multisystem diseases having different etiology and management; however, they have similar clinical and histological characteristics, that may rarely coexist. The emergence of Extensively Drug-Resistant Tuberculosis (XDR-TB) is a challenging paradigm shift faced by the TB control programs worldwide. The treatment is further compounded with unique management difficulties. Treatment of XDR-TB requires prolonged chemotherapy with second-line anti-TB drugs, which offer lesser potency and increased risk of drug related side effects. Sarcoidosis is a multisystem granulomatous disorder characterized pathologically by the presence of non-caseating granulomas in involved tissues. Depressed cellular immunity predisposes patients to infections with certain intracellular organisms, mostly fungi, *Mycobacterium tuberculosis* and Nocardia. As these infections are mainly insidious and difficult to differentiate from the underlying disease, a possible misdiagnosis may lead to fatal complications. This case highlights the high index of suspicion required in order to identify any possible infection in a case of sarcoidosis. A case of a 66-year-old female with 3-months history of fever, exertional dyspnea and dry cough, in whom extensively drug resistant tuberculosis was documented with co-existence of sarcoidosis. This case highlights the high index of suspicion required in order to identify any possible infection in a case of sarcoidosis.

Keywords: Extensively drug-resistant tuberculosis • Sarcoidosis • Hilar lymphadenopathy • Non-caseating granuloma

Introduction

Extensively Drug-Resistant Tuberculosis (XDR-TB) is caused by strain of *Mycobacterium tuberculosis* resistant to isoniazid and rifampicin (multidrug-resistant tuberculosis), with resistance to a fluoroquinolone and to at least one injectable second-line drug (amikacin, capreomycin, or kanamycin). According to the WHO 2015 report, XDR-TB has been reported in 105 countries and approximately 9.7% of MDR-TB cases are caused by XDR strains globally. Treatment of XDR-TB is prolonged chemotherapy with second-line antitubercular drugs, which have lower potency compared to adverse effect. Sarcoidosis is a multisystem granulomatous disorder of uncertain etiology, characterized pathologically by the presence of non-caseating granulomas in involved tissues [1]. Approximately, half of cases are diagnosed incidentally by radiographic abnormalities on a routine chest radiograph. Depressed cellular immunity predisposes patients to opportunistic infections with certain intracellular organisms, mostly fungi, *Mycobacterium tuberculosis* and Nocardia species. As these infections are mainly insidious and difficult to differentiate from the underlying disease, a possible misdiagnosis may lead to fatal complications for the patient. We present a case of XDR-TB and sarcoidosis managed with drug sensitivity-based second-line anti-tubercular drugs regimen. This case highlights the high index of suspicion required in order to identify any possible infection in a case of sarcoidosis.

Case Report

A 66-year-old female presented with complaints of low-grade intermittent fever, which was not associated with chills, and rigors, dyspnoea on exertion, cough for previous 3 months. The patient also had complaints of loss of appetite and weight loss. Patient had a significant past medical history of taking Anti-Tubercular Therapy (ATT) DOTS-category I, which was started on clinicoradiological basis and took treatment for 6 months, well tolerated and completed course. The patient had no other past medical history. She had never smoked and had not taken any medication in the past. She had no environmental or occupational history of beryllium or other metal exposure. She had never travelled outside India. She never had a tuberculin skin test before [2].

On physical examination, patient appeared to be in good condition, mildly dyspneic with 22 breaths per minute, a temperature of 39.4°C, blood pressure of 110/70 mmHg and a heart rate of 90 beats per minute. Apart from mild bilateral inspiratory fine crackles in

***Address for Correspondence:** P. Prasanth, Department of Chest and Tuberculosis, Government Medical College, Punjab, India, Tel: 8754349180; E-mail: drprasanth1392@gmail.com

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the lower lung fields, no other physical abnormalities were observed. Laboratory investigations showed normocytic normochromic anemia (hemoglobin 11.8 g/dl), white blood count 6370/mm^3 (neutrophils-67%, lymphocytes-30%), erythrocyte sedimentation rate 95 mm/hour. Patient had serum electrolytes within normal range and was non-reactive for HIV, HCV, HBsAg. Serum Angiotensin Converting Enzyme (ACE) was 128 U/L (normal 8-65 U/L) [3]. The sputum smear for AFB by ZN staining was negative and subsequently samples were sent for sputum CBNAAT testing. The tuberculin skin test was positive (>10 mm). A chest X-ray on admission disclosed bilateral hilar lymphadenopathy together with bilateral interstitial lung densities in the lower lung fields (Figure 1). USG abdomen showed grade 1 fatty liver. CT scan showed multiple nodular opacities diffusely distributed in bilateral lung fields. A sub segmental consolidation with cavitation seen in right lower lobe with bilateral hilar lymphadenopathy (Figure 2) [4]. An ophthalmologic evaluation was normal. Patient also underwent diagnostic bronchoscopy through which Bronchoalveolar Lavage (BAL) and Transbronchial lung biopsy was obtained. Meanwhile, sputum CBNAAT report detected the presence of *Mycobacterium tuberculosis*, which was resistant to Rifampicin. The BAL AFB smear and AFB BACTEC culture detected the presence of *Mycobacterium tuberculosis*. BAL cytology showed presence of lymphocytes, pigment laden macrophages and occasional neutrophils, with a differential count of neutrophils-30% lymphocytes-53% macrophages-43%. Transbronchial lung biopsy showed many well formed non-caseating epitheloid granulomas containing multinucleated giant cells (Figure 3). The patient was initially started on conventional multidrug resistant regimen; DOTS-category IV, prescribed under RNTCP programmatic management of drug resistant tuberculosis by awaiting Line Probe Assay (LPA) to detect sensitivity to second line anti tubercular drugs. The LPA report on arrival detected that the smears were resistant to fluoroquinolones and aminoglycoside, the two most commonly used second line anti tubercular agents. Now the patient is a documented Extensively Drug Resistant Tuberculosis (XDR-TB) and was started with extended second-line Antitubercular chemotherapy (ATT) under RNTCP programmatic management of drug resistant tuberculosis [5].

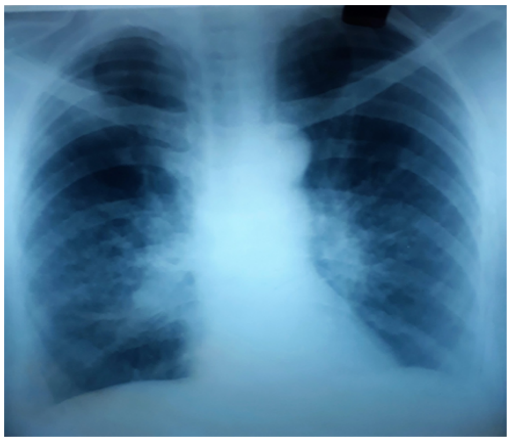

Figure 1. Chest X-ray showing bilateral hilar lymphadenopathy together with bilateral interstitial lung densities in the lower lung fields.

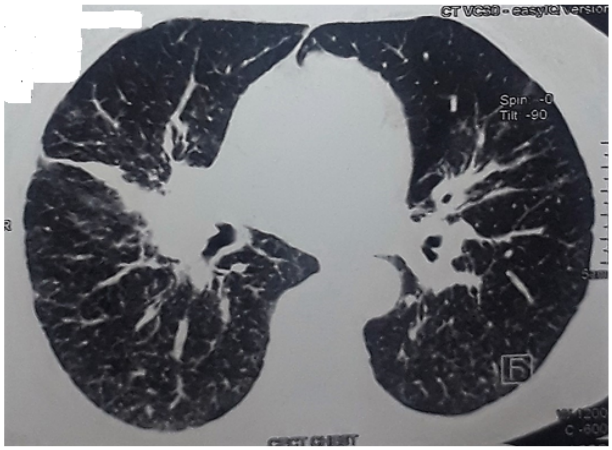

Figure 2. CT scan showing multiple nodular opacities diffusely distributed in bilateral lung fields and sub segmental consolidation seen in right lower lobe with bilateral hilar lymphadenopathy.

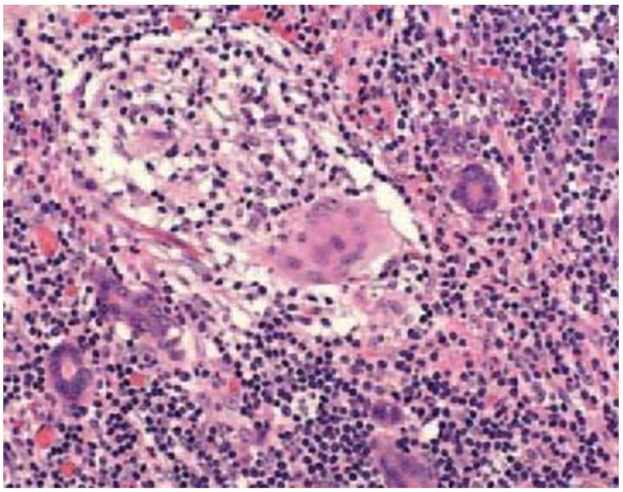

Figure 3. Transbronchial lung biopsy showing well-formed non-caseating granuloma.

Discussion

India is endemic for TB infection. High index of suspicion and a low threshold for initiation of empirical anti tuberculous treatment is usually noted among the treating physicians. However, the case highlights the fact that a Drug Sensitivity Testing (DST) is imperative for assessing the sensitivity pattern of the *Mycobacterium* strain, to detect the primary MDR or XDR-TB strains [6]. Failure to do so leads to ineffective treatment and further emergence of drug resistance. The combination of chronic bilateral hilar lymphadenopathy, the histopathological detection of non-caseating granulomas and the exclusion of other diseases with similar presentation suggested the diagnosis of sarcoidosis in our patient. Approximately, 75% of patients with stage I disease may experience regression of hilar nodes in 1 to 3 years while 10% develop chronic enlargement that

exists for 10 years or more [7]. Cutaneous involvement is seen in up to 20% of patients with sarcoidosis, with maculopapular eruption being the most common subacute lesion. The association of sarcoidosis with TB still remains complex, although it has been thoroughly studied. Coexistence of both these entities has sometimes been referred to as tuberculous sarcoidosis. It shows mainly of three patterns: Patients who have TB subsequently develop sarcoidosis, patients develop the concomitant sarcoidosis and TB, patients with chronic sarcoidosis develop TB due to treatment-related immunity suppression [8].

RNTCP is the state-run TB control initiative by the Government of India. The development of Programmatic Management of Drug-Resistant Tuberculosis (PMDT) is the RNTCP's fight against drug-resistant TB, adhering to the WHO guidelines [9]. The regimen for XDR-TB under PMDT includes 6-12 months intensive phase and 18 months continuation Phase. Drugs given in intensive phase includes capreomycin, high dose moxifloxacin, ethambutol, pyrazinamide, cycloserine, ethionamide, clofazimine, linezolid and continuation phase includes high dose moxifloxacin, ethambutol, cycloserine, ethionamide, clofazimine, linezolid [10]. The drugs to which patient demonstrates resistance should be withdrawn and replaced with at least two new drugs to which the patient has not previously been exposed. Although, interstitial parenchymal opacities are not common in HIV-negative patients with pulmonary TB, Chin et al. have recently reported that in a series of 22 patients with fever of unknown origin finally diagnosed with mycobacterial infection, including 19 TB patients, 41% of them had an interstitial pattern on chest radiographs [11].

Treatment success is dependent on several factors such as host immunity, extent of drug resistance, and disease severity. However, favorable outcomes, which are defined as cure or treatment completion, are very low (16%-44%) in patients with XDR-TB. The successful outcome in the present case can be attributed to strict compliance, directly observed therapy, guided multidisciplinary team management.

Conclusion

We have presented the case of a sarcoidosis who developed extensively drug resistant TB and have emphasized the diagnostic dilemmas that may occur when these conditions coexist. Although infections with certain intracellular organisms, including *M. tuberculosis*, are probably infrequent in patients with sarcoidosis, there needs to be a greater awareness among physicians in order to rule out any possible infection in cases of sarcoidosis. The initiation of steroid therapie in the patients with an underlying infections may accentuate any of possible life-threatening complications. Appropriate sensitivity-based chemotherapy, given ensuring good compliance to the regimen for an extended period, is the key to ensure effective treatment of XDR-TB patients.

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