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Case Report

Delayed Diagnosis of Vasopressor-induced Symmetrical Peripheral Gangrene in Septic Shock Patient

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ABSTRACT

Vasopressors are powerful vasoconstrictors used in critically ill patients to raise blood pressure after volume resuscitation attempts fail. These medications, while lifesaving, carry the risk of severe and under-reported side effects, digital ischemia, and gangrene due to decreased digital perfusion. We here present a case of vasopressin-induced digital gangrene in a female patient who underwent elective surgery for nephrolithiasis without any pre-existing peripheral vascular disease or smoking. The patient developed bilateral upper and lower limb symmetrical acronecrosis. The causality assessment as per the World Health Organisation - Uppsala Monitoring Centre scale was suggestive of a "Possible adverse" event. The patient denied surgical intervention, eventually developed multiorgan failure, and died of cardiopulmonary arrest. Although lifesaving, vasopressors due to alpha constricting activity can cause severe limb ischemia with dreadful consequences. These drugs should be used judiciously with careful monitoring and tapering as soon as possible when the condition improves. The consequences could be dreadful if timely surgical intervention and measures are not taken.

KEYWORDS: Acronecrosis; Adverse event; Sepsis; Symmetrical digital gangrene; Vasopressin

INTRODUCTION

Vasopressors, powerful vasoconstrictors, are used for resuscitation in critically ill patients who are experiencing circulatory shock and are not responding to volume resuscitation.[1] These medications, while lifesaving, hold the risk of severe side effects. Ischemia, a consequence of decreased digital perfusion, can have serious consequences, such as symmetrical peripheral gangrene (SPG) and amputation.

SPG is an infrequent but catastrophic condition described as multiple extremity ischemia involving two or more sites in the absence of large vessel obstruction.[2,3] The etiology remains multifactorial, including its treatment.

This case report aims to report a tragic occurrence of SPG due to vasopressor use in a middle-aged female soon after nephrolithotomy for a left ureteric stone.

CASE PRESENTATION

A 46-year-old woman presented to the emergency triage area of a tertiary care hospital on postoperative day 10 of percutaneous nephrolithotomy (PCNL) for a left-sided ureteric stone in a private hospital with chief complaints of pain in the abdomen, dysuria, hematuria, and bluish-black discoloration of bilateral peripheral extremities of the upper and lower limbs. On postoperative Day 2 in the same hospital, the patient

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developed hypotension, altered mental status, nausea, cold, and pale extremities. The blood pressure remained persistently low despite adequate fluid resuscitation, requiring the addition of vasopressor support. A provisional diagnosis of septic shock was made and was managed with intravenous fluids and inotropic support along with vasopressin. However, the detailed records (dose and duration) of vasopressin were unavailable from the patient or the discharge summary. The patient deteriorated and started developing blackish discoloration of bilateral upper and lower limbs, because of which she was referred to a higher center on postoperative Day 10.

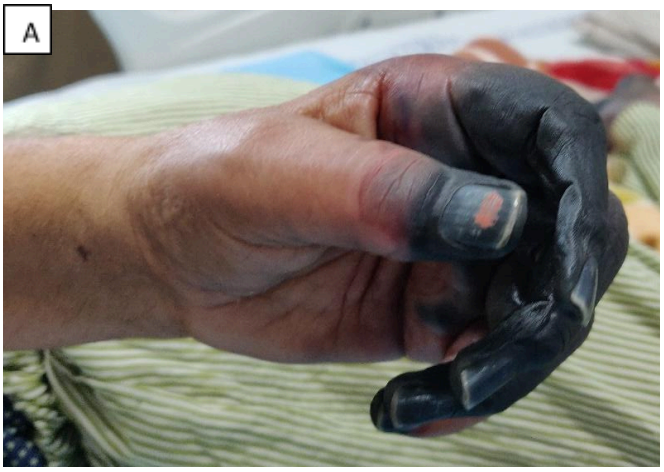
There was no past or present history suggestive of intermittent claudication, peripheral vascular disease, Raynaud's phenomenon, vasculitis, hypertension, diabetes, or connective tissue disorders. The patient did not have a history of smoking, alcohol consumption, or any drug abuse. There was no history suggestive of ergot poisoning, and she did not report neurological symptoms such as convulsions or hallucinations to suggest this as a potential explanation. The patient had a history of Sheehan syndrome, for which she was taking prednisolone 10 mg once a day, and hypothyroidism, for which she was regularly taking thyroxine 62.5 microgram once a day for the last 6-7 years.

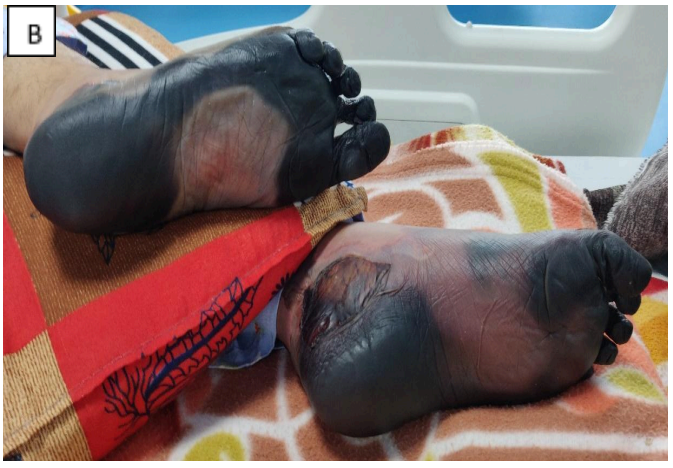
On presentation to the emergency, the patient was intubated with a Glasgow Coma Scale of $E_4V_tM_6$. Her vitals were as follows: blood pressure=102/72 mm Hg, heart rate= 103 per minute, respiratory rate=22 per minute. She had a body temperature of 38.3 degrees Celsius but no lymphadenopathy. On skin examination, there were dry gangrenous changes associated with blistering on the bilateral upper and lower limbs (Fig 1A-B). All peripheral pulses, i.e., brachial, radial, femoral, and dorsalis pedis, were present.

She was admitted to the Department of General Medicine and started on supportive therapy and empirical antibiotics because of suspected infective etiology (injection colistin and meropenem) in addition to cilostazol and nifedipine. Doppler ultrasound of both upper and lower limbs was done. The Doppler study revealed normal flow in visceral arteries without evidence of thrombus. Ultrasound of the abdomen revealed minimal ascites and 2-dimensional echocardiography showing an ejection fraction of 60% with mild tricuspid regurgitation without septic foci. Anti-nuclear antibody, anti-neutrophilic cytoplasmic antibody, anti-cyclic citrullinated peptide, and rheumatoid factor were negative. Liver function tests showed deranged SGOT/AST and SGPT/ALT values of 113 and 130 IU/L, respectively. She had lactate levels of 1.52 mmol/L. Urine and blood cultures sent at admission yielded no growth. Platelet count was 581000/µL with an international normalized ratio (INR) of 1.2 and D-dimer 2460 ng/ml (fibrinogen was not done in-house), ruling out disseminated intravascular coagulation (DIC) as per the International Society of Thrombosis and Haemostasis score.

The patient was managed by a multidisciplinary Cardiothoracic vascular surgery, Plastic surgery, and Orthopaedics team. Along with ongoing treatment, aspirin (75 mg once daily), nicorandil (5 mg twice daily), and the local application of nitroglycerin ointment was advised. The patient was diagnosed as a case of symmetrical peripheral gangrene (SPG) and was advised amputation and reconstructive surgery. The patient denied amputation and did not provide informed consent for surgical intervention. Non-surgical management was continued, but the patient developed multiorgan failure with cardiopulmonary arrest after two days of admission and expired.

Figure 1: Vasopressor-induced symmetrical peripheral gangrene of bilateral upper (A) and lower (B) limb**s**





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SPG is an exclusion diagnosis, which means that all other causes of gangrene must be conquered. According to the patient's history and investigations, patient had symmetrical gangrene involving more than two distal extremities on examination, and all of her peripheral pulses were present. The history was not suggestive of Raynaud's disease, connective tissue disorder, vasculitis, peripheral vascular disease, or any poisoning (ergot). The Doppler study revealed normal flow in visceral arteries with no evidence of thrombus. Anti-nuclear antibody, anti-neutrophilic cytoplasmic antibody, cyclic citrullinated peptide and rheumatoid factor profile were negative. LFT were deranged and lactate levels were found to be higher supporting the diagnosis of SPG. Urine and blood culture were found to be negative (to note that the patient was receiving broad spectrum antibiotic outside as well as on admission). Outside treatment history was suggestive of the use of vasopressin for resuscitation suggestive of positive temporal association. However, the dose and duration of vasopressin use were unclear. The causality assessment as per the World Health Organisation-Uppsala Monitoring Centre scale was suggestive of "Possible" causality.

DISCUSSION

We present a case of symmetrical peripheral gangrene (SPG) in critically ill post-operative patient with suspected septic shock associated with use of high dose vasopressin. SPG is an infrequent but dreadful condition. The etiology remains multifactorial like sepsis and septic shock, small vessel obstruction, malignancy including myeloproliferative disorders, connective tissue disorders such as systemic lupus erythematosus, antiphospholipid antibody syndrome, ergotism, protein C deficiency, use of high dose vasopressors, DIC[2-12]. The common organisms implicated in infective etiology include *Pneumococcus, Staphylococcus, Streptococcus* and some gram-negative organisms [6]. SPG has high mortality (upto 40 %) and more than half of patients who survive end up having amputation of the affected limb[3,8]. According to Molos et al, DIC is a substantial underlying factor in 85% of patients diagnosed with SPG[8]. Immunosuppression, asplenism, hypothermia, diabetes mellitus, and renal failure are also the aggravating risk factors for SPG[8-11].

Vasopressors are lifesaving if used promptly and judiciously in intensive care setting in presence of shock. However, vasopressors with alpha constricting property can lead to peripheral digital ischemia owing to reduced digital blood supply especially when the intraluminal pressure falls below a critical value. However, the existing evidence largely comes predominantly from case reports and case series [4,13,14,15]. Lewy et al in the review article tried to see correlation of ischemic limb necrosis in septic shock with the use of high dose vasopressor therapy (>0.5 mcg/kg/min). In the review, three of the eight studies included showed that digital ischemia or SPG is associated with use of high dose vasopressors. The vasopressor doses required to maintain target blood pressure ranged from 0.5 to 4 mcg/kg/min with mean duration 84.7 hours in the study. Vasopressors increased the risk of SPG with relative risk (RR) of 4.85, CI 2.81- 8.39, I^2 = 26%, although the risk factors (DIC, coagulopathy) were not mentioned in the study[16].

SPG presents with early sign of pallor, cyanosis, coldness and pain in the extremity. If appropriate care and tapering of vasopressors is not done at early stage especially in unconscious patients, it may progress to digital bullae, blisters, discoloration and subsequently gangrene[3]. Ischemic changes typically begin in the periphery and advance proximally. The pulses remain intact in early stages with sparing of large vessels despite occlusion of microcirculation. This may be further aggravated by use of vasopressors even at recommended doses leading to more sluggish flow and hence ischemia of digits[17,18].

The first line of management includes vigorous fluid resuscitation with aim to stop vasopressors as early as possible along with empirical antibiotics if sepsis and anticoagulation for DIC[3,8,19]. It is essential to have a high index of suspicion and identify the underlying cause early in order to save life and limb before irreversible ischemia and gangrene are set in. Although digital ischemia early signs are not viewed as emergency due to medical adage "Life over Limb" and is a secondary diagnosis but it has long term psychosocial effect and impact quality of life if patient survives and amputation is done[20]. Amputation may be required in many cases of the affected extremities when a clear line of demarcation appears along with plastic surgery involvement for skin grafting[19]. Various vasodilator therapies have been explored at early stages of discoloration including use of nitroglycerin paste[21], calcium channel blockers, temperature regulation, high dose continuous tissue plasminogen activator infusion with heparin and topical nitroglycerin[22], phentolamine[23] with an attempt to halt progression to gangrene with unproven results with limited evidence so far. More research is required to determine optimal treatment in early stages of SPG. All attempts should be made to wean the patient off vasopressors as early as possible to prevent such dreadful consequences. Appropriate dosage of intravenous vasopressors to treat

hypovolemic shock, septic shock or other life-threatening cardiovascular instability should be individualised according to age, mean arterial pressure and cardiovascular status of the patient.

CONCLUSION

Early diagnosis of SPG and attempts to stop the vasopressor therapy at the earliest possible point could prevent dreadful complications such as acronecrosis, limb loss, or even death. Prompt management of sepsis and optimization of fluid status can help wean off the vasopressors as soon as possible and avoid catastrophic consequences. Although no clear recommendations exist for using vasodilators to manage SPG, some agents such as nitroglycerin, tissue plasminogen activator, and phentolamine have been tried and found helpful.

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CONFLICT OF INTERESTS STATEMENT

The authors declare no conflict of interest

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ETHICS STATEMENT INCLUDING PATIENT CONSENT

Written informed consent was obtained from the patient's husband. Confidentiality of the patient was maintained in the article.

AUTHORS' CONTRIBUTIONS

RR: Methodology; Data curation; Analysis; Writing the draft

DC: Review & editing; Supervision; Validation

AA: Review & editing; Supervision; Validation

PSD: Methodology; Data curation;Analysis; Writing the draft

AI DECLARATION

No AI tool was used to generate research data, perform data analysis, interpret findings, formulate scientific conclusions, or make editorial decisions. All AI-assisted content was critically reviewed, verified, and revised by the authors. The authors take full responsibility for the accuracy, originality, integrity, and final content of the manuscript.

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