Thromboembolic event in a patient of immune thrombocytopenic purpura: a case report

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Abstract

Immune Thrombocytopenia Purpura (ITP) is an autoimmune disorder characterised by a low blood platelet count, which is attributed to both decreased megakaryocyte production in the bone marrow and the generation of autoantibodies causing platelet destruction in the spleen. Individuals with autoimmune conditions are highly susceptible to pulmonary embolism. This case involves a 39-year-old female with ITP who developed thromboembolisms. A comprehensive investigation into prothrombotic risk factors, including obesity, smoking, family history of thromboembolism, and ITP-related interventions such as prolonged corticosteroid use or splenectomy, revealed insignificant results, except for the patient's history of receiving corticosteroid therapy. Despite the disparate pathogenesis of thromboembolism (TE) and ITP, recent events of TE in ITP patients have been observed. This report underscores the potential life-threatening complications in ITP and aims to explore their causes and pathogenesis for ensuring optimised patient care.

Keywords: Immune thrombocytopenia, autoantibodies, autoimmune, thromboembolism, corticosteroid therapy, splenectomy.

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Introduction

Immune thrombocytopenic purpura (ITP) is a rare, heterogeneous autoimmune blood disorder characterised by a reduced peripheral blood platelet count below 100 $\times 10^9$/L.[1] In ITP, platelet destruction is mediated by autoantibodies in the spleen, and there is also decreased production of megakaryocytes in the bone marrow. A patient with ITP is prone to bruising and bleeding, including epistaxis and gum bleeding. Although the pathogenesis of thromboembolism and ITP appears contradictory, recent cases of thromboembolisms in patients with ITP have been reported. Studies have shown that autoimmune diseases such as ITP and SLE place patients at a higher risk for developing thromboembolism (TE) as compared to a healthy individual.[3-5] Patients receiving TPO receptor agonist therapy for ITP have also been reported to develop thromboembolic events.[6] Certain prothrombotic risk factors including obesity, smoking, family history of TE and ITP-related treatments such as long-term corticosteroid use or splenectomy, may increase the risk of TE in ITP, although the distribution and influence of these factors have not been fully described.[7] This presented case study describes a female with immune thrombocytopenic purpura (ITP) complicated by pulmonary embolism.

Case Report

A 39-year-old unmarried female, diagnosed with Immune Thrombocytopenic Purpura (ITP) for 20 years and with a recent onset of pulmonary thrombosis, presented to the Emergency department of the Pakistan Institute of Medical Sciences (PIMS), Islamabad, on May 7, 2023. She complained of fever, headache, altered sensorium for two days and prolonged gum and per vaginal bleeding since the last 60 days. Two days prior to hospitalisation, the patient experienced a sudden onset of high-grade fever (104°F) accompanied by a severe headache, which was relieved by antipyretics. Two months earlier, she had experienced heavy menstrual bleeding which had lasted 60 days and was resolved 10 days before admission. Additionally, the patient reported decreased vision over the past 2 years and a history of HCV infection, which was treated 15 years ago with a complete IV course.

The patient's current medications include Azathioprine for 3 years, steroids (prednisolone and deltacortril) for 1 month, and Tazobactam and Amikacin for 4 days. Steroids were indicated as the patient presented with a low platelet count of 22,000/µL and gum bleed. Tapering steroids led to a decrease in her platelet level, and immunosuppression with azathioprine was initiated. The

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Table: Diagnostic parameters with pertinent positive and negative findings

Diagnostic Parameter	Findings
Procalcitonin	Normal
Urine Routine Exam	Normal
Renal Function Tests	Normal
Liver Function Tests	Normal
C Reactive Protein	Unraised
White Blood Cells	Normal
Blood Culture	Negative
Platelet Count	22000/µL
Haemoglobin	10.2 g/dL
D Dimer Levels	Elevated
CT (PA view)	Segmental lung thrombi
X-Ray Chest	Inconclusive
Ultrasound Abdomen	Inconclusive
Doppler Ultrasound Legs	Inconclusive
Bone Marrow Biopsy	Identified megakaryocytes
Nocturnal Haemoglobinuria (PNH)	No abnormalities

patient's vital signs showed a Blood Pressure of 120/80 mm Hg, regular pulse of 82 beats per minute, respiratory rate of 20 breaths per minute and temperature of 37 degree Celsius. Physical examination revealed shortness of breath, subconjunctival haemorrhages, oral ulcers, facial flushing, moon face, central obesity, abdominal striae with no organomegaly, peripheral muscle wasting, and bilateral limb bruising. The patient was tachypnoeic with bilaterally equal chest movements and bilateral crepitations throughout the chest.

Suspecting a thrombotic event secondary to sepsis or Disseminated Intravascular Coagulation, a musculoskeletal workup and thorough investigation [Table 1] was conducted, ruling out Systemic Lupus Erythematosus (SLE), Thrombocytopenic Purpura (TTP), and Haemolytic Uraemic Syndrome (HUS).

The patient was offered a splenectomy for the haematological disorder, which was declined. A subsequent follow-up appointment was scheduled. Thrombosis was treated with rivaroxaban, with a weekly follow-up for the first month and then monthly for the next six months. After six months, complete resolution of the thrombus was confirmed by computed tomography pulmonary angiography (CTPA). In the context of existing literature, this case tentatively suggests that prolonged steroid usage may be a potential thrombotic risk factor in patients with immune thrombocytopenic purpura (ITP), although definitive evidence remains elusive.

Discussion

The presented case of ITP was diagnosed 20 years ago, and the patient has been on medication since then. Two months ago, the patient had a relapse, and reports showed that in addition to thrombocytopenia and anaemia, the patient also had developed segmental thrombosis in the right lung. The patient's past medical and surgical history were non-contributory, although the patient did suffer from HCV confirmed by HCV PCR, after being diagnosed with ITP, and received interferon based treatment for 6 months, from March to July 2008. There was no family history of ITP. The patient had no previous history of thromboembolic events, but these events were encountered after initiating steroids.

Although the patient had been taking azathioprine for the past 3 years, which has a documented good response rate in ITP cases,[8] she experienced a relapse. Although leukopenia is a known side effect of azathioprine, the patient has maintained a normal WBC count. The patient also showed increased D-dimer levels, which was suggestive of thrombosis and was subsequently confirmed as pulmonary thrombosis on further investigation.

Steroids, in addition to immunosuppressant medications, were started. As the patient has had thrombocytopenia, her developing thrombosis looks likely to be due to the medication for ITP and the use of corticosteroids. The patient's anaemia can be attributed to the immunosuppressant drugs, which likely caused bone marrow suppression. A few studies mention that corticosteroids can lead to thrombus formation in autoimmune diseases and increase the risk of TE in ITP.[9,10] Studies have demonstrated the association between the short term use of oral corticosteroids by patients and increased risk of thromboembolic events.[11] However, this conclusion cannot be made with complete confidence due to the limited research on the subject.

Conclusion

The body of published evidence on the risk of thromboembolism (TE) should be carefully considered by the healthcare professionals while treating the patients with Immune Thrombocytopenia Purpura (ITP). The coexistence of TE and ITP raises important questions, yet no studies have been conducted so far to fully explain the underlying pathophysiology of this condition. This study highlights the need for more research and data on the contributory factors to better understand why TE is higher in the ITP population. It will also help in developing a more effective management approach on a broader level.

Consent: written consent was obtained from the patient for publishing her case.

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References

1. Provan D, Stasi R, Newland AC, Bussel JB, Chong BH, Cines DB, et al. International consensus report on the investigation and management of primary immune thrombocytopenia. Blood. 2010;115:168-86. doi: 10.1182/blood-2009-06-225565.
2. Audia S, Mahévas M, Samson M, Godeau B, Bonnotte B. Pathogenesis of immune thrombocytopenia. Autoimmunity reviews. 2017; 16:620-32. doi: 10.1016/j.autrev.2017.04.012.
3. Ekstrand C, Linder M, Baricault B, Lafaurie M, Sailler L, Lapeyre-Mestre M, et al. Impact of risk factors on the occurrence of arterial thrombosis and venous thromboembolism in adults with primary immune thrombocytopenia - Results from two nationwide cohorts. Thromb Res. 2019; 178:124-31. doi: 10.1016/j.thromres.2019.04.016.
4. Hannah JR, D'Cruz DP. Pulmonary Complications of Systemic Lupus Erythematosus. Semin Respir Crit Care Med. 2019; 40:227-34. doi: 10.1055/s-0039-1685537.
5. Sulit C, Hashemzadeh M, Hashemzadeh M. CRT-500.12 Evaluating the Association Between Immune Thrombocytopenic Purpura and Pulmonary Embolism. J Am Coll Cardiol Intv. 2023; 16: S74.https://doi.org/10.1016/j.jcin.2023.01.235
6. Wu C, Zhou XM, Liu XD. Eltrombopag-related renal vein thromboembolism in a patient with immune thrombocytopenia: A case report. World J Clin Cases. 2021; 9:2611-8. doi:10.12998/wjcc.v9.i11.2611
7. Tjepkema M, Amini S, Schipperus M. Risk of thrombosis with thrombopoietin receptor agonists for ITP patients: A systematic review and meta-analysis. Crit Rev Oncol Hematol. 2022; 171:103581. doi: 10.1016/j.critrevonc.2022.103581.
8. Chang H, Tang TC, Hung YS, Li PL, Kuo MC, Wu JH, Wang PN. Immune thrombocytopenia: effectiveness of frontline steroids and comparison of azathioprine, splenectomy, and rituximab as second-line treatment. Eur J Haematol. 2018; 101:549-55.doi: 10.1111/ejh.13144
9. Liu X, Peng X, Rong C, Zhang W. Acute pulmonary embolism following corticosteroid administration in acute severe ulcerative colitis with gastrointestinal bleeding: A case report. Front Cardiovasc Med. 2022; 9:1018462. doi: 10.3389/fcvm.2022.1018462.
10. Severinsen MT, Engebjerg MC, Farkas DK, Jensen AØ, Nørgaard M, Zhao S, et al. Risk of venous thromboembolism in patients with primary chronic immune thrombocytopenia: a Danish population-based cohort study. Br J Haematol. 2011; 152:360-2.doi: 10.1111/j.1365-2141.2010.08418.x.
11. Waljee AK, Rogers MAM, Lin P, Singal AG, Stein JD, Marks RM, et al. Short term use of oral corticosteroids and related harms among adults in the United States: population based cohort study BMJ. 2017; 357:j1415. doi:10.1136/bmj.j1415

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MN: Concept, data interpretation, draft writing, proofreading, final approval and responsible for all aspects of this work.
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LS: Literature search, data interpretation, draft writing, proofreading, final approval and responsible for all aspects of this work.
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