Immune thrombocytopenic purpura in a case of tubercular pleural effusion: A rare presentation

Sir,

Patients with both pulmonary and extrapulmonary tuberculosis may demonstrate peripheral blood abnormalities and the findings may be minimal or profound.\(^1,2\) 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.\(^3\) However, immune thrombocytopenic purpura (ITP) in association with tuberculosis is extraordinarily a rare event.

A 23-year-old previously healthy, non-smoker male was admitted in our hospital with history of fever and productive cough for 1 month and purpuric spots all over the limbs for the last 2 weeks, purpuric spots on oral cavity [Figure 1], respiratory distress and hematuria for 1 day. There was no history of arthralgia and weight loss. He was not on any medication at the time of admission. Past history and family history were non-contributory. On physical examination, vitals were stable. He had non-tender, non-palpable purpuric spots all over the four limbs and wet purpura on mouth. He had mild pallor, no sternal tenderness. There was no hepatosplenomegaly or
lymphadenopathy. Left-sided vesicular breath sound was grossly reduced in mammary and inframammary region with stony dull percussion note.

Serial investigations are shown in Table 1. His prothrombin time was 13.7 sec with control 11.2 sec and INR was 1.2 and APTT was 25.6 sec (n-22.6-35 sec). Clinically he was diagnosed to be immune thrombocytopenic purpura and intravenous methylprednisolone was started. Emergency chest X-ray showed left-sided pleural effusion. Pleural fluid was aspirated for diagnostic purpose and it was reddish in color.

Next day patient complained of blurring of vision and ophthalmoscopy revealed hemorrhagic spots in retina of both eyes. Reports of biochemical analysis of pleural fluid which came on day 3, showed glucose 10 mg/dl, protein 6.5 gm/dl (serum protein 7.3 gm/dl), LDH 1100U/L (serum LDH 317 U/L), and ADA 80.3 U/L. We have started ATD CAT I.

Bone marrow aspiration was done on day 4 and it revealed a cellular marrow with normal maturation of myeloid and erythroid series. Megakaryocytes were increased in number [Figure 2]. No granuloma and abnormal non-hematopoietic cells were detected. Bone marrow culture for Mycobacterium tuberculosis was negative.

The platelet count normalized on seventh day and remained normal during the course of treatment. Sputum smear was negative for AFB initially and at the end of 2nd, 4th and 6th month of chemotherapy. Pleural fluid was positive for AFB by BACTEC culture on day 14. Pleural effusion was subsided on second week. Patient was discharged on the 21st day. Thrombocytopenia did not recur during follow-up for 1 year after completion of chemotherapy.

A causal association between TB and immune thrombocytopenia is extremely rare. ITP is an acquired disorder in which there is immune-mediated destruction of platelets and possibly inhibition of platelet release from megakaryocytes. The pathogenesis of immune thrombocytopenia in tuberculosis is thought to be generation of lymphocyte-borne antiplatelet antibodies as a result of clonal proliferation of B-lymphocyte due to host’s immune response to the tuberculous pathogen. It was supported by presence of antiplatelet antibodies in few reports. However, according to The American Society

| Parameters                | Day 1 | Day 2 | Day 3 | Day 5 | Day 7 |
|---------------------------|-------|-------|-------|-------|-------|
| Hb% (g/dl)                | 6.9   | 6.7   | 6.8   | 9.7   | 10.1  |
| Erythrocyte count (million/cu mm) | 2.47  | 2.48  | 2.48  | 3.70  | 3.74  |
| TLC                       | 9200  | 9500  | 9600  | 9900  | 11800 |
| DC                        | N63L29M4E4 | N66L27M3E4 | N71L21M4E4 | N79L14M4E3 | N77L16M5E4 |
| Platelet count            | <5000 | <5000 | <5000 | 30000 | 1.5 Lac |
| PCV (%)                   | 22.1  | 22    | 22    | 30.5  | 30.5  |
| MCV (fl)                  | 89.4  | 88.7  | 88.7  | 82.4  | 81.6  |
| MCH (pg)                  | 27.9  | 27    | 27.4  | 26.2  | 27    |
| MCHC (g/dl)               | 31.2  | 30.5  | 30.9  | 31.8  | 33.1  |
| RDW-CV (%)                | 19.3  | 19.2  | 17.9  | 14.4  | 14.4  |
| ESR (mm/1st Hr)           | 90    | 101   | 89    | 74    | 55    |

TLC: Total leucocyte count, DC: Differential count, PCV: Packed cell volume, MCV: Mean corpuscular volume, MCH: Mean corpuscular haemoglobin, MCHC: Mean corpuscular haemoglobin concentration, RDW-CV: Red cell distribution width - Coefficient of variance, ESR: Erythrocyte sedimentation rate

Figure 1: Wet purpura on palatal mucosa

Figure 2: Bone marrow aspiration smear showing mature megakaryocyte with normal morphology (x40), Leishman Stain
for Hematology’s (2011) guidelines for the diagnosis and management of ITP, absence of antiplatelet antibodies in no way invalidate the diagnosis of ITP. Moreover, they labelled antiplatelet antibodies as an ‘unnecessary’ test for the routine evaluation of ITP patients.[6]

However, many mechanisms specific for the disease itself can produce thrombocytopenia. Bone marrow changes like myelofibrosis, granulomatosis, amyloidosis, hemophagocytosis and necrosis can cause thrombocytopenia along with decrease in other cell lines.[7] Bone marrow aspiration of our patient showed only increased number of megakaryocytes which not only support the diagnosis of ITP but also excludes other production defect and hemophagocytic syndrome. Thrombocytopenia in TB is usually a complication of therapy with antituberculous drugs like rifampicin, ethambutol, and pyrazinamide.[8,9] Our patient had not received any ATT prior to presentation to our institution. So ATT-induced thrombocytopenia was ruled out. Absence of spleenomegaly excludes consumptive thrombocytopenia as may occur in disseminated tuberculosis in the context of tubercular splenic abscess. Absence of renal insufficiency, hemolytic anemia and neurological signs made TTP as a cause of thrombocytopenia unlikely. DIC was excluded as P-time and APTT was normal.

The above case could be confused with coincidental presentation of ITP and tuberculosis. But temporal association of TB with immune thrombocytopenic purpura (ITP) purpura, recovery of platelet count after starting antituberculous drugs and steroids, and absence of recurrence of thrombocytopenia after stopping antituberculous drugs are further evidences to suggest that thrombocytopenia was not co-existent with TB but was causally related to it.

The case we described was negative for acid-fast bacilli in sputum. Depending on facts like pleural fluid analysis which showed high ADA (80.3 U/L) and high lymphocyte to neutrophil ratio, age of the patient which is below 35 years and from an area of India with high prevalence of tuberculosis, we diagnose it as a case of tubercular pleural effusion. This view is supported by some studies which showed non-invasive diagnosis using a ADA cut-off level of 40 IU with lymphocyte/neutrophil ratio above 0.75 can be used to diagnose pleural tuberculosis in patients <35 years old from countries with a high prevalence of tuberculosis and a low level of mycobacterial resistance.[10,11] So we started antitubercular therapy, to which our patient readily responded both clinically and radiologically. This was further confirmed by positivity by BACTEC culture.

Most of the such cases published in the literature, are associated with sputum-positive pulmonary tuberculosis and tubercular lymphadenitis, disseminated tuberculosis, military tuberculosis with and without tubercular meningitis and one case of knee joint tuberculosis.[12] Only one case report mentioned tubercular pleural effusion which in due course found to be disseminated tuberculosis on clinical and radiological evidence.[13] Immune thrombocytopenia associated with only tubercular pleural effusion has not been reported earlier. So in this respect our case was unique.

So, it is important that the medical community should recognize and consider TB as a treatable secondary cause of immune thrombocytopenia, especially in areas of high endemicity of TB.

**Financial support and sponsorship**
Nil.

**Conflicts of interest**
There are no conflicts of interest.

**Souren Pal, Nirendra Mohan Biswas, Saikat Dutta¹, Ramkrishna Brahmachari**

Department of General Medicine, Nil Ratan Sircar Medical College, ¹Department of Haematology, Institute of Haematology and Transfusion Medicine, Kolkata, West Bengal, India
Email: drsourenpal@gmail.com

**REFERENCES**

1. Kumar S. Haematological manifestations of tuberculosis. In: Sharma SK, Mohan A, editors. Tuberculosis. 2nd ed. New Delhi: Jaypee Brothers Medical Publishers; 2009. p. 542-52.

2. Mert A, Bilir M, Tabak F, Ozaras R, Ozturk R, Senturk H, et al. Miliary tuberculosis: Clinical manifestations, diagnosis and outcome in 38 adults. Respirology 2001;6:217-24.

3. Ghozrial MW, Albornoaz MA. Immune thrombocytopenia: A rare presenting manifestation of tuberculosis. Am J Hematol 2001;67:139-43.

4. Krishnamurthy S, Yadav S. Immune thrombocytopenic purpura as a presentation of childhood tuberculosis. Indian J Pediatr 2007;74:853-5.

5. Madkaikar M, Ghosh K, Jiijina F, Gupta M, Rajpurkar M, Mohanty D. Tuberculosis and immune thrombocytopenia. Haematologica 2002;87:ELT38.

6. Neunert C, Lim W, Crowther M, Cohen A, Solberg L Jr, Crowther MA. American Society of Hematology, The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. Blood 2011;117:4190-207.

7. Avasthi R, Mohanty D, Chaudhary SC, Mishra K. Disseminated tuberculosis: Clinical manifestations, diagnosis and outcome in 38 adults. Respirology 2001;6:217-24.

8. Laniado-Laborín R. Adenosine deaminase in the diagnosis of tuberculous pleural effusion: Is it really an ideal test? A word of caution. Chest 2005;127:417-8.

9. E-mail: drsourenpal@gmail.com

10. Souren Pal, Nirendra Mohan Biswas, Saikat Dutta¹, Ramkrishna Brahmachari

Department of General Medicine, Nil Ratan Sircar Medical College, ¹Department of Haematology, Institute of Haematology and Transfusion Medicine, Kolkata, West Bengal, India
Email: drsourenpal@gmail.com

**REFERENCES**

1. Kumar S. Haematological manifestations of tuberculosis. In: Sharma SK, Mohan A, editors. Tuberculosis. 2nd ed. New Delhi: Jaypee Brothers Medical Publishers; 2009. p. 542-52.

2. Mert A, Bilir M, Tabak F, Ozaras R, Ozturk R, Senturk H, et al. Miliary tuberculosis: Clinical manifestations, diagnosis and outcome in 38 adults. Respirology 2001;6:217-24.

3. Ghozrial MW, Albornoaz MA. Immune thrombocytopenia: A rare presenting manifestation of tuberculosis. Am J Hematol 2001;67:139-43.

4. Krishnamurthy S, Yadav S. Immune thrombocytopenic purpura as a presentation of childhood tuberculosis. Indian J Pediatr 2007;74:853-5.

5. Madkaikar M, Ghosh K, Jiijina F, Gupta M, Rajpurkar M, Mohanty D. Tuberculosis and immune thrombocytopenia. Haematologica 2002;87:ELT38.

6. Neunert C, Lim W, Crowther M, Cohen A, Solberg L Jr, Crowther MA. American Society of Hematology, The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. Blood 2011;117:4190-207.

7. Avasthi R, Mohanty D, Chaudhary SC, Mishra K. Disseminated tuberculosis: Clinical manifestations, diagnosis and outcome in 38 adults. Respirology 2001;6:217-24.

8. Laniado-Laborín R. Adenosine deaminase in the diagnosis of tuberculous pleural effusion: Is it really an ideal test? A word of caution. Chest 2005;127:417-8.

9. E-mail: drsourenpal@gmail.com

**REFERENCES**

1. Kumar S. Haematological manifestations of tuberculosis. In: Sharma SK, Mohan A, editors. Tuberculosis. 2nd ed. New Delhi: Jaypee Brothers Medical Publishers; 2009. p. 542-52.

2. Mert A, Bilir M, Tabak F, Ozaras R, Ozturk R, Senturk H, et al. Miliary tuberculosis: Clinical manifestations, diagnosis and outcome in 38 adults. Respirology 2001;6:217-24.

3. Ghozrial MW, Albornoaz MA. Immune thrombocytopenia: A rare presenting manifestation of tuberculosis. Am J Hematol 2001;67:139-43.

4. Krishnamurthy S, Yadav S. Immune thrombocytopenic purpura as a presentation of childhood tuberculosis. Indian J Pediatr 2007;74:853-5.

5. Madkaikar M, Ghosh K, Jiijina F, Gupta M, Rajpurkar M, Mohanty D. Tuberculosis and immune thrombocytopenia. Haematologica 2002;87:ELT38.

6. Neunert C, Lim W, Crowther M, Cohen A, Solberg L Jr, Crowther MA. American Society of Hematology, The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. Blood 2011;117:4190-207.

7. Avasthi R, Mohanty D, Chaudhary SC, Mishra K. Disseminated tuberculosis: Clinical manifestations, diagnosis and outcome in 38 adults. Respirology 2001;6:217-24.

8. Laniado-Laborín R. Adenosine deaminase in the diagnosis of tuberculous pleural effusion: Is it really an ideal test? A word of caution. Chest 2005;127:417-8.
comparative study. Eur Respir J 2003;22:589-91.
12. Khan MA, Mohammed FR, Shams MZ, Sarker S, Alam MB. Knee joint tuberculosis presenting as immune thrombocytopenia. J Med 2009;10:28-30.
13. Kalra A, Kalra A, Palaniswamy C, Vikram N, Khilnani GC, Sood R. Immune thrombocytopenia in a challenging case of disseminated tuberculosis: A case report and review of the literature. Case Rep Med 2010;2010. pii: 946278.

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.