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IMMUNE THROMBOCTYOPENIC PURPURA A RARE COMPLICATION OF TUBERCULOSIS : A CASE REPORT

Pediatrics

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ABSTRACT

The haematological abnormalities associated with active pulmonary tuberculosis were known to human beings since decades but Immune Thrombocytopenic Purpura (ITP) secondary to extra pulmonary tuberculosis have been reported only in a few instances. We report a 8 year-old female patient who was admitted to our hospital with ecchymotic patches over thighs, arms and patechie over legs. No complain of shortness of breath, cough, fever, haematuria, epistaxis, bleeding from any site and trauma .HRCT thorax shows multiple enlarged mediastinal lymphadenopathy. The ultrasound guided FNAC shown granulomatous changes and gene Xpert was positive for Mycobacterium tuberculosis. Effective Anti Tubercular Therapy (ATT) and appropriate immune modulator therapy (steroids/IVIG) together are important in the management of ITP associated with TB and hence both were started in this patient.1 Clinical and laboratory parameters including patients response to the treatment confirms the diagnosis of ITP secondary to extrapulmonary TB. Patient was put on Directly Observed Treatment and Short course (DOTS) category-1 Anti-Tuberculosis Therapy (ATT) and dexamethasone following which thrombocytopenia was corrected and there was complete recovery of the patient without recurrence of thrombocytopenia.

KEYWORDS

Immune Thrombocytopenic Purpura, Lymphadenopathy, Tuberculosis , Dexamethasone, Anti Tubercular Treatment

INTRODUCTION

We present an interesting case of extrapulmonary tuberculosis, complicated by isolated thrombocytopenia which was diagnosed as immune thrombocytopenic purpura. This is a rare haematological manifestation of tuberculosis.

Tuberculosis (TB) has variable presentations ranging from classical respiratory symptoms to less common presentations like involvement of lymph nodes and gastrointestinal system and rarely hematological manifestations.[2] Hematological manifestations of TB vary from anemia and pancytopenia to rare presentations like immune thrombocytopenia. Thrombocytopenia can be either due to bone marrow infiltration with granuloma or immune-mediated thrombocytopenia presenting as immune thrombocytopenic purpura (ITP).[2,3,] ITP in association with TB has rarely been reported. Here we describe a case of ITP that was later found to be secondary to TB; unfortunately, the diagnosis of TB was delayed because the patient was suspected initially as ITP. The purpose of this report is to highlight the association between the two conditions because early diagnosis and treatment are important to avoid an extreme outcome.

CASE STUDY

A 9 year old female admitted with chief complaints of patechie over legs, thighs, arms and back for 15 days. Patient had no history of fever, respiratory distress, weight loss, bleeding tendency, hematuria, and trauma.

On examination patient was active, alert, conscious and well oriented. Vitals were normal with no positive finding in systemic examination. There was no associated Hepatosplenomegaly or lymphadenopathy. Local examination shows multiple non tender and non palpable purpuric lesions over lower limbs and arms.

Routine workup revealed severe thrombocytopenia (Platelet 20,000/ul) with normal white blood cell and hemoglobin count. Dengue serology was negative and malarial parasite was not seen on smear. Liver function test, renal function test and coagulation profile were normal. Erythrocyte sedimentation rate was 28mm/h, C-reactive protein was negative , COVID-19 RT PCR was negative. Chest X ray shows no opacity. Mantoux test was negative after 48 hours.

To evaluate the underlying etiology, serological tests (hepatitis A, B, C, HIV, Epstein–Barr virus and cytomegalovirus), autoimmune profile (rheumatoid factor, antinuclear antibody, anti-double-stranded DNA antibody, antinuclear cytoplasmic antibody and complement C3 and C4), were carried out. The results of all these tests were negative. Absence of pancytopenia rule out BM infiltration as cause of thrombocytopenia hence BM biopsy was not done.

Hence at this stage diagnosis of ITP was made as no other cause for thrombocytopenia was revealed. Because of the initial severe thrombocytopenia, the patient was started on pulse steroid therapy in the form of prednisolone 2mg/kg/day orally in divided doses for 7days followed by tapering dose in next 7 days. Platelet count shows no improvement therefore intravenous immunoglobulin (IVIG) was given at 1 g/kg/day for 2 days .Platelet count done daily and no improvement was seen even after IVIG.

In view of no response to the given treatment further investigations were done. HRCT thorax shown multiple large midiastinal lymphadenopathy. USG guided lymphnode biopsy was done which shows granulomatous changes negative for gram stain for AFB but gene xpert for MTB was positive. On Day 16th of admission ATT was started (2HRZE +4HRE) with dexamethasone 20mg/day for four days in a week fortnight. Inj Romiplostim 75microgram/weeks subcutaneous was started and patient is still receiving weekly injections (At present 12th week of Rmiplostim).

Child responded to the treatment and platelet count improved to 60,000/ul on day7 of ATT and steroid therapy. Patient got discharged on day 14 of the treatment with platelet count of 1,50,000. Patient was kept on regular weekly follow up.

DISCUSSION:

Tuberculosis is one of the world's most challenging communicable diseases. The hematological abnormalities associated with tuberculosis are well recognized but thrombocytopenia is rarely seen in such patients[1]

Hematological manifestations of TB includes anemia, leukocytosis, leucopenia, thrombocytosis, or thrombocytopenia (rarely).[4] The mechanism of isolated thrombocytopenia in tuberculosis is believed to be immune mediated, through anti platelet antibodies or platelet-associated immunoglobulin G, which are generated by proliferating lymphocytes as a part of the immune response to infection.[2,5,6,7,] Most of the hematological abnormalities, including pancytopenia, have been noted to respond to ATT.

Our patient had extrapulmonary tuberculosis with persistent isolated thrombocytopenia and petechie. Other hematological manifestations

of disseminated tuberculosis include leucopenia, anemia, pancytopenia, myelofibrosis, and the hemophagocytic syndrome, which can occur due to direct bone marrow involvement in tuberculosis.[4]

Our patient had not received any ATT prior to presentation to our institution. Hence ATT-induced thrombocytopenia was ruled out. In our patient, ecchymosis and platelet count did not respond to steroid and IVIG ,which were given for suspected immune thrombocytopenic purpura (ITP) ; but responded favorably to ATT , steroids and Romiplastin together.

TB was diagnosed based on histological and radiological evidence. Secondary causes for immune thrombocytopenia such as drugs, infections, autoimmune conditions and malignancy were ruled out. The absence of pancytopenia excludes bone marrow infiltration as the cause of thrombocytopenia. Improvement of platelet counts after initiation of ATT with steroids and Romiplostim suggests Tuberculosis as the etiology of the thrombocytopenia.

ITP is a disorder in which antiplatelet antibodies cause accelerated destruction of platelets, resulting in thrombocytopenia and a varying propensity for bleeding.[8] In addition, it is now recognized that these antibodies may also impair platelet production, creating a dual cause of thrombocytopenia. The diagnostic criteria[11] for ITP are (1) isolated thrombocytopenia with otherwise normal peripheral complete blood count and smear, (2) an absence of hepatosplenomegaly and lymphadenopathy on physical examination, and (3) platelet response to classic ITP therapy (usually intravenous immunoglobulin, IV anti-D, and possibly steroids). Our patient met the first two of the above-mentioned criteria for ITP. Also, her thrombocytopenia improved only after ATT along with steroid and Romiplastim. This further supports the diagnosis of **ITP secondary to tubercular lymphadenitis** in our patient.

ITP in conjunction with tuberculosis has not been reported frequently. A study from Saudi Arabia of 846 patients reported that only 1% of these had ITP as the presenting feature; all these patients had increased megakarycocytes in the bone marrow.[9]

A case report from Turkey describes a child diagnosed with ITP, not responding to standard therapy with IVIG and pulsed steroids. Radiological investigations were suggestive of pulmonary infiltrates and the patient responded to the combination of ATT and steroids.[10] Thrombocytopenia associated with tuberculous gumma has been reported from Japan.[11] Tuberculous splenic abscess has been reported in a known case of ITP. The patient was a 14-year-old male, on steroids for his ITP, who developed a tuberculous splenic abscess.[12] Thrombocytopenia has also been found with tuberculous lymphadenitis.[13]

Effective ATT and appropriate immunomodulatory therapy (steroids/IVIG) are both important in the management of ITP associated with TB.[5]

CONCLUSIONS

The incidence of tuberculosis continues to rise due to evolution of bacteria resistant to anti-tuberculous agents and spread of human immunodeficiency virus (HIV) worldwide. Tuberculosis has varied manifestations, and the clinicians must also recognize tuberculosis-mediated immune thrombocytopenia as a manifestation of the disease. The pathophysiologic mechanisms behind it remain unclear. Adherence to anti-tubercular therapy with initiation of immune modulator therapy defines the treatment of this specific condition.[4.] It is important to recognize TB as a treatable cause of immune thrombocytopenia and to initiate anti-TB medications early to avoid a serious or prolonged illness, as was the case with the reported patient. It is also vital to anticipate that the use of steroids without anti-TB medications can lead to disseminated TB.

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