Case Report

Immune thrombocytopenic purpura secondary to tuberculosis

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INTRODUCTION

Immune thrombocytopenic purpura (ITP) is a clinical syndrome characterized by reduced number of circulating platelets. The cause of ITP remains unknown in most cases, although it can be triggered by a viral infection or other immune trigger. Although tuberculosis is associated with a wide range of hematological manifestations, ITP secondary to tuberculosis is a very rare manifestation, especially in children. We describe an 11-year-old female child who presented with skin and mucosal bleeds, thrombocytopenia and chronic submandibular lymphadenitis. Blood and bone marrow investigations were suggestive of ITP. She received IVIg, but response was unsatisfactory, hence she was started on steroids. Concurrently, GeneXpert of lymph node biopsy was positive for tuberculosis. A diagnosis of ITP secondary to tuberculous lymphadenitis was made. She received 6 months of anti-tuberculosis therapy. Steroids were tapered and stopped within 2 months. She responded well with restoration of normal platelet counts and regression of lymphadenopathy. Tuberculosis should be considered as one of the secondary causes of ITP, especially in highly endemic countries.

Keywords: Immune thrombocytopenic purpura, Tuberculosis, Tuberculous lymphadenitis

ABSTRACT

Immune thrombocytopenic purpura (ITP) is a clinical syndrome characterized by reduced number of circulating platelets. The cause of ITP remains unknown in most cases, although it can be triggered by a viral infection or other immune trigger. Although tuberculosis is associated with a wide range of hematological manifestations, ITP secondary to tuberculosis is a very rare manifestation, especially in children. We describe an 11-year-old female child who presented with skin and mucosal bleeds, thrombocytopenia and chronic submandibular lymphadenitis. Blood and bone marrow investigations were suggestive of ITP. She received IVIg, but response was unsatisfactory, hence she was started on steroids. Concurrently, GeneXpert of lymph node biopsy was positive for tuberculosis. A diagnosis of ITP secondary to tuberculous lymphadenitis was made. She received 6 months of anti-tuberculosis therapy. Steroids were tapered and stopped within 2 months. She responded well with restoration of normal platelet counts and regression of lymphadenopathy. Tuberculosis should be considered as one of the secondary causes of ITP, especially in highly endemic countries.

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INTRODUCTION

Immune thrombocytopenic purpura (ITP) is a clinical syndrome characterised by reduced number of circulating platelets. ITP in the absence of other causes or disorders that may be associated with the thrombocytopenia is known as primary ITP. Secondary ITP refers to immune-mediated thrombocytopenia with an underlying cause, such as drug-induced, or associated with systemic illness. Tuberculosis is one of the most widespread communicable diseases in developing countries, due to a wide variety of well documented predisposing factors. As of 2016, India has the highest incidence of the disease with an estimated 2.79 million cases, accounting for about 25% of the global incidence according to the World Health Organization statistics. A wide spectrum of hematological manifestations of tuberculosis has been observed, although an association with immune thrombocytopenia is quite rare and there have been few reports to date. We report the case of an 11-year-old girl diagnosed with tuberculous lymphadenitis induced immune thrombocytopenic purpura, who responded well to anti-tuberculosis therapy and steroids.

CASE REPORT

An 11-year-old girl was admitted to our hospital with complaints of new onset petechiae, ecchymoses and gum bleeds. She was recently evaluated for chronic right submandibular lymphadenitis. Her FNAC showed inflammatory changes and was attributed secondary to dental caries for which she was treated with antibiotics. On examination, she had petechiae and ecchymoses all over the body, more over the lower limbs. An isolated submandibular lymph node of approx. 2.5 cm × 2.5 cm was palpable on the right. Initial laboratory investigations

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revealed Hemoglobin 10.9 g/dL, WBC count 4.6x10^9/L and platelets 5x10^9/L. The peripheral smear showed marked thrombocytopenia with occasional giant platelets. In view of significant lymphadenopathy, skin bleeds and thrombocytopenia, bone marrow aspirate was done which showed increase in size and number of megakaryocytes, with normal erythroid and myeloid maturation, suggestive of ITP. The child received 1g/kg of IVIg. There was no satisfactory response, hence intravenous Methylprednisolone was given for 3 days.

On further evaluation, Ultrasonogram (USG) of neck showed lymph node with central caseation. USG abdomen showed multiple enlarged lymph nodes in retroperitoneum and paraaortic region. Computed tomography of abdomen showed multiple enlarged lymph nodes with ileocaecal thickening. Mantoux test was positive (20 mm induration with 2 TU). Hence, a lymph node excision biopsy was done which revealed confluent granulomatous lymphadenitis, suggestive of tuberculosis. Gene Xpert was positive. On careful probing, it was revealed that there was household contact with tuberculosis in a paternal uncle, who had completed treatment recently. She was started on anti-tuberculous therapy (ATT) - Category I. Steroids were switched to oral Prednisolone. Platelets gradually increased to 79x10^9/L. She was discharged on Prednisolone (2mg/kg/day) and ATT. On follow up, her platelet counts improved further, and steroids were tapered.

She developed ATT induced hepatitis, ATT was stopped and re-introduced in a phased manner. ATT was given for 6 months (2HRZE + 4HRE). On a year follow up, her CBC showed Hemoglobin 11.1 g/dL, WBC count 5.2x10^9/L and platelets 245x10^9/L and she had no significant lymphadenopathy.

**DISCUSSION**

Various hematologic abnormalities such as anemia, leukocytosis, monocytes, lymphopenia, leucopenia, thrombocytopenia, thrombocytosis, leukemoid reactions and pancytopenia have been seen in tuberculosis. The occurrence of thrombocytopenia in tuberculosis could be due to a variety of causes such as granulomatous infiltration of bone marrow causing pancytopenia, thrombotic thrombocytopenic purpura or hemophagocytic lymphohistiocytosis.

Immune thrombocytopenic purpura in association with tuberculosis infection is extremely rare in the paediatric population which is evidenced by the paucity of literature on the same. A review of the published paediatric case reports of immune thrombocytopenia associated with tuberculosis has been summarised (Table 1).

The mechanism of TB-related immune thrombocytopenia is not clear. One theory is that antiplatelet antibodies may be produced by activation of a clone of B-lymphocytes by Mycobacterium tuberculosis. Another is, Mycobacterium tuberculosis may share antigen with platelets leading to antiplatelet antibody. In two case reports immunofluorescence studies with platelets and mycobacteria showed the presence of platelet surface membrane IgG.

Although we could not perform immunofluorescence studies to detect anti-platelet antibodies, it does not invalidate the diagnosis of immune thrombocytopenia. The American Society of Haematology’s 2011 guidelines considered platelet associated IgG assay unnecessary to confirm the diagnosis of ITP.

| Report                | No. of cases | Pathology          | Plt on admission | Treatment                  |
|-----------------------|--------------|-------------------|-----------------|---------------------------|
| Present report        | 1            | Cervical lymphadenitis | 5000/cu.mm     | IVIg + ATT + steroids     |
| Jurak et al⁹          | 1            | Cervical lymphadenitis | 42000/cu.mm    | ATT only                  |
| Singh et al¹⁰         | 1            | Cervical lymphadenitis | 29000/cu.mm    | ATT + steroids            |
| Bakhshi et al⁶        | 1            | Cervical lymphadenitis | 28000/cu.mm    | ATT only                  |
| Krishnamurthy et al⁵  | 1            | Mediastinal lymphadenitis | 21000/cu.mm   | ATT only                  |

Immune thrombocytopenic purpura is a diagnosis of exclusion. In the patient, there was no hepatosplenomegaly to suggest platelet consumption. Bone marrow study was also highly suggestive of ITP and excluded any production defect or hemophagocytosis. Absence of renal insufficiency, hemolytic anemia and neurological signs made TTP unlikely.

Although it could be considered that immune thrombocytopenia was a coincidental presentation with TB lymphadenitis, the temporal association of both and the response of the child to ATT was quite significant in establishing tuberculosis as the trigger for ITP. Treatment decisions in the paediatric population have varied between ATT only or a combination of ATT with steroids. Steroids were administered to our patient in combination with ATT as there was active mucosal bleeding.

To summarize, a high index of suspicion for TB is essential and should be considered as one of the
secondary causes of ITP, more so in high endemic countries.

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