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Dr. Srisanat Srinivasan Rao
Deenanath Mangeshkar Hospital and Research Center, Deenanath Mangeshkar Hospital Road, Near Mhatre Bridge, Erandwane, Pune, Maharashtra, India

Dr. Chandrashekhar Sahebrao Sonawane
Deenanath Mangeshkar Hospital and Research Center, Deenanath Mangeshkar Hospital Road, Near Mhatre Bridge, Erandwane, Pune, Maharashtra, India

Dr. Hemant Madhukar Wakankar
Deenanath Mangeshkar Hospital and Research Center, Deenanath Mangeshkar Hospital Road, Near Mhatre Bridge, Erandwane, Pune, Maharashtra, India

Corresponding Author:
Dr. Srisanat Srinivasan Rao
Deenanath Mangeshkar Hospital and Research Center, Deenanath Mangeshkar Hospital Road, Near Mhatre Bridge, Erandwane, Pune, Maharashtra, India

Antiphospholipid antibody syndrome presenting as foot gangrene after bilateral total knee arthroplasty: A case report

Dr. Srisanat Srinivasan Rao, Dr. Chandrashekhar Sahebrao Sonawane and Dr. Hemant Madhukar Wakankar

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Abstract
Case: A 71 years old female who underwent bilateral total knee replacement, noted discolouration of toes and plantar aspect of right foot, along with cold right foot, 1 week after surgery due to thrombosis of dorsalis pedis artery in spite of adequate anticoagulation. She was eventually diagnosed with Anti phospholipid antibody (APLA) syndrome.
Conclusion: APLA is not routinely investigated in preoperative workup for arthroplasty. It is also not a common condition in orthopaedic practice. Some patients may develop thrombosis after arthroplasty in spite of adequate thromboprophylaxis and a rare cause like APLA has to be kept in mind to help in ensuring appropriate treatment.

Keywords: Antiphospholipid antibody syndrome, total knee arthroplasty, dorsalis pedis thrombosis, arterial thrombosis, foot gangrene

Introduction
Total Joint Arthroplasty (TJA) has revolutionised the field of orthopaedic surgery. With increase in the number of arthroplasties performed, there is also an increase in the number of complications. The overall incidence of arterial complications after Total Knee Arthroplasty (TKA), including arterial occlusion, arteriovenous fistula, arterial aneurysm, and arterial severance varies between 0.03% and 0.17% in reports published in the orthopaedic literature [1]. Of these, popliteal artery thrombosis is the most frequent, accounting for 65.9% of all arterial problems [2].
One medical condition that carries higher risk for development of thromboembolism (TE) is antiphospholipid antibody (APLA) syndrome. APLA are a class of autoantibodies which can be divided into anticardiolipin antibodies (aCL), anti-beta 2 glycoprotein 1(aβ2GP1), and lupus anticoagulants (LA). These autoantibodies have been shown to be associated with both venous and arterial thromboembolic complications [3]. A study by Conduah *et al*. has evaluated the prevalence of APLA in patients having prior history of thromboembolism (either self or family) and undergoing joint replacement surgery. This study reported that 25% of patients had LA and 25% had aCL. None of their patients had abnormal aβ2GP1 [4]. Though the prevalence seems to be significant, the clinical manifestations of APLA are seldom seen in elderly population. Hence, preoperative screening for APLA is not done in all patients who are about to undergo joint replacement surgery. Here we report a rare case of an elderly female without any prior relevant history of thromboembolism who developed clinical complication of APLA after undergoing joint replacement surgery and was eventually diagnosed to have APLA.

Case history
The authors of the following case report obtained the patient's consent to having her date being submitted for publication. A 71 year old female with hypertension, Body mass index (BMI) of 22.4, presented with both knee osteoarthritis. She underwent bilateral Total Knee Arthroplasty (TKA) (Fig. 1). As part of routine perioperative drug protocol, she received a total 3 doses of 1g of tranexamic acid intravenously (1 dose preoperatively and 2 doses post-operatively 3 hours apart), in addition to receiving 1g of the same intraarticularly. She also received TE prophylaxis in the form of stocking and enoxaparin injection until discharge and tablet rivaroxaban 10 mg, once a day after discharge, as a part of standard post operative

protocol. On post operative day 7, she noticed discolouration of the right great toe, 4th toe and little toe (Fig. 2). It gradually extended to the lateral and plantar aspect of the right foot along with decreasing sensation and coldness in the same areas in the following days. She consulted us for the same on post operative day 10 and on clinical assessment, all peripheral pulses were palpable. An arterial and venous doppler was performed. There was intimal thickening in arteries of the right lower limb with no stenosis or thrombosis in the arterio-venous system. On post operative day 15, patient had absent dorsalis pedis pulsation and a Computed Tomography (CT) angiogram for right lower limb was performed which showed occlusion of right dorsalis pedis artery in distal third of foot with slow flow in mid foot. There was no floating thrombus in abdominal aorta, bilateral common iliac, external and internal iliac arteries and femoral arteries. Patient was admitted and started on injection prostacyclin infusion, injection enoxaparin, tablets rosuvastatin and aspirin along with analgesics. She was discharged in stable condition along with antiplatelet agents and statins. On post operative day 23, she presented with persistent severe pain in the toes and worsening discolouration (Fig. 3). On admission, her dorsalis pedis artery was found palpable in contrast to not being palpable on day 15. Opinion was sought from a haematologist to find out the cause of thrombosis. Investigations were sent to evaluate tumour markers and infective foci which were found to be negative. She eventually tested positive for Anticardiolipin IgM antibody and Anti beta 2 glycoprotein IgM antibody. Thus, diagnosis of Antiphospholipid antibody syndrome was established in a patient without any prior history of self or family for thrombosis. No vascular surgical intervention was done as dorsalis pedis artery pulsation was palpable clinically and confirmed on doppler. Patient was started on tablet warfarin after establishing diagnosis of APLA and discharged on the same. She was followed up at 6 weeks postoperatively, wherein she had bilateral knee range of movement 0-120 degrees. She had reperfusion of right little toe with dry gangrene of right great and 4th toes (Fig. 4) which was being managed by a vascular surgeon.

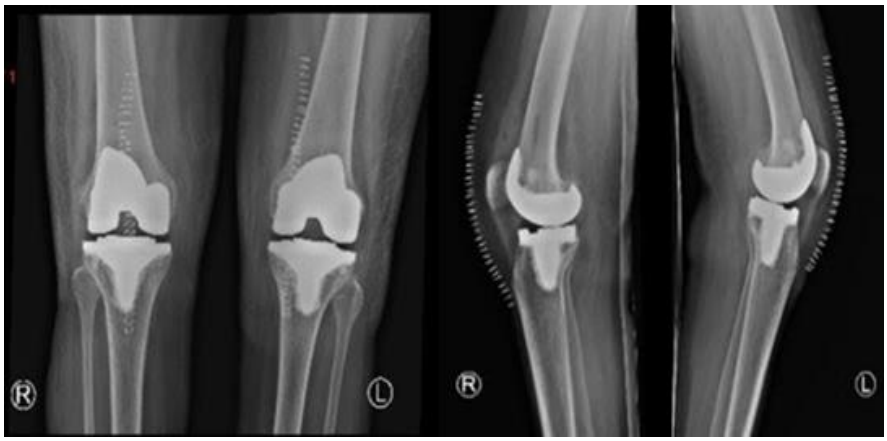

Fig 1: Immediate anteroposterior and lateral postoperative radiographs of the knee

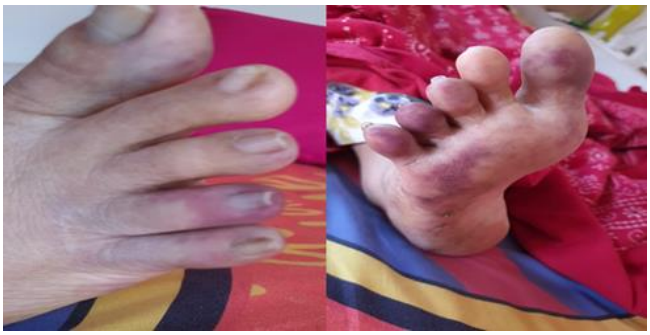

Fig 2: On post operative day 7, discolouration of the right great toe, 4th toe, little toe, lateral and plantar aspect of the right foot

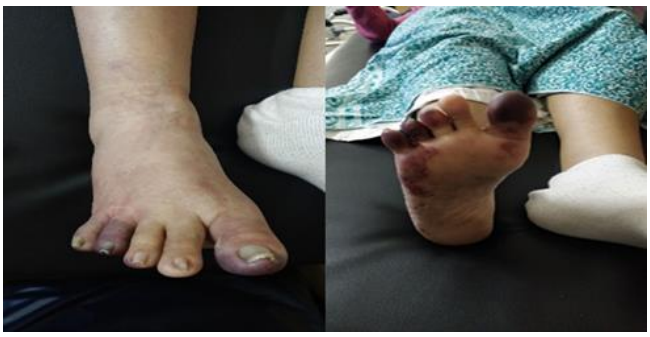

Fig 3: Clinical status on post operative day 23.

Fig 4: Dry gangrene at 6 weeks follow up.

Discussion

Knee arthroplasty improves pain and function in patients with end-stage osteoarthritis of the knee. Thromboembolic events after arthroplasty can cause significant morbidity and mortality and can occur despite aggressive perioperative thromboprophylaxis. Reports of arterial complications following TKA mostly occur in patients with an existing history of peripheral vascular disease(PVD), prior bypass surgery, arterial calcification on radiographs, revision surgery, renal failure, coagulopathy and metastatic cancer [5, 6, 7]. These patients usually present with a history of intermittent claudication, pain at rest, ischemic ulcers and absent or asymmetric pedal pulses [8].

Absence of distal pulse usually within 24 hours of TKA is the most common presentation of arterial injuries as reported by Li *et al*. [9]. We present a unique case of delayed arterial thrombosis after 7 days of primary TKA with initial complaints of discolouration of foot. APLA as an etiological factor in such rare vascular events still is less explored and discussed. The evidence to prove an association of APLA and thromboembolic event is still vague with evidence both in favour of as well as inconclusive [3, 10, 11]. In a study by Biggioggero *et al*., patients scheduled for hip or knee arthroplasty were tested for APLA prior to surgery and after surgery and found that the prevalence of APLA positivity preoperatively was 44% compared to 3 to 10% in the general population [12]. Such a wide variation in rate can be because with advancing age, incidence of APLA generally tends to increase and patients for joint replacement are usually elderly.

Patients having comorbidities like hypertension and coronary artery disease are more prone for development of arterial complications after surgery and are commonly diagnosed within the first few days of surgical event. In comparison with these cases, our patient's diagnosis was delayed. This case report agrees with the previous literature that there is no consensus on optimum management and intervention must be determined by the specific pathology [13].

Irrespective of the time of presentation as well as establishment of diagnosis, there is a need for further studies to investigate a larger population, measure all participants prospectively with prolonged follow up, measure APLA in the postoperative period, and correlate APLA results with clinical outcomes. Among all patients undergoing arthroplasty, identification of a subgroup of patients carrying higher risk for development of TE is of importance. This would enable us to further understand the association of APL antibodies with thromboembolic events. Patients may benefit from aggressive thromboprophylaxis if these patients are identified earlier.

Summary

Although no conclusions may be drawn from this case report alone, the fact that about 0.2 % of the population undergoing joint replacement can be expected to develop arterial thrombosis is evidence that a subset of patients exists for whom TE continues to be a concern. Among the risk factors that should be investigated in this group are APLA.

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