Symmetrical Peripheral Gangrene due to Postpartum Cardiomyopathy: A case series

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Abstract

Background: *symmetrical peripheral gangrene (SPG) of two or more extremities without large vessel obstruction or vasculitis is seen in various medical conditions. It has high morbidity with an increasing frequency of multiple limb amputations in survivors.* ***Objective:*** *The objective of these case series is to highlight SPG as a cause of multiple limb amputation and the benefits of a multidisciplinary team approach in its management.* ***Methods:*** *We report three cases of SPG caused by sepsis within the peripartum period. All the patients were referred to our facility because of progressive darkening of the extremities following unsupervised home deliveries. Two of the patients were booked multigravida with regular clinic visits at a peripheral hospital, while one is an unbooked primigravida. They all had urgent resuscitation and subsequent multiple amputations and disarticulations of affected extremities to save their lives. Multidisciplinary pain management involving nursing care, dietetics, physiotherapy, and social care was involved in the care of the patients till discharged. The pain intensity was measured to be at ten on the verbal rating scale (VRS) pre-operation, and functional disability of 30% on Barthel's index (BI).* ***Results:*** *Seven days post-operation, all the patients' pain has remarkably reduced with an average VRS = 2 and enhanced functional disability BI = 70%. All three patients now ambulate on a pair of auxiliary crutches.* ***Conclusion:*** *Early recognition of symmetrical peripheral gangrene and prompt referral for immediate resuscitation and active treatment of sepsis may prevent further progression of the condition and, thus, saves the person's life.*

Keywords: **S**ymmetrical, Gangrene, Postpartum, Cardiomyopathy

Introduction

Symmetrical peripheral gangrene (SPG) is a rare syndrome defined by a peripheral ischemic lesion of two or more extremities in the absence of major vascular obstructive disease(Albano *et al*., 2018; Ghosh *et al*., 2010; Prati *et al*., 2018). It was first described

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in 1891 by Hutchinson in a clinical case of sepsis with intravascular disseminated coagulopathy (Ghosh *et al*., 2010).

Clinically, it presents with signs of ischemic limb injury, which is sharply demarcated and strikingly symmetrical and often progresses rapidly to gangrene, however, with palpable pulses. The pathogenesis of the condition is not fully understood. However, it was thought to be related to conditions that decrease blood supply and consequently the delivery of nutrients and oxygen to the more peripheral regions for an extended time (Knight Jr *et al*., 2000).

The features of symmetrical two or four limbs and mono-limb ischemic necrosis are similar to micro thrombosis, which is caused by a disturbed procoagulant balance(Ghosh *et al*., 2010; Sharma *et al*., 2012). There is also a risk of developing deep vein thrombosis in mono-limb ischemic necrosis. Although deep vein thrombosis is not usually present in patients with polymyopathy or superficial vein thrombosis, it can result from disseminated intravascular coagulation (DIC) (Ikezoe, 2015). According to some authors, this condition is caused by reduced antithrombin levels. In addition, there is an increase in the expression of a plasminogen activator inhibitor (Ikezoe, 2015; Moake, 2020).

It is also theorized that the development of SPG is caused by the reduction in the level of pro-coagulant factor VII and protein C deficiency. In severe sepsis, the increase in protein consumption and the downregulation of the activation of the cytokines are some of the factors that contribute to the development of this condition (MEYERS *et al*., 1970). In patients with meningococcal septicemia, conditions that are characterized by the lack of protein C can be caused by the Shwartzman reaction. On the other hand, conditions that are caused by the reduction in the level of pro-coagulant factor VII can be caused by complicated cancer patients (Ikezoe, 2015; MEYERS *et al*., 1970; Moake, 2020).

CASE REPORT 1

A 30-year-old with four children and one week postpartum was referred to the orthopaedic unit with complaints of progressive darkening of her forefoot and toes, pregnancy was unbooked, and home-conducted delivery with an alive infant. She was admitted with a history of dyspnea, orthopnea, cough with pink frothy sputum, decreased urine output, and bilateral feet swelling. At admission, the patient was afebrile, with a blood pressure of 96/60 mm of Hg, pulse rate of 100/min, and respiratory rate of 28/min. On examination, There was Pedal edema and bluish discoloration of the fingers of both hands (fig 1). Bilateral toes showed symmetrical gangrenous changes with eschar formation (fig 1.1). All peripheral pulses were palpable, regular, and of normal volume. Investigations showed hemoglobin of 8 g% total leukocyte count 15,600/cumm, Peripheral blood smear revealed normocytic hypochromic anaemia with neutrophilia and a left shift. Biochemical parameters revealed Random blood glucose-118 mg%, SGOT-110 IU/L, SGPT-102 IU/L, alkaline phosphatase-90 IU/L, albumin-3.0 g%, urea-120 mg%, creatinine-1.5mg%. Electrolytes, lipid profile, and coagulation profile were normal. Doppler study for upper and lower limb arteries was normal.

After 10 days of hospital treatment, gangrenous changes demarcated and became confined to the bilateral forefoot and toes. All the toes were dry and shriveled with features of auto amputation. Due to multiple joint involvement and her cardiomyopathy a diagnosis of SPG was reached.

She was counseled and subsequently had a forefoot amputation on the right and left below knee amputation. She was ambulatory at discharge, normotensive, and referred to the orthosis and prosthesis unit for a limb-fitting prosthesis. The pain intensity and functional ability of the patient were measured with the verbal rating scale (VRS) and Barthel's index, which were found to be 10 and 30% respectively before the surgery but reduced to 2 on discharge from the hospital. The patient was asked to continue hospital visitation on an outpatient basis.

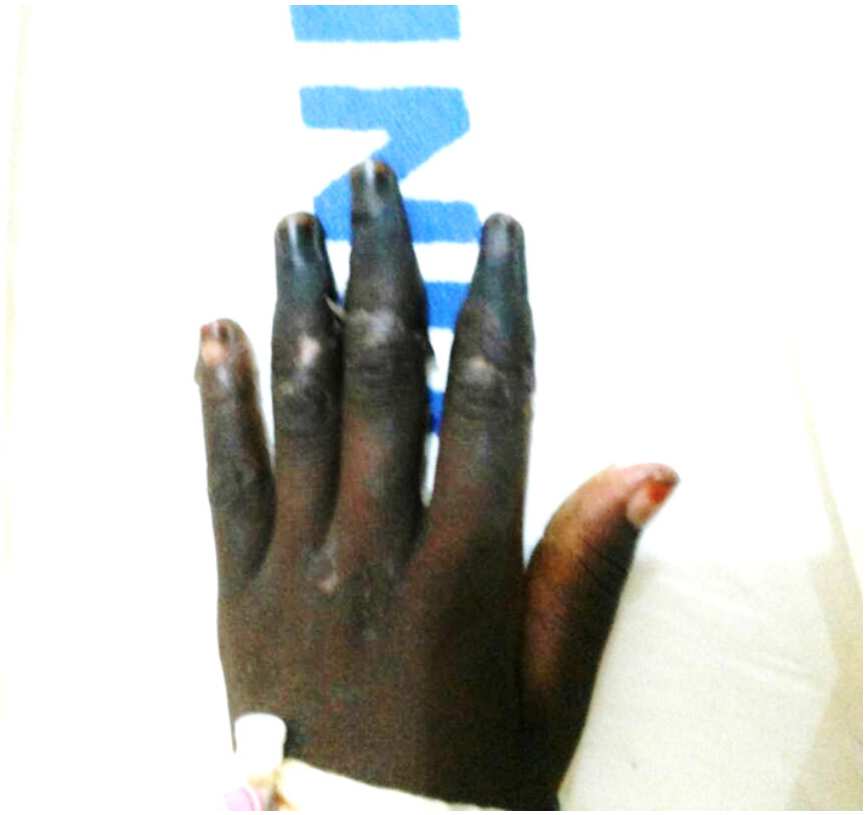

Figure 1: Pedal edema and bluish discoloration of fingers of the hands

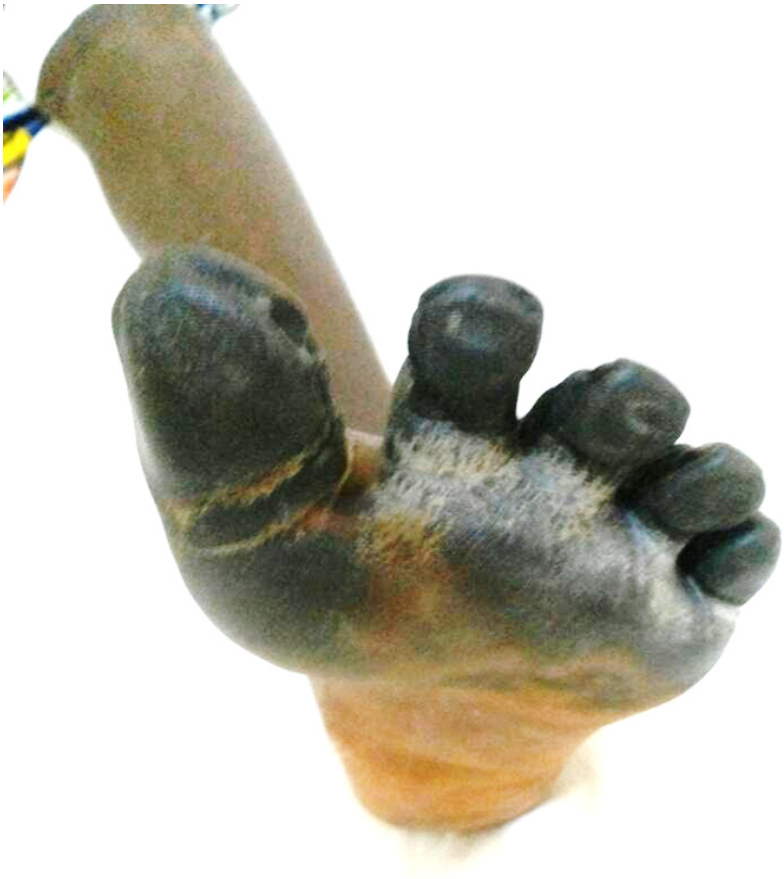

Figure2: Bilateral toes showed symmetrical gangrenous changes with eschar formation

CASE REPORT 2

A 20-year-old primigravid was booked and delivered at a peripheral hospital. She presented with bilateral leg swelling and darkening of her toes two weeks after childbirth. She has a history of post-partum bleeding necessitating multiple blood transfusions at the health centre. She was admitted to the accident & emergency department 10 days following discharge from the health centre due to coldness in the feet, pain, and progressive gangrene. On examination the vital signs were stable, and all peripheral pulses were palpable.

She has no prior history of intermittent claudication, cold or heat intolerance, tobacco smoking, collagen vascular disease, or use of ionotropic drugs. Laboratory results on admission showed; haemoglobin (Hb) was 9.0 g/dL; white blood cell (WBC) count 12.470/mm3; platelet counts 674.000/mm3 and on clotting profile, prothrombin time (PT) was 12 sec. and partial thromboplastin time test kaolin (PTTK) 32 seconds. Color Doppler ultrasound of the lower extremity vessels showed a tri-phasic pattern of normal circulation. Her medical treatment consisted of broad-spectrum antibiotics and low molecular-weight heparin. The gangrenous appearance of the feet demarcated itself to just above the malleoli on the left leg, fig 2. Due to multiple joint involvement and cardiomyopathy a diagnosis of SPG was reached. The patient was counselled and prepared for surgery. She had a below-knee amputation on the left leg.

The pain intensity and functional ability of the patient were measured with the verbal rating scale (VRS) and Barthel's index, which were found to be 9 and 40% respectively before the surgery but reduced to 2 on discharge from the hospital. The patient was asked to continue hospital visitation on an outpatient basis.

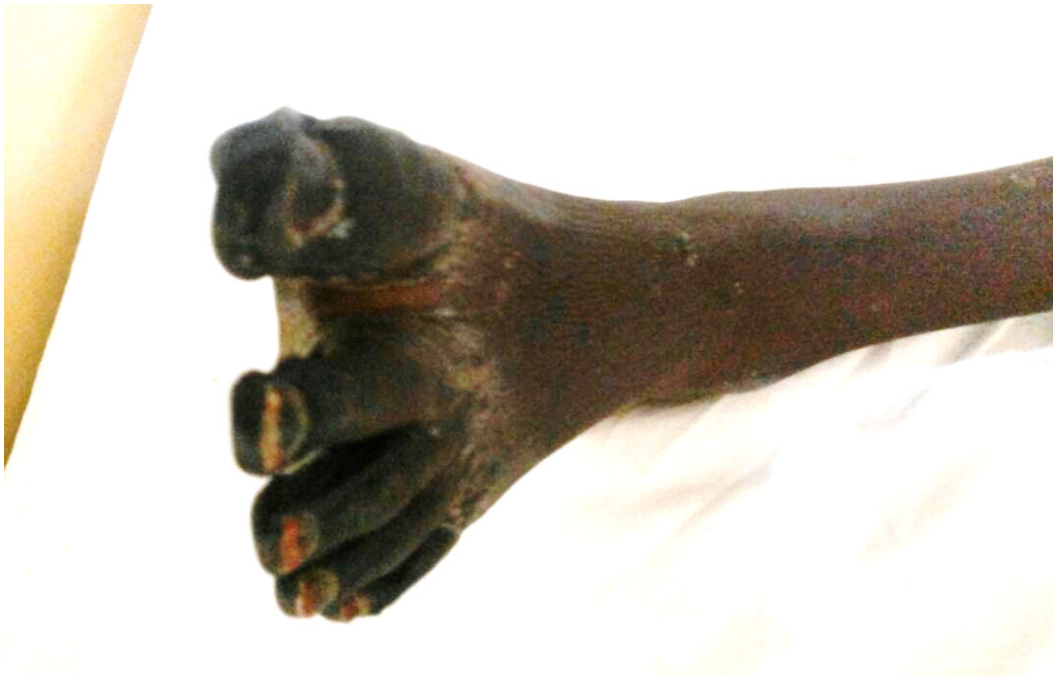

Figure 2: The gangrenous appearance of the feet demarcated itself to just above the left malleoli on the leg

CASE REPORT 3

A 23-year-old Gravida with one child presented to the accident and emergency department of Aminu Kano Teaching Hospital with the complaint of bilateral lower limb pain, paresthesia, numbness, and dark discoloration of her forefoot and toes. She also complained of shortness of breath and cough

She was four weeks post-partum, following a home delivery, supervised by a traditional birth attendant. Delivery was uneventful. She has no personal or family history of cardiomyopathy and no history of use of ionotropic agents. Her remaining history was unremarkable.

On examination, gangrenous changes were found on her left lower limb up to the mid-leg region and on the right limb on her toes and the posterior aspect of the foot. See fig. 3 & 3.1

Echo-cardiography showed an ejection fraction of 24% with the dilated left ventricular wall, chest x-ray showed interstitial oedema and pleural effusion. Due to multiple joint involvement and cardiomyopathy a diagnosis of SPG was reached. After medical management by the cardiologist and the ICU experts, appropriate counselling for amputations was scheduled. She had above-knee amputation on the left and below-knee amputation on the right.

The pain intensity and functional ability of the patient were measured with the verbal rating scale (VRS) and Barthel's index, which were found to be 10 and 30% respectively before the surgery but reduced to 2 on discharge from the hospital. The patient was asked to continue hospital visitation on an outpatient basis.

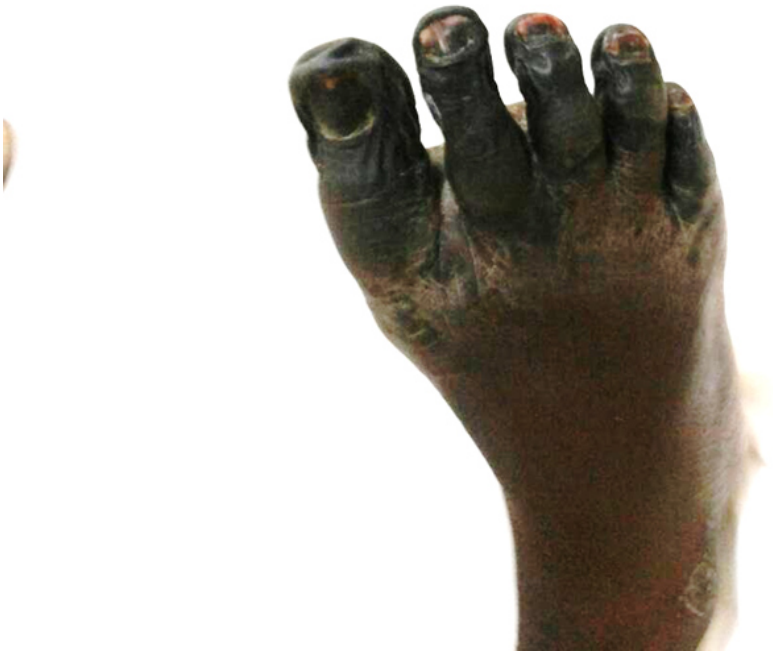

Figure 3: gangrenous changes seen on the right limb on her toes and the posterior aspect of the foot.

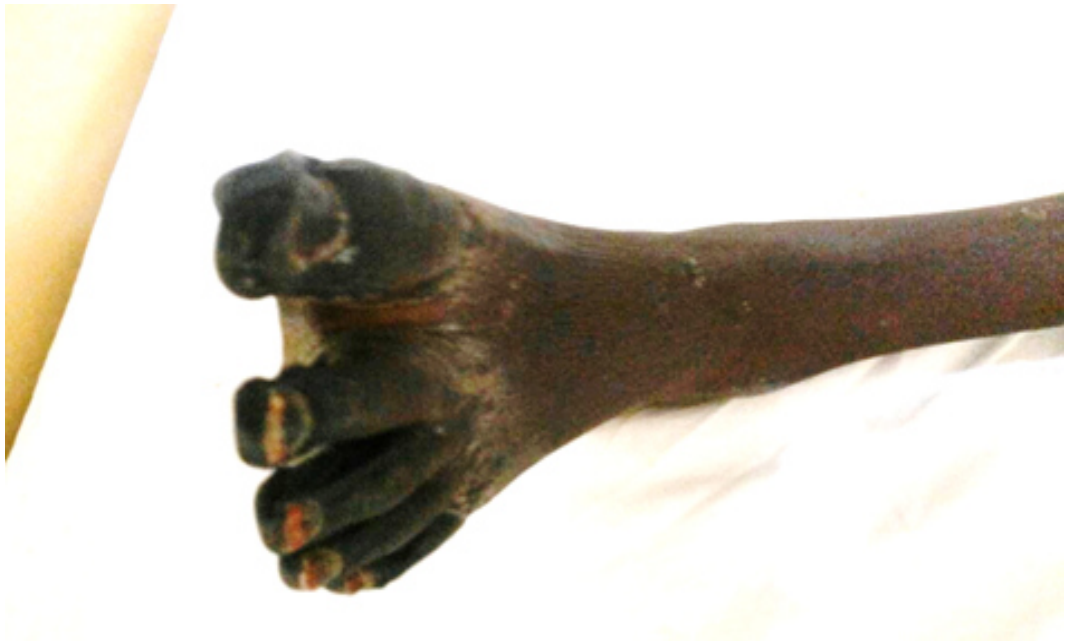

Figure3.1: Gangrenous changes seen on the left lower limb up to the mid-leg region.

Discussion

We report three cases of symmetrical peripheral gangrene (SPG) caused by cardiomyopathy within the peripartum period. All the patients were referred to our facility on account of progressive darkening of the extremities following unsupervised home deliveries. Two patients were booked multigravida with regular clinic visits at a peripheral hospital while one is an unbooked primigavid. They all needed urgent resuscitation which was carried out by the ICU experts and subsequent multiple amputations and disarticulations to save their lives were done. All the amputations were done under various nerve blocks with sedation as the patients were not stable to undergo general anesthesia or neuraxial blocks. We report these cases to highlight the importance of early identification and treatment of pre-gangrenous changes in SPG to avoid multiple limb amputation. Previously, early identification and treatment helped with resolving gangrenous changes in SPG and other causes of gangrene (Liao *et al*., 2015; Sharma *et al*., 2012).

Symmetrical peripheral gangrene is a clinical entity that manifests as ischemic changes occurring in two or more extremities without any evidence of major vascular obstruction or vasculitis (Ghosh *et al*., 2010). The ischemic changes usually affect fingers or toes but can also involve lips, ear lobules, nose, and external genitalia.

The etiology of SPG is multifactorial, in general, it has been divided into two main categories which are infective and noninfective factors common Infective etiology of SPG includes bacterial infections such as pneumococcus, staphylococcus, meningococcus, and streptococcus (Prati *et al*., 2018; Sharma *et al*., 2012). Other established causes are falciparum malaria and viral gastroenteritis. Noninfective etiology of SPG refers to conditions that precipitate SPG occurrence such as myocardial infarction, cardiac failure, hypovolemic shock, hypertension, pulmonary embolism, supraventricular tachycardia, Hodgkin's lymphoma, lung adenocarcinoma, adenocarcinoma-associated thrombotic endocarditis, systemic lupus erythematosus, polymyalgia rheumatica, antiphospholipid syndrome, congenital and acquired protein C and S deficiencies, sickle cell disease, cryoglobulinemia, and idiopathic (Abdali *et al*., 2014). SPG can also be caused by drugs such as dopamine, noradrenaline, adrenaline, warfarin, and propylthiouracil (Sharma *et al*., 2012).

The affected limb may appear pale or bluish, swollen, and painful. Bullae (often hemorrhagic) may develop over the distal part of the limb, indicating tissue necrosis. The dermal lesions are sharply demarcated and symmetric, with initial grayish-blue or purple discoloration that will quickly turn gangrenous. The distal pulses are still palpable even though discolorations of distal fingers or toes have occurred. Peripheral Doppler ultrasonography shows that large peripheral arteries are not involved in thrombosis.

Most authors reported that SPG is a result and manifestation of DIC based on the finding that in DIC, there is a reduction of antithrombin (AT) level and an increase in the expression of plasminogen activator inhibitor-1 which is mediated by endotoxin and tumor-necrosis-factor-α (Albano *et al*., 2018; Ghosh *et al*., 2010; Prati *et al*., 2018; Sharma *et al*., 2012). The exaggerated coagulation together with impaired anticoagulant

and fibrinolysis system leads to continuous thrombus formation, especially in small-sized and medium size vessels This will eventually lead to multiorgan dysfunction and SPG. Clinically, there are two types of DIC, one which develops slowly and causes thrombotic and/or embolic manifestations and one that develops rapidly and causes bleeding SPG is thought to be the result of the second type of DIC (Albano *et al*., 2018; Ghosh *et al*., 2010). SPG has also been theorized to occur due to protein C deficiency and reduced pro-coagulant factor VII (Prati *et al*., 2018). Severe sepsis causes increased protein C consumption, protein S inactivation, downregulation of cytokine-mediating signaling, leading to increased proteolytic enzymes release, which in turn favour microvascular thrombosis and increased leukocyte adhesion. A biopsy is the most reliable form of diagnosis for the pathology of SPG. Most SPG specimens show microthrombi in the capillary lumen of the superficial and deep vascular plexus, accompanied by the deposition of fibrin and subtle extravasation of red blood cells.

Postpartum gangrene during pregnancy has been reported, sparsely. However, in most of these cases, it is thought that the existing peripheral vascular disorder may be caused by the use of ergot alkaloids usually used in relieving pain during labour (Sharma *et al*., 2012). Other studies have also found a relationship between SPG following sepsis (Ruffin *et al*., 2018; Shenoy *et al*., 2013). In addition, it has also been reported that high doses of inotropic agents such as dopamine and noradrenaline may lead to vasoconstriction with ischemia, and ultimately lead to gangrene. However, the extent of the effect of these drugs is not known (Albano *et al*., 2018).

SPG is a rare complication, with a high mortality and about half of the patients will require amputation of multiple limbs. The ischemic changes usually begin distally and progress proximally to involve the entire limb. It can usually be differentiated from other causes of acral gangrene such as thromboangiitis obliterans, atherosclerosis, thromboembolic gangrene, secondary Raynaud's phenomenon, diabetes, neuropathy, chemical or toxic agents, calciphylaxis, and vasculitides by a thorough history of the natural causes (Jung *et al*., 2018; Ruffin *et al*., 2018). The absence of vasculitides features, and the sparing of major arteries, of which pulses can still be palpable, should be able to rule out SPG from other conditions (Jung *et al*., 2018; Ruffin *et al*., 2018).

The complexity of the conditions that can affect a person with SPG makes it important that the multiple medical specialists working together are able to provide effective and efficient management. Multi-disciplinary teams are also beneficial in the treatment of this condition. Besides being able to provide effective and efficient management, multi-disciplinary teams can also improve the communication between patients and their healthcare providers in the management of SPG (von Kodolitsch *et al*., 2016). Specialists involved in the management of these case series include ICU experts, cardiologists, nurses, surgeons, physiotherapists, orthotics, and dieticians.

No treatment has been universally effective in reversing the condition (Macheka *et al*., 2020). Intravenous prostaglandins like (epoprostenol), nitroprusside, topical nitroglycerine, papaverine, reserpine, streptokinase, dextran, hyperbaric oxygen, and sympathetic blockade have all been tried with variable and unequivocal degrees of success (Macheka *et al*., 2020). Treatment is usually individualized according to the

underlying etiology and the patient's general condition. However early recognition of the condition and immediate reversal of the underlying cause (if possible) may prevent its further progression. Patients are usually treated with appropriate antibiotics for sepsis. If there is evidence of DIC, heparinization may be effective. Other aggravating factors like cold, renal failure, diabetes mellitus, and immunosuppression are identified early and managed accordingly.

The affected limb should be protected from trauma, cold, and secondary infection. Amputation of the gangrenous area is usually required. However, the Patient should be continuously monitored for gangrene to become demarcated, and only then should amputation be attempted. The initial nonsurgical approach helps in avoiding the loss of viable tissue and gives time for the patient's condition to stabilize.

Conclusion

Symmetrical peripheral gangrene (SPG) is a rare, debilitating condition that deserves more widespread concern among medical practitioners. About 18%–40% mortality rate has been reported, and survivors have a high frequency of multiple limb amputations. We report these cases to highlight the importance of early identification and treatment of pre-gangrenous changes in limbs to avoid amputation.

Conflict of interest: The authors declare no conflict of interest in the study.

Ethics: The three patients gave verbal consent for the pictures of their limbs to be photographed and published.

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