Unusual Presentation of ITP in a Young Male Patient: A Management Dilemma

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ABSTRACT

Immune thrombocytopenic purpura (ITP) is an autoimmune acquired bleeding disorder characterized by isolated thrombocytopenia with the absence of a systemic illness. The usual clinical manifestations of ITP results from increased bleeding tendency and usually include petechiae, purpura and ecchymosis that most commonly affect the upper and lower extremity. It can also be associated with spontaneous widespread hematomas if platelets count falls < 10,000 u/L.

Paradoxically, ITP has also been suggested to increase the risk of venous thromboembolism. This poses a clinical challenge especially if anticoagulation is to be initiated.

We present a case of a previously healthy 37 years old male, who presented with a history of exertional dyspnea and palpitations associated with retrosternal chest pain. CTPA revealed extensive bilateral pulmonary embolism (PE). Routine blood investigations were unremarkable apart from an isolated thrombocytopenia with a platelet count of 11,000 u/L.

Keywords: Immune Thrombocytopenic Purpura, Anticoagulation, Pulmonary Embolism

INTRODUCTION

Immune thrombocytopenic purpura (ITP), a hallmark of acquired bleeding disorders, is an auto-immune disorder characterized by low platelets count (<150,000 u/L) and mucocutaneous bleeding[1].

It is reported in roughly 2 per 100,000 adults with mean age of diagnosis of 50 years[2]. Although the pathogenesis is unclear, a widely accepted theory states that it results from the development of autoimmune IgG targeting glycoproteins 2b-3a on platelets membrane. Consequently, platelets become susceptible to phagocytosis by splenic macrophages and Kupffer cells in the liver[2,3].

Clinical manifestations include petechiae, purpura and ecchymosis that most commonly affect the upper and lower extremity. It can also be associated with spontaneous widespread hematomas and more serious internal bleeding if platelets count falls < 10,000 u/L[2].

Despite thrombocytopenia, aplenty of arterial and venous thrombosis cases has been identified in ITP patients. Furthermore, plenty of studies had sufficient evidence of increased risk of thromboembolism in ITP patients. That potential comorbidity might require an exceptional attention as management of thromboembolism may be challenging especially in very low platelets count[4].

The aim of this report is to present a case of recurrent venous thromboembolism (VTE) in a patient with newly diagnosed ITP.

THE CASE

A 37-year-old male, not previously known to have any medical illness, presented to the pulmonology clinic with three weeks history of exertional dyspnea and palpitations associated with retrosternal chest pain. Upon presentation, patient was vitally stable and systemic examination was unremarkable. Full blood count was sent as part of the initial work up and was normal apart from thrombocytopenia with a platelet count of only 11,000 u/L. Blood film was unremarkable apart from thrombocytopenia with some giant forms. Baseline renal and liver function tests were normal. Coagulation profile showed normal PT, APTT and Fibrinogen but high D-Dimer of 9.46. Chest x-ray was normal. Given the high D-Dimer and patient's clinical presentation, urgent CTPA was arranged, which came back positive for extensive bilateral pulmonary embolism (PE) extending from the main pulmonary arteries to the sub segmental branches (Figure 1).

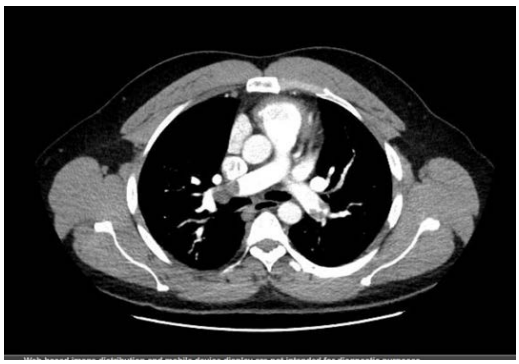

Figure 1: Bilateral extensive PE

Doppler ultrasound of both lower limbs was negative for deep vein thrombosis (DVT) and echocardiogram was unremarkable.

The patient was then admitted directly to the hospital. Patient that time denied any active bleeding symptoms including skin bruising, epistaxis, and gum bleeding. There were no symptoms suggestive of active infection or underlying connective tissue disease. Patient denied alcohol consumption. He was not taking any medication at home. Family history was unremarkable.

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Given the severity of the thrombocytopenia and the need for rapid platelets increment to introduce anticoagulation, patient was transfused 6 units of platelets and started on Dexamethasone 40 mg IV OD and IVIG 0.5 gm/ Kg for total of four days. Initially he was kept on prophylactic Low Molecular Weight Heparin (LMWH) as his platelets increased to more than 25,000 u/L. Platelets count raised to 59,000 u/L the next day, so the patient was started on heparin infusion and subsequently therapeutic LMWH.

As part of the thrombocytopenia work up, ANA profile, routine viral serology, CMV and EBV serology, serum folate and vitamin B12 level were sent, and all were normal. Bone marrow examination was unremarkable except for reactive marrow with increased megakaryocytes number, compatible with ITP.

Inherited and acquired thrombophilia screens were negative as well as PNH screen. Tumor markers were all normal. CT abdomen and pelvis with IV contrast showed no evidence of underlying malignancy but revealed a partially thrombosed Superior Mesenteric Vein (SMV). JAK-2 mutation was negative.

Based on patient's clinical picture along with the above laboratory, radiological and bone marrow findings, diagnosis of ITP with multiple venous thromboses; PE and SMV thrombosis was made.

During the hospital course, the patient had clinically improved. His platelets count continued to rise reaching up to 202,000 u/L. Therapeutic Clexane was switched to Dabigatran 150 mg twice daily upon discharge and patient was followed up regularly in hematology clinic to monitor his platelets count and any bleeding complications.

One month after discharge, patient represented to the emergency department with sudden onset of left sided chest pain associated with shortness of breath and palpitations. He also gave a history of right lower limb pain and swelling for two days duration. Upon presentation, patient was vitally unstable with heart rate of 112 bpm and oxygen saturation of 87% on on room air, so he was kept on oxygen supplement. BP was normal. Systemic examination was unremarkable except for right lower limb swelling and tenderness.

Repeated echocardiogram this time showed a high SPAP pressure of 44 mmHg along mild RVOT dilatation and dysfunction.

An urgent CTPA revealed progression of the previously noted PE with saddle thrombus formation (Figure 2).

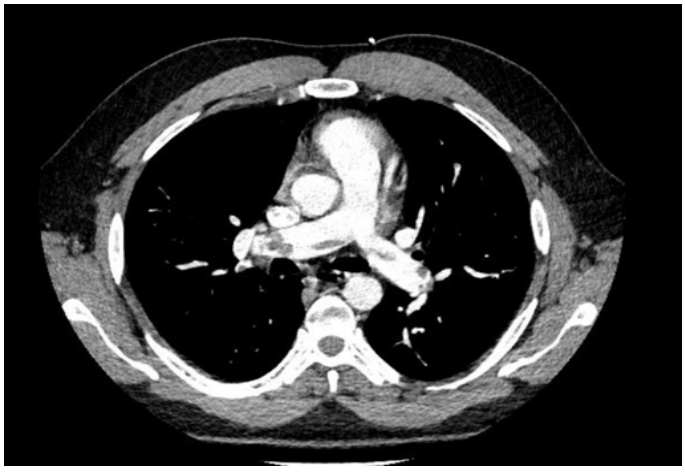

Figure 2: Saddle Pulmonary Embolism

Right lower limb Doppler revealed a distal Deep Femoral Vein (DFV) thrombus with extension to the popliteal and infra popliteal veins. Platelets count was 136,000 u/L on presentation. The patient was started on unfractionated heparin (UFH) infusion with higher APTT targets and shifted to the ICU for close monitoring and further management.

Subsequently he underwent IVC filter insertion as a preventative measure. Patient condition improved, UFH infusion was switched to therapeutic LMWH with 20% dose increment and later bridged with warfarin with target INR between 3-4. Patient was discharged from the hospital and is following up regularly in the hematology and anticoagulation clinic. During the first year post discharge, patient remained in complete remission of ITP with no clinical evidence of recurrent VTE.

DISCUSSION

Thrombocytopenia is not a protective factor against thromboembolic disease in ITP patients. Furthermore, there have been a lot of papers reporting cases of thromboembolism in ITP patients. Aledort et al. reported 18 thrombotic/ ischemic events that occurred in 10 of 186 adults diagnosed with ITP (5%), 11 of which happened after the diagnosis of ITP[5].

Another larger study evaluated the incidence of thromboembolic events (TEEs) in 1070 adult patients with ITP and 4280 primary ITP disease free patients over a median of 47.6 months of follow up. The cumulative incidence of venous TEEs was 2.9% in the primary ITP cohort and 1.9% in the primary ITP disease free cohort. The IRR of venous TEEs was 1.57 (95% CI: 1.04-2.37). These results suggest increased risk of venous TEEs in patients with ITP[4].
The exact pathophysiology behind the increased risk of venous and arterial thromboembolic events in ITP remains questionable. However, a widely accepted theory states that platelets microparticles, which is a result of autoantibody induced platelets fragmentation, activates the platelets. Moreover, the higher percentage of the young and large platelets may be thrombotically active[6]. Contradictory, the risk of thromboembolism seems to be higher with lower platelets counts[7].

Additionally, ITP treatment itself is associated with thrombotic complications. IVIG is thought to increase plasma viscosity, compliment activation and platelets aggregation. Corticosteroids were described in previous studies to also play a role in thrombosis[6,8].

Initiation of anticoagulation was a clinical challenge in our case because it is usually contraindicated in thrombocytopenia with platelets count of <50,000 u/L. In case of severe thrombocytopenia with <50,000 u/L and acute thrombotic event, anticoagulation should be started with half-therapeutic or prophylactic dose (UFC preferred over LMWH). Simultaneously, corticosteroids and IVIG are given to raise platelets to a safe level (> 50,000 u/L). Once platelet count rises above 50,000 u/L, standard-dose therapeutic anticoagulation can be administered. Anticoagulation should be avoided in patients with life threatening bleeding or bleeding requiring transfusion. IVC filters can be considered in DVT patients[7].

Our patient was readmitted with new saddle PE and DVT despite being on Dabigatran. A similar case was documented in the literature, where a 54-year-old male with ITP and bilateral lower limb DVT developed pulmonary embolism 1 week after starting Dabigatran[6]. Both cases raise the question whether or not Direct Oral Anticoagulants (DOACs) are effective in preventing thrombosis in patients with ITP without Antiphospholipid Syndrome (APS) or should vitamin K antagonist be the drug of choice in managing thrombosis in such patients?

CONCLUSION

Although the majority of ITP patients present with active bleeding symptoms, ITP has also been shown to increase the risk of thromboembolism. The unique presentation of our patient with multiple acute thrombosis along with severe thrombocytopenia made his management challengeable. The initial step in managing such case is to rapidly raise platelet count to a safe level before starting anticoagulation. Anticoagulation choice and dosage highly depends on the patient clinical condition and platelet count.

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