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Case Report

Surgery Section

Takayasu Arteritis Presenting with Gangrene: A Case Report

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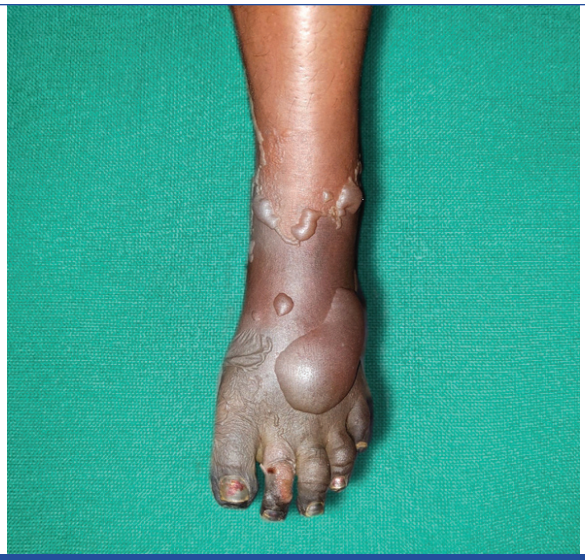
ABSTRACT

Takayasu Arteritis (TA) is a chronic inflammatory disease affecting large blood vessels, particularly the aorta and its branches, making it a type of vasculitis. It is reported to be highly prevalent in Southeast Asian countries. Clinical presentations may vary, including headache, weight loss, malaise, fever, hypertension, visual disturbances, and musculoskeletal symptoms. Gangrene is a rare manifestation of TA, with relatively few cases reported globally. If gangrene is present, it is commonly noted in the lower limbs. Inflammation of the blood vessels caused by TA might lead to stenosis of the affected vessels. The underlying pathophysiology of gangrene development in TA is poorly understood but is mainly attributed to the occlusion of blood vessels. It is associated with inflammatory markers produced by lymphocytes and macrophages. Immunosuppressive drugs are recommended for symptomatic relief. Early diagnosis and intervention can be useful in managing TA, preventing adverse outcomes, and reducing its financial, social, and psychological consequences. This is a case report of a 32-year-old female, presented with gangrene and a history of rheumatoid arthritis. Further examination revealed a presentation of TA. The patient was managed by below-knee amputation for gangrene of the left leg and medical management for TA. Therefore, authors aim to draw attention to the diagnosis of TA and the rare associated morbidity, 'gangrene,' and the importance of timely intervention.

Keywords: Below knee amputation, Critical limb ischaemia, Limb claudication, Pulselessness, Vasculitis

CASE REPORT

A 32-year-old female visited the Outpatient Department with complaints of pain in her left foot for the past six months, along with blackish discolouration of the skin over the foot and loss of sensation in the left foot. The patient did not had any significant medical history. The first instance of developing pain in the left foot was noted six months ago, with an insidious onset and gradual progressive and throbbing type of pain, aggravated by physical activity and not relieved by rest. The pain was described as throbbing, intermittent, non radiating, and localised to the left leg. The patient also reported tingling and numbness in the left foot, as well as claudication. Upon physical examination, the patient's vitals were stable, with pallor noted. Discolouration of the same foot had been observed for the last 15 days, starting from the tip of the toes and gradually progressing towards the ankle. Blackening was observed in the great toe of the left foot extending to the distal one-third of the foot [Table/Fig-1].

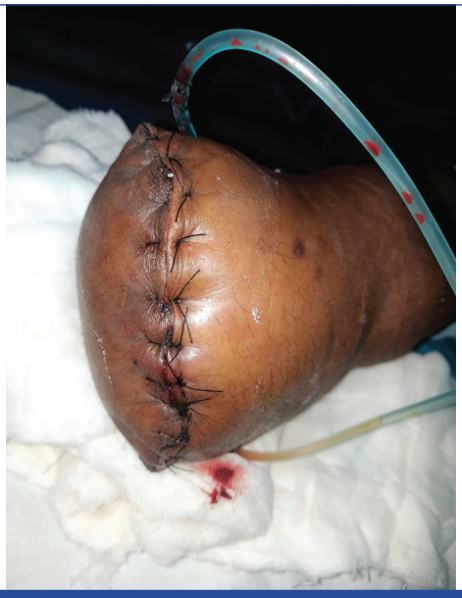


[Table/Fig-1]: Physical presentation of the patients' foot.

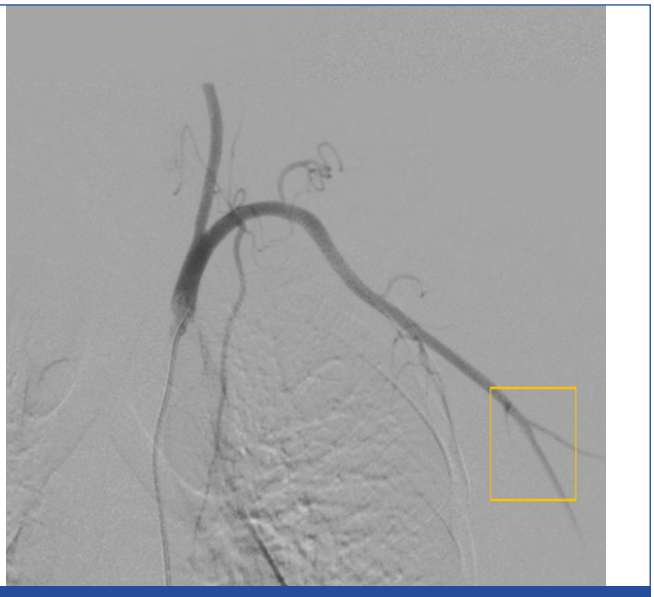
The foot was cold with no palpable dorsalis pedis artery, anterior tibial artery, or posterior tibial artery. The left popliteal artery was palpable, with a preserved full range of motion at the ankle and knee. The right limb was normal, with all palpable peripheral pulses in the upper and lower limbs. There was no history of trauma, fever, ulcers, dilated veins in the left leg, or dyspnoea. The patient had a history of rheumatoid arthritis and was being medically managed with regular medications (Methotrexate and Folic acid). Upon admission, the colour Doppler study indicated biphasic flow in the left popliteal artery, anterior tibial artery, posterior tibial artery, and dorsalis pedis artery. The patient underwent surgical management for intra-arterial thrombolysis of the left lower limb along with dual-action blood thinners. The foot appeared pale with blackish discolouration, a foul smell, and a clear line of demarcation at the ankle joint, indicative of gangrene. Antibiotic and supportive medications were started preoperatively, and routine blood investigations revealed anaemia, which was managed by blood transfusion. Preoperative blood investigations are detailed in [Table/Fig-2]. Thyroid profile, liver function tests, and serum electrolytes were within normal limits. The patient underwent below-knee amputation under spinal anaesthesia for the left foot due to gangrene. Postoperatively, the patient was transferred to the Intensive Care Unit (ICU) for close monitoring with routine supportive medications [Table/Fig-3]. A postoperative colour Doppler study revealed a chronically narrowed left radial artery and biphasic flow in the left ulnar artery, with normal findings in bilateral upper limb colour Doppler. Subsequently, the patient underwent Magnetic Resonance (MR) angiography, which indicated Takayasu Arteritis (TA), and was started on steroids, antimetabolites, and anticoagulants [Table/Fig-4,5]. The patient's hospital course was uneventful, and she was discharged 15 days postprocedure. Ecosprin and Clopidogrel were prescribed for three months, with potential modifications during the next follow-up visit. The patient was advised to have three-monthly follow-ups for a period of one year.

Test parameter	Patient value	Normal range
Haemoglobin (gm/dL)	10.5	12.0-16.0
MCHC (gm/dL)	32.6	32-36
MCV (fl)	76.1	83-101
MCH (picograms/cell)	24.8	27-31
Total WBC count (cells/cumm)	15700	4,000-10,000
Total platelet count (lac/cumm)	4.65	1.5-4.1
INR	1.08	<1.1
D-Dimer (mg/L)	2002	<0.50
ESR (mm/hr)	104	Male: ≤15 Female: ≤20
Anti-Nuclear Antibodies (ANA)	6.370	<0.9- negative/ undetectable, 0.9-1.1- Borderline, >1.1- Positive
C3 (mg/dL)	110	90-180
C4 (mg/dL)	42.6	15-45
CRP (mg/dL)	289.05	<0.3
Urea (mg/dL)	13	19-43
Creatinine (mg/dL)	0.5	0.66-1.25

[Table/Fig-2]: Blood investigation profile of the patient.
MCHC: Mean corpuscular haemoglobin concentration; MCH: Mean corpuscular haemoglobin; WBC: White blood cell; INR: International normalised ratio; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein



[Table/Fig-3]: Postoperative image of the patient managed by below knee amputation for the management of TA associated gangrene.



[Table/Fig-4]: Highlighted area shows the abrupt blood flow in the peripheral blood vessels.

[Table/Fig-5]: Highlighted area shows the reduced flow in left radial artery.

DISCUSSION

The TA is more prevalent in Asia, approximately 100 times higher than in the rest of the world. Clinical presentations vary, with common symptoms including dyspnoea, musculoskeletal symptoms, claudication, weight loss, fatigue, syncope, and visual disturbances [1]. TA is characterised by arterial inflammation of large blood vessels such as the brachiocephalic artery, subclavian arteries, and renal arteries and their branches. It is considered an autoimmune disorder and has been associated with various underlying factors such as endothelial inflammation and injury, microbial infections, and genetic factors. Some genes associated with TA include human leukocyte antigen I and II, with strong evidence of the gene HLAB52. Other genetic markers associated with TA are immuno-regulatory genes (LILRA3, IL38, and RPS9/LILRB3) and cytokines (IL12B, IL6, and MLX) [2]. TA can be diagnosed if any three of the following criteria are observed: a) lower pulse in the upper limb, limb claudication, >10 mmHg blood pressure difference between both limbs; b) onset of symptoms in patients <40 years old; c) detection of bruit from the aorta and subclavian artery supported by angiographic findings [3]. Clinical presentations of patients with TA commonly include weight loss, malaise, fever, muscle aches, hypertension, visual disturbances, and joint stiffness. Some patients may also present with arterial bruits and limb claudication [4]. This case had a similar presentation with a positive history of rheumatoid arthritis and limb claudication. Females are suggested to be more prone to TA, with a reported male to female ratio of 1:5, with renovascular hypertension as a predominant risk factor [4,5]. Positron Emission Tomography-Computerised Tomography (PET-CT) can be used to detect arterial wall thickness and vessel hypermetabolism [6]. Vessel hypermetabolism refers to increased metabolic activity within the blood vessels, which can occur in various physiological and pathological contexts, including angiogenesis, inflammation, tumour growth, and vascular diseases. Occasionally, individuals may experience a sudden development of vascular stenosis, leading to severe limb ischaemia or gangrene. Gangrene is an uncommon presentation of TA, with very few reported cases in available research literature [7,8].

The management of TA typically involves the use of immunosuppressive medications to control inflammation, with the goal of alleviating symptoms, preserving vascular function, and preventing complications such as gangrene [7-9]. Corticosteroids, immunosuppressive agents, and antitumour necrosis factor therapy are recommended for disease management and prevention of relapse [10]. Additionally, revascularisation of renal arteries and percutaneous transluminal angioplasty are recommended to improve outcomes in renal artery stenosis resulting from TA [1,11]. Gangrene in TA is rarely reported, with very few cases documented worldwide. A research report by Misra DP et al., described three

similar cases involving two females and a male aged 14, 24, and 18 years, respectively, who presented with gangrene and were diagnosed with TA. Pulselessness, a common symptom of TA, may contribute to the development of gangrene in this patient group [9]. Angiography reports indicated Numano's type V in the majority of the patients. Clinical presentations of these patients included a history of hypertension, arterial bruits, and lower limb claudication [4,7].

Gangrene is more commonly observed in the lower limbs compared to the upper limbs, a similarity noted in this patient. The presentation of gangrene is attributed to the production of inflammatory markers induced by the infiltration of lymphocytes, killer cells, and macrophages, which can cause damage through the production of perforin, leading to vascular damage [4,5]. The incidence of TA has also been linked to microbial infections such as *Mycobacterium tuberculosis* and Streptococcal infections, contributing to its multifactorial and elusive aetiology [5]. Gangrene in extremities or digital gangrene is considered an unusual primary presentation of TA, with only a few cases documented in medical literature [4,12]. Partial or complete occlusion of the common carotid artery has been reported as a common underlying cause of digital gangrene in such cases [7]. The management of TA with gangrene typically involves oral corticosteroids such as prednisolone and immunosuppressants for symptom relief and disease management [5,7,8]. Although timely diagnosis and medical management therapies are available, approximately 20% of patients with severe disease presentation may require aggressive management through surgical modalities [13]. Early diagnosis and intervention can be beneficial in the management of TA and in preventing adverse outcomes through timely intervention. However, in cases with severe complexities, endovascular management and surgery may be necessary. Prolonged medical management with regular follow-up is essential to avoid exacerbation and acute disease presentation.

CONCLUSION(S)

TA is a rare illness that predominantly affects women, presenting with either asymptomatic or varied clinical manifestations, with angiography as the primary method for diagnosis. Management typically involves steroids, methotrexate, and mycophenolate mofetil, primarily for symptomatic relief, restoration of absent pulses, and control while preserving vascular function. However, an alternative approach involving surgery has been practiced in patients with associated co-morbidities for better disease management or throughout disease progression. Regular monitoring and follow-up are crucial to evaluate disease activity and adjust the treatment plan as necessary, using interventional procedures or surgery to address arterial abnormalities.

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