

Case Report

Rare cause of paradoxical worsening of pleural effusion in a patient with tuberculosis

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ABSTRACT

A 33-year-old patient, Known case of chronic kidney disease on maintenance dialysis presented with complaints of low-grade fever and weight loss of 2 months duration. Computed tomography (CT) revealed bilateral mild pleural effusion with significant mediastinal and abdominal adenopathy. CT-guided fine-needle aspiration cytology of abdominal lymph nodes and bone marrow culture was suggestive of tuberculosis. The patient was started on four drug anti-tubercular therapy, post 6 weeks of initiation he developed new onset fever and chest X-ray revealed moderate right pleural effusion. Diagnostic thoracocentesis was suggestive of chylothorax. To the best of our knowledge, this is the first case report of chylothorax due to the paradoxical reaction in the HIV-negative tuberculous patient.

KEY WORDS: Chylothorax, immune reconstitution inflammatory syndrome, paradoxical reaction, tuberculosis

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INTRODUCTION

Paradoxical reaction (PR)/immune reconstitution inflammatory syndrome (IRIS) is an exaggerated and dysregulated inflammatory response to the microorganism. It manifests when a sudden shift of host immunity from an immunosuppressed and anti-inflammatory state toward a proinflammatory state.^[1,2] Here, we present a case, probable the first report in the literature about PR in HIV-negative tuberculosis (TB) patient presenting as chylothorax.

CASE REPORT

A 33-year-old man, diagnosed case of chronic kidney disease secondary to diabetes mellitus on maintenance dialysis presented to pulmonary medicine outpatient unit with complaints of intermittent fever and weight loss of 2 months duration. On examination, he was febrile (38.4 Celsius) with a respiratory rate of 20/min, pulse rate of 104/min, blood pressure of 140/90 mmHg, and oxygen

saturation of 96% on room air. General examination revealed pallor and bilateral pitting pedal edema. His respiratory-, cardiac-, abdominal- and neurological examination was within normal limits. Laboratory examination showed hemoglobin of 7.2 g/dL (normal 11.5–16.5), platelet count of $22 \times 10^9/L$ (normal 150–500), white cell count of $3.2 \times 10^9/L$ (normal 4.3–10.8) with neutrophils 65%, lymphocyte 32%, and monocyte of 3%. His glycated hemoglobin was 5.6% (normal <6.5%) and liver function test revealed albumin of 2.2 g/dL (normal 3.5–5 g/dL). Rest of the biochemical investigations were within normal limits. HIV serology was negative. Even though, the patient had normal blood picture and reticulocyte count, bone marrow study was done for his leukopenia.

Chest X-ray posteroanterior (PA) view revealed increased bronchovascular markings [Figure 1a] and computed tomography (CT) thorax with abdomen [Figure 1b] showed

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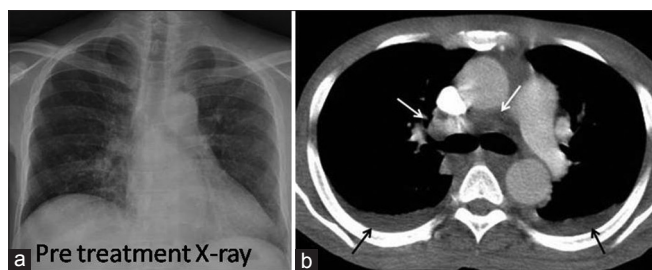


Figure 1: (a) Chest X-ray posteroanterior view showing increased bronchovascular prominence, (b) computed tomography thorax showing bilateral mild pleural effusion (black arrows) with significant mediastinal adenopathy (white arrows)

bilateral mild pleural effusion with significant mediastinal and abdominal adenopathy. Ultrasound chest was done and it revealed minimal pleural effusion and the same was not tappable. CT-guided fine-needle aspiration was done from paraaortic lymph nodes. Histopathology from bone marrow and cytology of paraaortic lymph nodes showed caseous necrotic granulomatous inflammation suggestive of TB. Acid-fast culture of bone marrow tissue and lymph node aspirate revealed growth of pansensitive mycobacterium TB. He was initiated on modified antitubercular treatment for his kidney disease and the regimen included rifampicin 450 mg daily, isoniazid 300 mg daily, ethambutol 800 mg thrice weekly, and pyrazinamide 1250 mg thrice weekly.

Six weeks postantitubercular treatment, he came to our casualty with complaints of fever and exertional breathlessness. Patient was febrile (38.6°C) with respiratory rate of 32/min, pulse rate of 120/min, blood pressure of 150/92 mm of Hg, and oxygen saturation of 92% at room air. Respiratory examination was suggestive of right pleural effusion. Rest of the examination was within normal limits. Chest X-ray PA view showed features suggestive of right moderate to massive pleural effusion [Figure 2a]. Diagnostic thoracentesis revealed milky white fluid and analysis showed total protein 4.1 g/dL, glucose 117 mg/dL, total cholesterol 68 mg/dL, triglycerides 751 mg/dL, and chylomicrons 1050 mg/dL. Cytology of the pleural fluid was negative for malignant cells, cultures for bacteria and mycobacteria were negative. Hence, a diagnosis of chylothorax was made. Repeat CT thorax with abdomen showed an increase in the size of mediastinal and abdominal lymphadenopathy. Hence, the acute worsening in patient clinical condition was attributed to be part of PR/IRIS, developing secondary to antitubercular treatment. His antitubercular therapy was continued and was managed symptomatically with parenteral nutrition, therapeutic thoracentesis, antipyretics, and oxygen; nonsteroidal anti-inflammatory drugs were deferred in view of renal disease. Despite these he was symptomatic, so initiated on tab prednisolone 1 mg/kg/day. In view of persisting breathing difficulty, increasing oxygen requirement and worsening pleural effusion radiologically after informed consent intercostal drain (ICD) was inserted. Post-ICD X-ray showed partial expansion of lung, so patient was connected to -20 cm water suction. Despite these lung

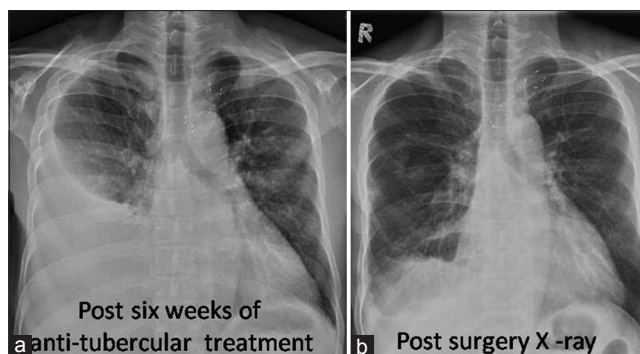


Figure 2: (a) Chest X-ray posteroanterior view post 6 weeks of antitubercular treatment showing moderate to massive right pleural effusion, (b) postsurgery chest X-ray posteroanterior view depicting resolving right pleural effusion

failed to expand, thoracic surgery opinion was obtained and he underwent decortication and interruption of the thoracic duct. Histopathology of the operated specimen showed fibrous connective tissue, fibrinous, and acute inflammatory exudates. Postoperative chest X-ray showed good lung expansion and resolution of right pleural effusion [Figure 2b]. Prednisolone 1 mg/kg daily was continued for 2 weeks, then, it was tapered to 0.5 mg/kg and the same was given for 2 more weeks. The patient was discharged on antitubercular treatment and was advised to continue the same for total of 6 months. On follow-up, patient showed good clinical recovery.

DISCUSSION

Paradoxical deterioration during anti-TB therapy defined as the radiological or clinical worsening of preexisting lesions or the development of new lesions in a patient who initially improves with anti-TB therapy. TB and HIV both cause immune dysfunction. TB is associated with depressed cellular immunity and other immunological abnormalities, which are restored to normal by effective anti-TB therapy. Hence, there is sudden shift of host immunity from an anti-inflammatory and immunosuppressive state toward a proinflammatory state. Poor drug compliance, the progression of the original disease, drug resistance, and other secondary diagnoses should be ruled out before diagnosing IRIS. The incidence, timing, and clinical spectrum of PR varies widely between studies.

The incidence of PR in HIV-negative patient varies from 2.4%^[1] to 28%.^[2] In one study, PR occurred in 28% of 50 HIV-positive TB patients and 10% of 50 HIV-negative TB patients.^[2] The median time from starting TB medication to the onset of PR was 33 days in the HIV-positive tuberculous patients (range 3–173 days) and 87 days in the HIV-negative tuberculous patients (range 23–157 days). Baseline anemia, low albumin, lymphopenia, and a greater change in lymphocyte count were independent risk factors for developing PR.^[1] Our patient had all the three risk factors. Chylothorax in adults is a rare cause of pleural effusion seen in approximately 2–3% of pleural

effusions can be divided in the nontraumatic cause (72%) and traumatic (28%). Malignancy accounts for more than 50% of chylothorax diagnosis. Nonmalignant etiology is separated into congenital, idiopathic, and miscellaneous. Miscellaneous causes include Castleman's disease, lymphangiomyomatosis,^[3] sarcoidosis, Kaposi sarcoma, Noonan syndrome, Yellow nail syndrome, TB,^[4] Down syndrome, congenital lymphangiectasia, Waldenstrom macroglobulinemia, filariasis, thoracic irradiation, subclavian vein thrombosis, constrictive pericarditis, and cirrhosis.^[5]

Pulmonary TB as a cause of chylothorax etiology was rare; with only a few cases reported in the world literature.^[6,7] Chylothorax is a rare manifestation of TB-associated PR in HIV-positive patients. To the best of our knowledge, PR presenting as chylothorax in HIV-negative patients is extremely rare and no cases reported till now.

In our patient, the cause for chylothorax possibly due to the mediastinal lymphadenopathy, which obstructed the thoracic duct flow and resulted in chyle leak into the pleural space. The administration of corticosteroid did not halt the progressive increase in chylous pleural effusion in our patient. To the best of our knowledge, we are the first to report a case of chylothorax due to PR in non-HIV tuberculous patient. There was no evidence/case report to suggest that chronic renal failure is a risk factor

for IRIS, just like HIV. This case illustrates the variable manifestations of TB-associated IRIS and suggests that close monitoring of clinical response.

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Conflicts of interest

There are no conflicts of interest.

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