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Respiratory Medicine Case Reports

Case report

Disseminated tuberculosis with severe immune thrombocytopenia

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ABSTRACT

Immune thrombocytopenia is an autoimmune condition with increased platelet destruction. Immune thrombocytopenic purpura is an uncommon and rare manifestation of tuberculosis. A search of the literature available on TB-associated ITP identified only around 50 cases published between 1964 and 2016. We present an uncommon and interesting case of severe isolated immune thrombocytopenia secondary to bilateral tubercular cervical lymphadenopathy and pott's spine in 26 year old Indian male. Due to severe thrombocytopenia patient was managed with IVIg and steroids along with anti tubercular therapy. Early diagnosis and treatment with Anti tubercular therapy is important for effective control of bleeding manifestations.

1. Introduction

Tuberculosis is still one of the leading causes of morbidity and mortality worldwide with varied presentations of multi-organ involvement.

Thrombocytopenia is a common hematological disorder where platelet count will be less than 100,000 per microliter. Immune thrombocytopenia is an autoimmune condition with increased platelet destruction. This disorder is either primary, characterized by isolated thrombocytopenia in the absence of any apparent cause of thrombocytopenia or secondary to underlying conditions like SLE, Lymphoproliferative diseases, medications and infections that might be benefited from treating the underlying cause.

Tuberculosis is associated with a variety of hematological abnormalities like anemia, leukocytosis, leucopenia, neutropenia, and thrombocytopenia. Hematological manifestations of TB can be due to the direct effect of the infectious process, or it may be due to the consequence of antitubercular treatment. Normochromic normocytic anemia or anemia of chronic disease and raised ESR is the most common hematological abnormality in tuberculosis. Thrombocytosis and thrombocytopenia both are seen in tuberculosis. Thrombocytosis is seen in pulmonary tuberculosis. Thrombocytopenia was commonly seen in disseminated Tuberculosis or miliary tuberculosis. Pathogenesis of thrombocytopenia is believed to be immune-mediated.

Immune thrombocytopenic purpura is an uncommon and rare manifestation of tuberculosis. We present an uncommon and interesting case of severe immune thrombocytopenia in disseminated tuberculosis. Severe ITP refers to thrombocytopenia with bleeding symptoms sufficient to require treatment; this occurs when the platelet counts are below 10,000 to 20,000 per microliter. A search of the literature available on TB-associated ITP identified only around 50 cases published between 1964 and 2016.

2. Case report

A 26 year old Indian male with no prior comorbidities and not on any recent medication presented with bilateral progressive non tender neck swelling for 40 days, weight loss of about 10 kgs in 2 months, bilateral multiple small and large joint pains of both legs and tingling and numbness of left 1st and 2nd toes for 26 days, petechial rash over lower limbs and trunk for 1 day. He had epistaxis for 1 hour for which he was rushed to emergency room.

On examination, the patient is pale, no icterus, and found to have bilateral enlarged, mobile, nontender cervical lymph nodes — no axillary and inguinal lymphadenopathy. Petechial rashes were found over lower limbs and trunk. He is afebrile with normal vitals. Active bleeding observed from the right nostril. His blood count revealed Hb – 9.70 gm %, TLC- 9100 cells/cumm, platelets – 3000 cells/cumm, ESR- 12mm/hr. Liver function tests, coagulation profile, blood urea, serum creatinine, CUE, serum electrolytes were within normal range. Peripheral smear showed microcytic hypochromic RBC, Neutrophilic predominance, platelets on smear were reduced and no abnormal cells were found. HIV, HCV, HBsAg, VDRL were Non-reactive. ANA was negative. His Chest X-ray and ultrasound abdomen were normal. B12, folic acid, procalcitonin levels were normal. Coombs test is negative. Serum LDH is 710 U/L.

In the further workup, USG guided FNAC of the right cervical lymph node is suggestive of granulomatous lymphadenitis with caseous

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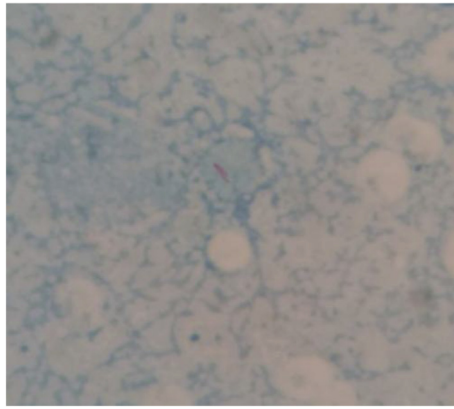 *E-mail address:* dr.uma3700@gmail.com (U.S. Gottam).

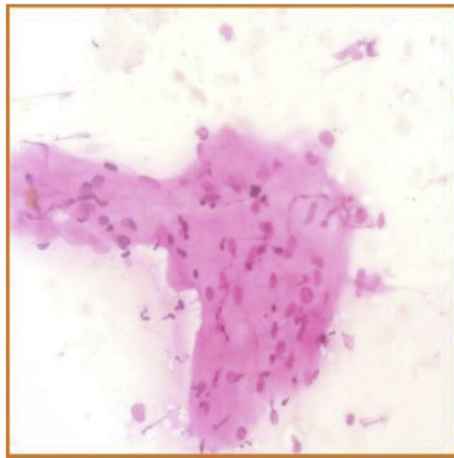**Fig. 1.** FNAC of Lymph node showing Acid fast bacillus.

Fig. 2. Cytology showing Granuloma.

necrosis. AFB Smear and Genexpert were positive and rifampicin sensitive (Figs. 1 and 2).

Bone marrow study suggestive of peripheral bicytopenia with cellular marrow, normoblastic erythropoiesis, and megakaryocytic thrombocytopenia. (Fig. 3). MRI of lumbosacral spine was showing (Fig. 4) altered signal intensities in multiple vertebral bodies in whole spine suggestive of TB osteomyelitis. Small abscess in paraspinal muscles at the level of D12 – L1 on the left side. Pus aspirated from the abscess showed AFB and Genexpert positive and rifampicin sensitive,
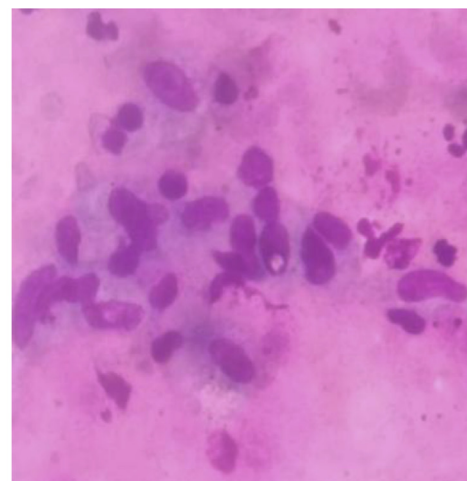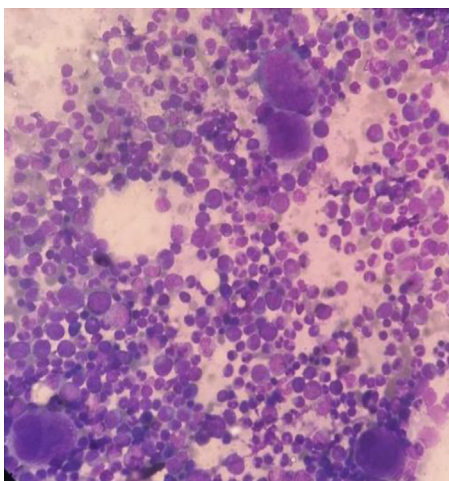
Suggestive of Pott's spine.

In view of severe thrombocytopenia and active uncontrolled epistaxis considered platelets products transfusion. After transfusion of one SDP platelet count increased from 3000 to 5000 per microliter and patient, continue to have epistaxis. So we Considered IVIg 1 gm/kg body weight as a single dose and corticosteroids dexamethasone along with second SDP transfusion. Dexamethasone 40mg IV for four days given followed by tapering the dose of prednisolone. Epistaxis controlled with all the above measures and nasal pack. The patient was started on category −1 ATT according to RNTCP guidelines.

Platelets count increased to 80,000 per microliter after one week and reached to above 1,50,000 per microliter after two weeks of the ATT and prednisone therapy. There was no fresh bleeding from any sites, and no new petechiae and purpura. Prednisone was then tapered off over a period of one month. The patient was followed-up for ten months in the outpatient department, and there was no recurrence of thrombocytopenia. Follow up MRI spine after 9 months was showing completely resolved paraspinal abscess. After exclusion of all other secondary causes of thrombocytopenia and failure of first-line ITP treatment and prompt response to Anti-tuberculosis treatment it is highly suggestive of TB is the causality of ITP.

3. Review of literature

Disseminated tuberculosis refers to concurrent involvement of at least two non-contiguous organ sites of the body or involvement of blood or bone marrow by tuberculosis process [1].

Immune thrombocytopenia (ITP) is an auto-immune condition that results in isolated thrombocytopenia associated with possibly lethal hemorrhage. In its secondary form, ITP can be triggered by many infectious and non-infectious conditions. Secondary ITP associated with tuberculosis (TB) has rarely been described in the literature. A search of the literature available on TB-associated ITP identified 50 cases published between 1964 and 2016 [2].

The mechanism of isolated thrombocytopenia in tuberculosis is believed to be immune-mediated, through antiplatelet antibodies as mycobacterium TB may share antibodies with platelets or platelet-associated immunoglobulin G, which are generated by proliferating lymphocytes as a part of the immune response to infection. Most of the hematological abnormalities, including pancytopenia, have been noted to respond to ATT [3–5]. Thrombocytopenia in TB may occur owing to defective platelet production in the context of pancytopenia due to bone marrow infiltration, histiophagocytosis, thrombotic thrombocytopenic purpura, disseminated intravascular coagulation, immune-mediated platelet destruction or as an adverse effect of therapy with rifampicin and isoniazid [4,6]. Henceforth a patient with newly-
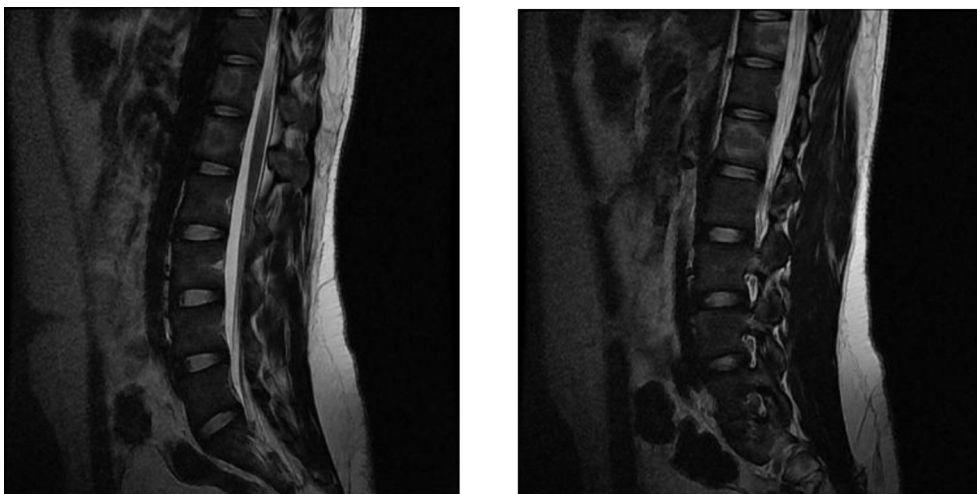

Fig. 3. Bone marrow study showing megakaryocytes.

Fig. 4. MRI spine showing altered signal intensities in multiple vertebrae.

diagnosed thrombocytopenia should be evaluated for symptoms associated with disorders causing secondary ITP. Rifampicin is also known to cause hematological abnormalities, which can be via autoimmune mechanisms, such as rifampicin-induced autoimmune hemolytic anemia and thrombocytopenia. The latter is thought to be mediated via antibodies directed against Glycoprotein Ib/IX and is more frequently observed with an intermittent schedule of rifampicin [7]. Our patient had not received any ATT before presentation to our institution. Hence ATT induced thrombocytopenia was ruled out.

Bleeding is the most common clinical manifestation of ITP, presenting as mucocutaneous bleeding involving the skin, oral cavity, and gastrointestinal tract. Purpura, usually on the extremities ("dry purpura") may often appear without an obvious precipitating event. Mucosal bleeding includes epistaxis, menorrhagia, and gingival and gastrointestinal bleeding [8]. Intracranial hemorrhage is the most feared complication of ITP.

The diagnosis of ITP is one of exclusion, and antiplatelet antibody testing is not recommended because of high inter-laboratory variability and poor sensitivity [9]. Essential components required for making the diagnosis include: personal history, family history evaluating for inherited thrombocytopenias, physical examination, and complete blood count with differential, reticulocyte count, and review of the peripheral blood smear [10–12]. Additional testing for HIV and hepatitis C is recommended for all adult patients with ITP [10,12] because both can be associated with ITP and treatment depends upon the management of the underlying condition.

Traditional first-line agents include corticosteroids, IVIg, and anti-D immunoglobulin (anti-D). Corticosteroids are the standard initial treatment. Prednisone is the standard initial first-line therapy for ITP patients. Prednisone is usually given at 0.5–2 mg/kg/d until the platelet count increases (> 30–50×10^9/L), which may require several days to several weeks [10,13,14]. Although the treatment is effective, patients are at risk of developing corticosteroid-related complications that vary with the dose and duration. To avoid corticosteroid-related complications, prednisone should be rapidly tapered and usually stopped in responders and especially in non-responders after 4 weeks [10,13]. Administration of dexamethasone 40 mg/day for 4 days (equivalent to 400 mg of prednisone per day) produced a sustained response in 50% of newly diagnosed adults with ITP [10,15,16]. Parenteral administration of high-dose methylprednisolone has been used in various regimens to treat patients failing first-line therapies, with 80% response rates. Due to the short-term responses to methylprednisolone, maintenance therapy with oral corticosteroids may be required.

The dose of IVIg is 0.4 g/kg/day for 5 day or infusions of 1 g/kg/day for 1–2 days. Up to 80% of Patients respond initially and achieve normal platelet counts. It appears that in some patients corticosteroids may enhance the IVIg response. In addition to this, the concomitant use of corticosteroids may reduce infusion reactions and prevent aseptic meningitis. IVIg influences humoral and cellular immunity by interacting with the regulation of Fc receptor expression [11,17]. IVIg recipients are more likely to attain a platelet increase within 24 hours at a dose of 1 g/kg (1–2 infusions over 2 days) compared with the historical treatment regimen (0.4 g/kg/d over 5 days) [10,18].

The treatment in secondary ITP is often the same to the one used for primary ITP, but the management must be focused to obtain complete remission of the underlying cause and not to treat the decreased platelet number. Indication for treatment: platelets $< 20/30,000$/mm3, active bleeding or high bleeding risk associated with platelets $< 50,000$/mm3 [10].

4. Conclusion

The incidence of tuberculosis still in the rise due to the evolution of bacterial resistance to antituberculosis therapy and also due to rising in the multiple comorbidities like diabetes mellitus, CKD, Immunocompromised states and at the same time tuberculosis manifestations also varying. Every clinician must recognize and correlate it to the cause for a better outcome and early intervention. Rare hematological manifestations of a common disease require more research and publications.

Conflicts of interest

The authors report no conflict of interest and no financial and non financial interest in the subject matter or materials discussed in this manuscript. The authors alone are responsible for the content and writing of this article.

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