A case of immune thrombocytopenic purpura with prolonged aPTT time: A clotter hidden in a bleeder?

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SUMMARY

We report the case of a 23-year-old woman who presented with prolonged menstruation and multiple bruises on the limbs and trunk. Investigations revealed severe thrombocytopenia and deranged coagulation profile with markedly prolonged activated partial thromboplastin time (aPTT). Lupus anticoagulant, anti-cardiolipin antibody and anti-beta-2-glycoprotein 1 antibody were positive. She was diagnosed with Immune Thrombocytopenic Purpura (ITP) with positive antiphospholipid antibody serology and given a course of intravenous methylprednisolone and tapering doses of oral prednisolone. She was steroid free and had no bleeding or thrombotic event over two years follow up.

INTRODUCTION

Immune Thrombocytopenic Purpura (ITP) is an acquired thrombocytopenia caused by autoantibodies against platelet antigen which can result in life threatening bleeding events. Antiphospholipid syndrome (APS) on the other hand, is characterised by venous or arterial thrombosis and adverse pregnancy outcome in the presence of persistent antiphospholipid antibodies (aPA). It has been recognised that patients with ITP might have aPA positivity. However, the underlying mechanism of the disease is not well established. The long-term risk of thrombotic event in ITP with aPA-positivity is also unclear and thus long-term follow-up is needed.

CASE REPORT

A 23-year-old woman with no past medical history presented with one week history of multiple bruises and petechiae over the limbs and trunk. She had menorrhagia for the past three months and spontaneous gum bleeding. There was no symptom suggestive of active lupus. She was nulliparous and had no prior history of thrombotic event. There was no significant family history of note.

On examination, she was pale. Her blood pressure was 106/84 mmHg, and pulse rate was 100 beats per minute. There was no oral ulcer, malar rash, discoid rash, or cutaneous vasculitis. There was no palpable lymph node. There were multiple bruises and petechiae over the limbs and torso, with different colour hues suggesting varying ages of the bruises. Other systemic examinations were unremarkable.

Blood investigations revealed haemoglobin of 8.4g/dL, platelet $4x10^9$/L, and a markedly prolonged aPTT of 105.3 seconds. Mixing test failed to correct the aPTT and suggested the presence of lupus anticoagulant. Further laboratory tests showed positive lupus anticoagulant, anti-cardiolipin antibody and anti-beta-2-glycoprotein 1 antibody. Anti-nuclear antibody (ANA), anti-double stranded DNA (anti-dsDNA) and complements (C3 and C4) were normal.

She was diagnosed with ITP with positive aPA serology. Intravenous methylprednisolone 250mg daily for three days was given followed by oral prednisolone 60mg daily. She did not develop new bruises or any other bleeding tendencies throughout her hospitalisation. Upon discharge home, her platelet count improved to $95x10^9$/L. She was subsequently monitored at outpatient clinic with slow taper of oral prednisolone. At two years follow-up, she was in clinical remission without corticosteroid or steroid-sparing immunosuppressant. Platelet count was normalised but aPTT remained slightly prolonged. Repeated antiphospholipid antibodies were still positive. There was no thrombotic or bleeding event during the two years follow-up.

DISCUSSION

Contrary to popular belief, it is not uncommon for patients with ITP to present with positive aPA serology. The reported prevalence ranges between 25–75%. Alternatively, it is also common for thrombocytopenia to occur in conjunction with antiphospholipid syndrome (APS), happening at a prevalence of 22-46%.[1] The exact mechanism of such coexistence remains a myth. However, it has been shown that the levels of aPA do rise during exacerbation of ITP and fall while in remission.[2] One explanation given for this occurrence was that the rise of the antibody levels might be the consequence of platelet destruction and the transient development of antibodies against the residue of the platelet. Others suggested that the severely low platelet count serves as a protective mechanism for the patient with underlying APS in preventing a thrombotic event.[3]

Despite the initial studies which found no correlation between thrombosis and aPA positivity in ITP patient,[4] subsequent reports showed that 10-61% of the ITP patients with aPA positivity developed complications.[1,3,5] Diz-Küçükkaya et al., found that there was a high risk of thrombosis (61%) in the aPA-positive group. They presented with deep vein thrombosis, pulmonary embolism, retinal

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with aPA positivity developed complications.[1,3,5] Diz-Küçükkaya et al., found that there was a high risk of thrombosis (61%) in the aPA-positive group. They presented with deep vein thrombosis, pulmonary embolism, retinal vein thrombosis, fetal losses, stroke and mesentery artery thrombosis. Conversely, aPA negativity significantly predicted the five years thrombotic free survival at 97.7%,[3] and this finding was consistent in report by Yang et al., in which none of the aPA-negative patients developed thrombosis. The subgroup that showed persistent aPA especially lupus anticoagulant despite in clinical remission may represent one end of a spectrum of overlapping syndromes of ITP and APS.[2]

The initial treatment strategy and treatment response in both aPA-positive and aPA-negative ITP do not differ. Methylprednisolone and oral prednisolone remain the mainstay of the treatment and both group respond similarly.[3,5] Proper follow-up, and risk stratification for aPA-positive patients are vital in early detection of the thrombotic event, as the catastrophic antiphospholipid syndrome is possible in such patient.

Despite all the findings, the benefit of prophylactic antithrombotic agent or antiplatelet was not established. Thus, the conflicting reports regarding the thrombotic risk imply that a larger scale of study is needed to establish the nature and significance of aPA.

CONCLUSION

ITP with positive aPA serology will present with bleeding episode, or at the other end of the spectrum, causing life threatening thrombotic event. The relationship between the risk of thrombosis and the duration of clinical remission of ITP remains unclear. Thus, long term monitoring is required to identify the complication.

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