Immune Thrombocytopenic Purpura in a Patient with Disseminated Tuberculosis: An Unusual Presentation

Prashant Nasa1, Deven Juneja1, Sudhish Sehra2, H. K. Singh2, Deen Bandhu Prasad2
Departments of 1Critical Care Medicine and 2Internal Medicine, Sri Balaji Action Medical Institute, New Delhi, India

Abstract

Pulmonary tuberculosis can have a wide variety of presentations including hematological manifestations. We report a case of a young male patient who presented with complaints of generalized petechiae, gum bleeding, systemic lymphadenopathy, and severe thrombocytopenia. His bone marrow revealed normal megakaryocytes, and in the absence of hepatosplenomegaly, a diagnosis of immune thrombocytopenic purpura (ITP) was made. The thrombocytopenia responded to course of intravenous immune globulin. The smear made from fine-needle aspiration of cervical lymph nodes showed acid-fast bacilli. This case highlights the rare association of extrapulmonary tuberculosis with ITP.

Keywords: Extrapulmonary tuberculosis with immune thrombocytopenic purpura, hematological manifestations of tuberculosis, immune thrombocytopenic purpura

Introduction

Extrapulmonary tuberculosis can have a wide variety of manifestations including hematological. Thrombocytopenia in tuberculosis is uncommon and if present, it is a diagnostic dilemma to clinicians. It occurs most commonly through nonimmunologic means and manifesting typically in relation to pancytopenia that may develop secondary to granulomatous infiltration of the bone marrow.1 However, immune thrombocytopenic purpura (ITP) in a patient with tuberculosis is exceedingly a rare event and is a diagnosis of exclusion.

Case Report

A 21-year-old male was admitted with complaints of high-grade fever, loss of appetite for 35–40 days, petechial rashes, and bleeding gums for the last 2 days. He had received intravenous ceftriaxone 1 g 12 hourly for 3 days in a nursing home before coming to our hospital. There was no other family and personal history and of any other major systemic disease. On examination, the patient had petechiae and purpuric rash on the trunk, neck, and both upper limbs. Furthermore, on palpation, there were nontender, multiple, soft, rubbery, discrete, and mobile lymph nodes (largest 3 cm × 2 cm), involving bilateral deep cervical, axillary, and inguinal areas. On taking further history, the patient confirmed the presence of these swellings for more than a month. He was hemodynamic stable. On systemic examination, liver and spleen were not palpable, with no other systemic findings. The significant investigational findings were thrombocytopenia (platelet count – 1000/mm³), multiple abdominal lymph nodes on ultrasound with no other organomegaly and multiple mediastinal lymphadenopathy with no lung parenchymal lesion on contrast-enhanced chest tomography chest. His other investigations are mentioned in Table 1. He was managed with single-donor apheresis platelets and other supportive management with a provisional diagnosis of hematological malignancy or ITP after performing bone marrow examination. On bone marrow aspirate, there were normal megakaryocytes with very few abnormal lymphocytes. He was started on intravenous immunoglobulin (IVIG) in view of persistent

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Address for correspondence: Dr. Prashant Nasa, Department of Critical Care Medicine, Sri Balaji Action Medical Institute, New Delhi, India. E-mail: dr.prashantnasa@hotmail.com

ORCID: https://orcid.org/0000-0003-1948-4060

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severe thrombocytopenia, 400 mg/kg/day for 3 days. The fine-needle aspiration of cervical lymph node showed multiple granulomas with central necrosis and acid-fast bacilli on smear [Figure 1]. He was started on the first-line antituberculosis treatment (isoniazid, rifampin, pyrazinamide, and ethambutol). His platelets showed improvement from day 4 (60 h after the first dose) and increased to 121,000/mm³ on day 8 [Figure 2]. The patient was discharged on day 10 on antituberculosis drugs as the final diagnosis of extrapulmonary tuberculosis and ITP with advice of regular follow-up.

**Discussion**

Tuberculosis is a major public health problem worldwide with not only challenges in management but also in the diagnosis. Extrapulmonary tuberculosis can present with a wide variety of hematological manifestations such as anemia, leukopenia, pancytopenia, thrombocytopenia, myelofibrosis, and the hemophagocytic syndrome.[1,2] Severe isolated thrombocytopenia in extrapulmonary tuberculosis is relatively uncommon. There are various pathophysiological hypotheses proposed for thrombocytopenia in tuberculosis which include defect in platelet production (marrow suppression), hemophagocytosis of all cell lineages in bone marrow, side effect of antituberculous therapy (especially rifampin), thrombotic thrombocytopenic purpura (TTP), or disseminated intravascular coagulopathy (DIC), and due to immune-mediated platelet destruction.[3,4]

The ITP in extrapulmonary tuberculosis is very rare with very few cases reported in the literature.[3‑7] It can be either due to the production of platelet antigen-specific antibodies or platelet surface membrane immunoglobulin G, which is generated by proliferating lymphocytes as a part of the immune response to infection.[3,5] The characteristics of these patients are as follows:[3]

1. More common in females
2. Middle aged to the elderly, third to eighth decades of life

**Table 1: Laboratory investigations**

| Investigations                  | On admission |
|---------------------------------|--------------|
| Hemoglobin (g %)                | 14           |
| Platelets count (mm³)           | 1000         |
| TLC: N, L, E, M (%)             | 6200: 65, 31, 0, 9 |
| Peripheral smear                | Thrombocytopenia with normal other cell lineage and no evidence of schistocytes, target cells |
| Hematocrit (%)                  | 43.8         |
| Blood urea (mg/dl)              | 14           |
| Serum creatinine (mg/dl)        | 0.6          |
| Sodium (mg/dl)                  | 139          |
| Potassium (mg/dl)               | 4.8          |
| HIV (spot test)                 | Nonreactive  |
| HbsAg                           | Nonreactive  |
| HCV antibody                    | Nonreactive  |
| Malarial antigen                | Negative     |
| Typhid IgM                      | Nonreactive  |
| Dengue IgM                      | Nonreactive  |
| Dengue NS-1 antigen             | Not detected |
| LDH                             | 303          |
| PT (s) test/control             | 19.1/14.3    |
| INR                             | 1.38         |
| PTT (s) test/control            | 23.5/25.1    |
| Fibrinogen (mg/dl)              | 302          |
| FDP                             | Negative     |
| Serum bilirubin (mg/dl) total/direct | 0.23/0.2 |
| Serum alkaline phosphatase (IU/L) | 138       |
| AST (IU/L)                      | 40           |
| ALT (IU/L)                      | 41           |
| Cholesterol/LDL/HDL (mg/dl)     | 182/95/34    |
| Serum triglycerides (mg/dl)     | 137          |
| Serum ferritin (ng/L)           | 389          |

ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, HDL: High-density lipoprotein, IgM: Immunoglobulin M, LDL: Low-density lipoprotein, PT: Prothrombin time, PTT: Partial thromboplastin time, FDP: Fibrinogen degradation product, LDH: Lactate dehydrogenase, TLC: Total lymphocyte count, HBsAG: Hepatitis B surface antigen, HCV: Hepatitis C virus, INR: International Normalized Ratio

**Figure 1:** Response of platelet count to intravenous immunoglobulin
3. Middle Eastern and Asian descent
4. Most commonly associated with pulmonary tuberculosis (33%)
5. Extrapulmonary tuberculosis and tubercular lymphadenitis are associated in only 19% of cases.

The principal diagnostic criteria for ITP are as follows:[7]
1. Isolated thrombocytopenia with otherwise normal peripheral complete blood count and smear and normal marrow production
2. Absence of hepatosplenomegaly
3. Platelets response to classic ITP therapy (usually IVIG, IV anti-D, and possibly steroids).

Our case was challenging and unique in several aspects, as our patient was young (21 years) male, nonimmunocompromised, and presentation was with systemic lymphadenopathy involving multiple noncontiguous groups of lymph nodes and severe thrombocytopenia. There was no hepatosplenomegaly and absence of pulmonary involvement. The bone marrow showed normal megakaryocytes and the absence of granuloma or hemophagocytosis. Absence of renal dysfunction, neurological abnormalities, and evidence of hemolysis on peripheral smear rules out TTP. DIC was ruled out with normal prothrombin time. There was also no history of any offending drug causing thrombocytopenia. The thrombocytopenia was very severe with platelet count <10,000/mm³ and showed a good response to IVIG. The presence of thrombocytopenia with tubercular lymphadenitis in adults is very rarely reported.[8-10]

CONCLUSIONS

ITP is a rare but potentially treatable presenting manifestation of extrapulmonary tuberculosis infection. It should be considered in differential diagnosis of patients with tuberculosis presenting with isolated thrombocytopenia. The early diagnosis with the use of specific therapies such as IVIG and antituberculosis therapy should be considered in these cases.

Declaration of patient consent
We certify that we have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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