CASE REPORT

An Uncommon Cause of Leg Swelling After Exercise: A Case Report on An Unprovoked Deep Vein Thrombosis in Young Healthy Man

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ABSTRACT

Antiphospholipid syndrome is a hypercoagulable autoimmune condition that predominantly affect the female and commonly manifest as arterio-venous thrombosis and recurrent miscarriage. Here, we present a unique case of a healthy young man who developed sudden onset of right leg swelling after exercise which was then found to be due to deep vein thrombosis via Doppler ultrasound. His blood investigations showed thrombocytopenia and prolonged coagulation profile. Therefore, antiphospholipid syndrome was suspected and later confirmed by positive autoimmune antibodies. He was treated with long term moderate intensity oral warfarin. The objective of this case report is to share the uncommon occurrence of an unprovoked deep vein thrombosis secondary to antiphospholipid syndrome in a healthy young man so that the possibility of deep vein thrombosis should be suspected in selected cases of non-resolving leg swelling after exercise as it can lead to fatal pulmonary embolism.

Keywords: Antiphospholipid syndrome; Hypercoagulable; Male; Deep vein thrombosis; Thrombocytopenia

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INTRODUCTION

Deep vein thrombosis (DVT) are said to occur in 0.1% of all adult populations (1). It commonly occurs in the presence of provoking factors such as prolonged immobilization, surgery, pregnancy and malignancy. However, it can also occur unprovoked in a healthy individual which once present warrants a detailed workup mainly to look for Antiphospholipid Syndrome (APLS). APLS is an autoimmune disorder that manifests as recurrent venous or arterial thrombosis. APLS can be primary which is the isolated form, or secondary which commonly seen in systemic lupus erythematosus. Although APLS patient usually has prolonged coagulation profile, they are usually prothrombotic rather than haemophilic. We reported a case of a healthy young man who developed spontaneous DVT after exercise as a presentation of APLS. To the best of our knowledge, there has been very limited case reported on APLS in male that presented with DVT.

CASE REPORT

A 21-year old male university student who was physically active presented with sudden onset of unilateral right leg swelling which associated with throbbing pain that occurred two days after he went for a jog. He denied having any chest and constitutional symptoms, as well as bleeding tendencies or symptoms suggestive of connective tissue disease. He seeks treatment in a private clinic where he was treated as soft tissue swelling after exercise and was given only analgesics. As there was no improvement, he eventually came to the emergency department. There was no significant past medical, surgical or family history of note. He was not taking any over the counter or traditional medications. He neither smokes nor consumes alcohol contained beverages. On arrival, his vital signs were stable. He has athletic body build. General examination reveals normal findings. He had unilateral, non-pitting right leg swelling extending to the knee, which was tender on palpation worst over the calf. His left leg was otherwise normal. His cardiovascular and respiratory examinations were all normal as were his abdominal examination. His preliminary blood investigations were taken (Table I). Electrocardiogram showed sinus rhythm. Ultrasound Doppler of right lower limb showed the presence of extensive thrombus involving the right external iliac, common femoral, superficial femoral and popliteal veins (as shown in Figure 1 and 2). In view of the presenting complaint and the findings of his preliminary blood test and Doppler ultrasound of the right lower limb, the diagnosis of Antiphospholipid

Table I: Preliminary blood investigations taken in the ward

Investigations	Results	Normal Range
Haemoglobin	14.8 g/dL	12 – 18 g/dL
White Blood Cell	13.9 x 10^9/L	4.0 – 11.0 x 10^9/L
Platelet	129 x 10^9/L	150 – 400 x 10^9/L
Creatinine Kinase	71 U/L	30-200 U/L
PT	13.8 second	11.8 -14.5 second
aPTT	61.5 second	30.0 - 44.5 second
INR	1.07	< 1.1
C3 (Nephelometry)	134 mg/Dl	90-180 mg/Dl
C4 (Nephelometry)	31.5 mg/Dl	10-40 mg/Dl
Antinuclear Antibody	Negative	
Anticardiolipin Antibody	Positive	
Beta-2-glycoprotein-1 IgG	Positive	
Lupus anticoagulant Antibody	Positive	

Blood results show thrombocytopenia and prolonged activated partial prothrombin time were suggestive of antiphospholipid syndrome and further confirmed by the presence of positive anticardiolipin, lupus anticoagulant and Beta-2 glycoprotein-1 IgG antibody. The antinuclear antibody was negative and the level of C3 and C4 was normal.

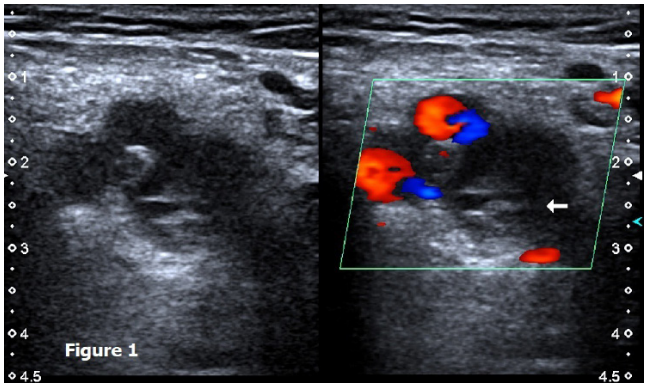

Figure 1: Ultrasound Doppler of right lower limb showed the presence of an echogenic thrombus (arrow) over the right common femoral veins which was not compressible

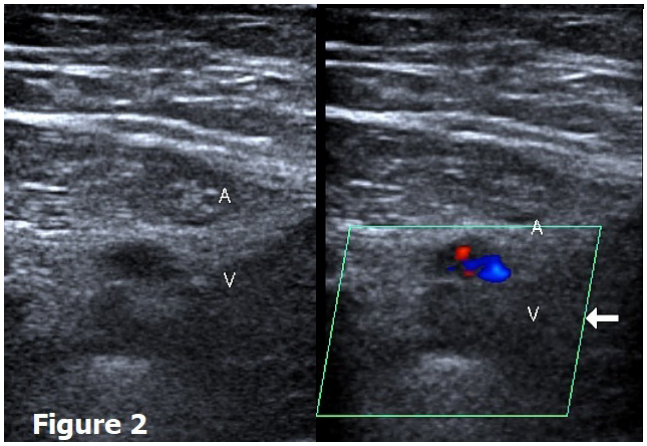

Figure 2: Ultrasound Doppler of right lower limb showed the presence of a non-compressible echogenic thrombus (arrow) over the right popliteal veins. A: Popliteal artery, B: Popliteal vein

Syndrome (APLS) was suspected. It was later confirmed with the positive test of Lupus anticoagulant, anti-Cardiolipin and anti-β2 glycoprotein-1 antibodies. Thence, anticoagulation therapy with oral warfarin 5mg once daily was commenced and overlapped with subcutaneous enoxaparin 60mg twice daily to achieve a target international normalization ratio (INR) of 2 to 3. However, there was a difficulty in achieving the target INR as expected of APLS. After almost one week on oral warfarin 5mg daily, he still failed to achieve the target INR. Thus, he was then subjected to a higher dose of 10mg daily for more than a week before he finally achieves it. The dose was continued to maintain the INR within the therapeutic range. The repeated Lupus anticoagulant, anti-Cardiolipin and anti-β2 glycoprotein-1 antibodies after 12 weeks were positive, which support the diagnosis of APLS. Repeated ultrasound Doppler of the right lower limb after 3 months of warfarin treatment noted resolved thrombus over the superior femoral vein and popliteal vein, with minimal remnant over the external iliac and common femoral vein. His warfarin was continued with target INR of 2 to 3.

DISCUSSION

Venous thromboembolism is a spectrum of disease that consist of deep vein thrombosis (DVT) and pulmonary embolism. It has an incidence of 1 per 1000 adult populations per year and mortality rate as high as 30% (1). It is imperative to be able to understand the risk factors of venous thromboembolism as early detection could maximise the efforts in preventing further sinister effects in high risk groups. Many studies have looked into the risk factors of venous thromboembolism, which then can be divided into provoked and unprovoked. Antiphospholipid syndrome (APLS) is one of the causes of thrombophilia disorder and has been positively associated as one of the causes of unprovoked venous thromboembolism.

APLS clinically manifests as arteriovenous thrombosis and usually associated with recurrent foetal loss, in the presence of antiphospholipid antibodies. The current gold standard in diagnosing APLS relies in the presence of anticardiolipin antibodies and lupus anticoagulant. Hence, confirming the presence of these antibodies in patients with thromboembolism is justified especially when there is a higher risk for recurrence, and ultimately will affect the subsequent management. APLS can be attributed to secondary causes, as most commonly seen in systemic lupus erythematosus, or it can also stand primarily on its own. According to the 5-years cohort study conducted by Duarte-Garcia et al. (2017) in United States of America, the annual incidence of APLS was about 2 per 100,000 populations, and the rates for both sexes were almost similar. The estimated prevalence for APLS was 50 per 100,000 population in a year (2). The common presentations for both male and female are different. In females, the common presentations are polyarthritis, livedo reticularis and migraine headache. Male patient frequently present with myocardial infarction, epilepsy and arterial thrombosis in lower legs (3).

Treatment for unprovoked DVT secondary to APLS is long term anticoagulant with warfarin. A moderate intensity anticoagulant with target international normalization ratio (INR) of 2 to 3 is adequate in preventing further episodes of thrombosis as what been suggested in a study that compared the outcome of high intensity warfarin to achieve target INR of more than 3.0. The study showed no difference in outcome and in fact increases the risk of bleeding in cases of high intensity warfarin (4).

With regards to our patient, he is a young and healthy man without any other substantive diagnoses. Arguably, whilst physical immobility, sedentary lifestyle, along with obesity have been acknowledged as a contributing factor to the formation of DVT, our patient actively engages in sports. The only striking resemblance seen in our patient with the ones seen in the other literatures is the presence of thrombosis in the lower limbs as the chief presentation. At the same time, our patient also had difficulty in achieving the target INR of 2 to 3 that necessitate him to be put on a high maintenance dose of oral warfarin.

One of the possibilities to be consider in spontaneous DVT in a healthy young man will be Factor XII deficiency. There is an article on incidental findings of Factor XII deficiency seen in a patient with elevated APTT, whom did not present with bleeding diathesis but with recurrent venous or arterial thromboembolism (5). However, in view of positive APLS antibody, we believe this patient has APLS instead of Factor XII deficiency.

CONCLUSION

In conclusion, this case report illustrates the importance to recognise that APLS can present in young man with thrombotic event as this could then help in targeting treatment and prevent catastrophic events, thus improving the outcome of the affected individuals.

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