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Case Report

Immune thrombocytopenia associated with pleural and pericardial tuberculosis: case report

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Background

Tuberculosis (TB) remains a major global health problem, responsible for the ill health of millions of people each year, and ranks as the second leading cause of death from an infectious disease worldwide.[1] A variety of clinical manifestations are associated directly or indirectly with TB. Among them, hematological abnormalities can be found in both the pulmonary and extrapulmonary forms of the disease, and though a myriad of hematological disorders have been described, anemia, leukocytosis, and pancytopenia are the most frequently cited.[2] Thrombocytopenia is usually associated with disseminated or miliary TB and when it occurs, it does so most commonly via non-immunologic means, typically manifesting in the context of pancytopenia that develops secondary to granulomatous infiltration of the bone marrow.[3] A causal association between TB and immune thrombocytopenia (ITP) is extraordinarily rare and, to our knowledge, this is the first documented case of pleural and pericardial TB and ITP.

Case report

60-year-old, previously healthy, Caucasian, male with a history of well-controlled hypertension was admitted to the Emergency Room with new-onset hematuria and generalized purpuric lesions. He also described a two-week history of fever, dry cough, shortness of breath and pleuritic chest pain. The patient was well nourished, with generalized nontender, nonpalpable purpuric lesions, most evident in the extremities and trunk. He had an auricular temperature of 37.8 °C and a respiratory rate of 22 breaths/min. His blood pressure and pulse were, respectively, 109/60 mmHg and 110 beats/min while supine. Breath sounds were diminished on the right side and the remainder of the physical examination was normal.

The initial complete blood count revealed a white blood cell (WBC) count of 9.8×10^9/L with 75.4% granulocytes, 13.1% lymphocytes, 11.1% monocytes, 0.3% eosinophils, and 0.1% basophils, hemoglobin of 10.8 g/dL with a mean corpuscular volume (MCV) of 85.6 fl and a mean corpuscular hemoglobin (MCH) of 30.0 pg, and platelet count of 2.0×10^9/L. A peripheral smear was remarkable for a paucity of platelets. The findings of blood chemistries were normal and the following laboratory studies were normal or negative: prothrombin time/partial thromboplastin time, fibrinogen, fibrin degradation products (FDP), antinuclear antibodies (ANA), rheumatoid factor, hepatitis C (HCV) and human immunodeficiency virus (HIV). Anti-platelet antibodies were not tested. A chest X-ray demonstrated bilateral pleural effusions, more pronounced on the right, a large heart shadow and clear lung fields. Computed tomography of the chest revealed massive right pleural effusion and a large pericardial effusion. M-mode and 2D transthoracic echocardiogram revealed an organized moderate-level anterior and posterior pericardial effusion, without right ventricular collapse.

The patient was admitted to the Hematology Clinic where he started a 5-day course of intravenous immunoglobulin (IVIg), followed by oral corticosteroid therapy with prednisone (1 mg/kg/day orally). The platelet count increased to 243×10^9/L and platelet transfusions were not required.

He was then transferred to our department to evaluate the pleural and pericardial effusions. A laboratory evaluation revealed a normal WBC count, normocytic normochromic anemia and normal platelet count. The erythrocyte sedimentation rate (ESR) was elevated at 88 mm/h. The result of tuberculin skin test was positive (22 mm). A thoracentesis was then performed, and the pleural fluid revealed glucose 37 mg/dL, protein 4.4 g/dL, lactate dehydrogenase (LDH) 890 U/L, adenosine deaminase (ADA) 90.1 U/L, with a WBC count of 8.0×10^9/L including 66% of lymphocytes and no malignant cells. Pleural fluid acid-fast bacilli (AFB) smears were negative but real-time polymerase chain reaction (PCR) for the detection of *Mycobacterium tuberculosis* complex was positive, posteriorly confirmed by cultures of pleural fluid with the identification of *M. tuberculosis*. Isoniazid, rifampin, pyrazinamide, and ethambutol were started immediately and the patient was discharged three weeks after admission. Prednisone was tapered over eight weeks and stopped. Four months after discharge, the patient, who was in stable health and with a platelet count of 253×10^9/L, was found to have abnormal liver enzymes with a cholestatic pattern, thought to be secondary to anti-tuberculous therapy (ATT). Doppler ultrasonography of the liver showed hepatomegaly (176 mm), dilated inferior vena cava and hepatic veins, with turbulent flow evidenced by color Doppler and a pulsatile waveform on pulsed Doppler, suggesting right-sided heart failure. A liver biopsy was performed which revealed sinusoidal dilatation and congestion, with no granulomas and no evidence of AFB or malignant cells. Cultures of the liver specimen were not performed. For further clarification, cardiac magnetic resonance imaging was then carried out which revealed thickening of the pericardium (6 mm) with signs of constriction, but without evidence of pericardial effusion, and the patient underwent pericardiectomy. Thrombocytopenia did not recur during the follow-up.

Discussion

ITP is an autoimmune disorder characterized by immunologic destruction of otherwise normal platelets most commonly occurring in response to an unknown stimulus. Classically it occurs as one of two forms: a childhood variety that is acute, without gender predilection, post-viral and self-limited, and the adult form that tends to be chronic. It may occur in isolation (primary) or in association with other disorders (secondary), including autoimmune diseases (particularly antiphospholipid antibody syndrome), viral infections (including HCV and HIV), and certain drugs. The diagnosis of ITP is made by exclusion of secondary causes of thrombocytopenia as there are no diagnostic tests to confirm ITP, and in general, bone marrow examination or assay of anti-platelet antibodies are not needed for diagnosis if typical features are present. In fact, anti-platelet antibodies were labeled as an 'unnecessary' test for the routine evaluation of patients presenting with ITP according to the 2011 guidelines of the American Society for Hematology, and the initial history and physical examination should aim at identifying evidence of bleeding and excluding other causes of thrombocytopenia including secondary ITP.[4] The association between TB and ITP is exceedingly rare, with few cases reported in the world literature.[3] An immune basis for TB-induced ITP was supported by the presence of either platelet antigen specific antibodies or platelet surface membrane IgG in three reports and by a salutary response to immunomodulating treatments, as observed in our patient. However, some cases failed to achieve a complete response to immunomodulating therapies alone, which was only obtained after ATT was started, supporting the etiologic role of TB in producing ITP. Most authors used anti-tuberculosis drugs combined with steroids and/or IVIg. Although rifampicin has been implicated in causing thrombocytopenia, four drug ATT regimens included rifampicin in all the cases without worsening the condition. The exact duration of the immunosuppressive therapy is not standardized and must be individualized according to the hematological response. However, in most of the reported cases steroids were withdrawn in 1–2 months.

In summary, TB-related ITP is a rare hematological manifestation of a common disease. The actual pathophysiology, clinical significance and optimal treatment is not fully known, but it should be recognized, especially in areas of high endemicity, that TB-related ITP is treatable.

Conflicts of interest

The authors declare no conflicts of interest.

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