Tuberculosis Presenting as Immune Thrombocytopenia: A case report and review of the literature

Hematology/Oncology Section, Medicine Department
Hamad Medical Corporation, Doha, Qatar

Abstract:
Various hematological abnormalities commonly occur in active tuberculosis (TB) but thrombocytopenia is exceedingly rare and immune thrombocytopenic purpura (ITP) is reported in only a few cases. A 28-year-old male presented with thrombocytopenia-induced epistaxis and generalized purpura that did not respond to intravenous immunoglobulin but did resolve after antituberculous treatment. The characteristics of this rarely documented association are reviewed.

Key words: Tuberculosis, immune thrombocytopenia, idiopathic thrombocytopenic purpura.

Introduction:
Tuberculosis (TB) is a health problem known worldwide in which many hematological problems have been described, monocytosis, basophilia, anemia, leukocytosis, leukopenia and pancytopenia\(^1\). When thrombocytopenia occurs in TB it does so most commonly in a non-immunologic form, typically as pancytopenia that develops secondary to a granulomatous infiltration of the bone marrow. The association between TB and immune thrombocytopenic purpura (ITP) is rare, this case being the fourteenth such report from all over the world and the first case reported in Qatar.

Case Report:
A 28-year-old Palestine male, well nourished and previously healthy, was admitted with epistaxis, a blood pressure of 130/80 mm Hg, pulse 85/minute and oral temperature 37°C. There were multiple non-tender non-palpable purpuric lesions in the extremities and multiple palpable non-tender mobile and firm cervical lymph nodes, 2-3 cm size. The spleen was palpable 3 cm below the left costal margin and was not tender; the rest of the physical examination was normal.

The initial blood count revealed a white blood cell count 2.9 x 10/L with 47.7% granulocytes, 35.7% lymphocytes, 12.3% monocytes 4.4% eosinophils, and no basophils; hemoglobin 126 gm/L, MCV 78.3 fl. and platelets 0.7 x 109/L. A peripheral smear showed severe thrombocytopenia. PT, a PTT were normal. HIV and hepatitis C and B serologies were negative. Bone marrow aspiration and biopsy revealed hypercellularity of all cell lines including megakaryocytes with normal morphology and multiple non-caseating granulomas (Figures 2, 3). A chest x-ray showed bilateral hilar prominences without military changes. A CT scan of the chest and abdomen revealed multiple enlarged mediastinal and hilar lymph nodes and homogenous hepatosplenomegaly. Fine needle aspiration (FNA) from a cervical lymph node showed non-caseating granulomas (Figure 3).

On the first day of admission and the following day the patient received intravenous immunoglobulin (IVIG) 1gm/Kg. each day which produced a mild increase of platelets to 5 x 10/L. He then was given multiple platelet transfusions. On the fifth day fever spiked to 39.5°C. On the seventh day, after receiving the result of the bone marrow aspiration and biopsy, the...
patient was started on anti-tuberculous therapy (isoniazid 300 mg, rifampin 600 mg, ethambutol 1000mg and pyrizinamide 1500 mg daily). After a total of three weeks as an in-patient he was discharged from hospital afebrile, with a white blood cell count of 3.6 x 10^9/L, Hb 119 gm/L, and platelets 72 x 10^9/L. Four weeks after discharge he was doing very well, physical examination was normal and blood count was white blood cell 4.0 x 10^9/L, Hb 120gm/L, and platelets 257 x 10^9/L.

Discussion:
The two principle diagnostic criteria for ITP are thrombocytopenia in the context of an otherwise normal blood count, a normal blood smear and the exclusion of conditions capable of inducing thrombocytopenia. There are two forms of ITP, the childhood variety that is acute, mostly post-viral and self-limited, and the adult form that tends to be chronic, more common in females and most frequently between the 2nd and 4th decades.

When thrombocytopenia occurs in TB 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. The association between TB and ITP is extremely rare; reviewing the world literatures only fourteen cases have been reported (Table 1). It has been postulated that the anti-platelet antibodies generated in some of TB-related ITP are secreted by lymphocytes born of a clonal proliferation which occurs in response to the tuberculosis pathogen. However, according to the American Society for Hematology's 1996 guidelines for the diagnosis and management of ITP, the absence of anti-platelet antibodies in no way invalidates the diagnosis of ITP. The anti-platelet antibodies were labeled as an unnecessary test for the routine evaluation. These guidelines also considered the platelet associated IgG assay as both an unnecessary and inappropriate test and further concluded that a diagnostic gold standard and definitive therapeutic strategy were lacking.

Other workers postulated that toxic thrombocytopenia might be related to the direct effect of the infecting organism, the acid-fast bacilli, or of immune complexes on the platelets during the most toxic period of infection. In the largest number of cases reported from Saudi Arabia the diagnosis of TB was not entertained initially but, after the start of a large dose of steroid and poor response in the platelet count, the manifestation of TB became obvious. In our case no steroid was given because the initial impression was immune thrombocytopenia secondary to a lymphoproliferative disorder but intravenous immunoglobulin, which was given, resulted in only a mild platelet increment. Two weeks after the start of anti-tuberculous therapy the platelet count improved rapidly and after six weeks the count was normal. We conclude that tuberculosis is a treatable cause of immune thrombocytopenia.
Table 1: Characteristics of TB-related cases reported in the literature

<table>
<thead>
<tr>
<th>Author</th>
<th>Country of report</th>
<th>No. of patients</th>
<th>Race</th>
<th>Pathology</th>
<th>Pts Count</th>
<th>Treatment modality and response</th>
<th>Response to anti TB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spedini et al. 2002(9)</td>
<td>Italy</td>
<td>1</td>
<td>----</td>
<td>Mediastinal nodal TB</td>
<td>1 x 10^7/L</td>
<td>Meth Prednisolone mild response</td>
<td>Yes</td>
</tr>
<tr>
<td>Ghoberail et al. 2001(10)</td>
<td>USA</td>
<td>1</td>
<td>----</td>
<td>Dissemin TB</td>
<td>2 x 10^7/L</td>
<td>IVIG, no response</td>
<td>Yes</td>
</tr>
<tr>
<td>Pezz, de Liano 1998(11)</td>
<td>Spain</td>
<td>1</td>
<td>----</td>
<td>Pulmonary TB</td>
<td>2 x 10^7/L</td>
<td>Prednisolone, IVIG</td>
<td>Yes</td>
</tr>
<tr>
<td>Talbot et al. 1998(12)</td>
<td>Australia</td>
<td>1</td>
<td>Bangalese</td>
<td>Mediastinal nodal TB</td>
<td>2 x 10^7/L</td>
<td>Prednisolone, improvement</td>
<td>Yes</td>
</tr>
<tr>
<td>Hernandez-Maraver 1996(13)</td>
<td>Spain</td>
<td>1</td>
<td>Caucasian</td>
<td>Dissemin TB</td>
<td>8 x 10^7/L</td>
<td>Meth, Prednisolone, and IVIG, mild response</td>
<td>Yes</td>
</tr>
<tr>
<td>Al-Majeed et al. 1995(14)</td>
<td>Saudia Arabia</td>
<td>9</td>
<td>Arabs</td>
<td>Dissemin TB Abdom. Abscess Pulmonary TB(6)</td>
<td>Ranged 4-20 x 10^7/L</td>
<td>Prednisolone in all patients and Cyclophosphamide/IVIG and Splenectomy improvement</td>
<td>Yes</td>
</tr>
<tr>
<td>Yusada et al. 1994(15)</td>
<td>Japan</td>
<td>1</td>
<td>----</td>
<td>TB Lymphadenitis</td>
<td>7 x 10^7/L</td>
<td>Prednisolone Recovery</td>
<td>Yes</td>
</tr>
<tr>
<td>Paviithran et al. 1993(16)</td>
<td>India</td>
<td>1</td>
<td>----</td>
<td>TB Lymphadenitis</td>
<td>46 x 10^7/L</td>
<td>Prednisolone Recovery</td>
<td>Yes</td>
</tr>
<tr>
<td>Boots et al. 1992(17)</td>
<td>Australia</td>
<td>1</td>
<td>Thai</td>
<td>Pulmonary TB</td>
<td>5 x 10^7/L</td>
<td>IVIG Recovery</td>
<td>Yes</td>
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<tr>
<td>Singh et al. 1986(18)</td>
<td>India</td>
<td>1</td>
<td>----</td>
<td>TB Lymphadenitis</td>
<td>29 x 10^7/L</td>
<td>Prednisolone Recovery</td>
<td>Yes</td>
</tr>
<tr>
<td>Jurak et al. 1983(19)</td>
<td>USA</td>
<td>2</td>
<td>Korean</td>
<td>Pulmonary TB TB Lymphadenitis</td>
<td>1 x 10^7/L</td>
<td>Steroid and Splenectomy +Vincristine Recovery</td>
<td>Yes</td>
</tr>
<tr>
<td>Chia et al. 1978(20)</td>
<td>UK</td>
<td>1</td>
<td>Indian</td>
<td>TB Splenitis (6 m after delivery)</td>
<td>&lt;1 x 10^7/L</td>
<td>Prednisolone+Splenectomy, no response</td>
<td>Yes</td>
</tr>
<tr>
<td>Cockcroft et al. 1976(21)</td>
<td>Canada</td>
<td>1</td>
<td>Chinese</td>
<td>Miliary TB</td>
<td>&lt;1 x 10^7/L</td>
<td>Prednisolone+Vincristine Recovery</td>
<td>Yes</td>
</tr>
<tr>
<td>Levy et al. 1964(22)</td>
<td>Canada</td>
<td>1</td>
<td>Greek</td>
<td>TB Lymphadenitis</td>
<td>8 x 10^7/L</td>
<td>Meth Prednisolone mild response</td>
<td>Yes</td>
</tr>
</tbody>
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References:

9. Spedini P. Tuberculosis presenting as immune thrombocytopenic purpura, Haematologica 2002; 87 (02) ELT 09.