Clinical Case Report

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Amputation of multiple limbs caused by use of inotropics

Case report, a report of 4 cases

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Abstract

Rationale: We present 4 cases of symmetrical peripheral gangrene (SPG) associated with use of inotropic agent to elevate blood pressure. SPG is a relatively rare phenomenon characterized by symmetrical distal ischemic damage that leads to gangrene of 2 or more sites in the absence of large blood vessel obstruction, where vasoconstriction rather than thrombosis is implicated as the underlying pathophysiology. We present 4 SPG cases of the multiple limbs amputation, associated with inevitable use of inotropic agents.

Patient concerns: Inotropic agents including dopamine and norepinephrine are used frequently in the treatment of hypotension, and its effectiveness in treating shock is firmly established. However, it can be caused peripheral gangrene by prolonged administration of high dose inotropics, inducing the constant contraction of the peripheral blood vessels.

Diagnosis: These 4 patients had different clinical histories and background factors, but each experienced sepsis. The level of amputation is determined by the line of demarcation in concert with considerations of the biomechanics of stump stability, weight bearing, and ambulation.

Interventions: After recovering of general conditions and completion of demarcation, these 4 patients underwent the amputation of multiple limbs.(bilateral amputations of upper extremities or bilateral amputations of lower extremities).

Outcomes: In each patient, there was no additional amputation caused by extension of SPG, and the rehabilitation with appropriate orthosis was performed. Treatment of underlying disease were continued too.

Lessons: It is important to alert the possibility of amputations, according to the use of inevitable inotropics. We recommended the careful use of the inotropic agents to the physicians in treating septic shock.

Abbreviations: DIC = disseminated intravascular coagulation, ICU = intensive care unit, SPG = symmetrical peripheral gangrene.

Keywords: amputation, dry gangrene, inotropics, symmetrical peripheral gangrene (SPG)

1. Introduction

Dry gangrene is common as a result of arterial occlusion. Typically affected parts of the body include toes, fingers, hands, feet, penis, and ear lobes. The common causes of dry gangrene are large vessel diseases such as diabetes mellitus, atherosclerosis, and long-term smoking.[1] Less frequently, microvessel angiopathy associated with autoimmune vasculitis and connective tissue diseases, such a scleroderma, infections, trauma, severe burns, and frostbite, cause gangrene.[2]

Symmetrical peripheral gangrene (SPG), also termed purpura fulminant, is uncommon but not rare in critically ill patients. SPG is a clinical syndrome characterized by bilateral distal ischemic damage leading to gangrene in the absence of major vascular occlusive disease.[3,4] Peripheral pulses are palpable as a result of sparing of larger vessels. The mechanism of vascular occlusion is disseminated intravascular coagulation (DIC). Various infective and noninfective etiological factors have been demonstrated with SPG.[5] It has been described in conditions associated with sepsis, low-flow states, vasospastic conditions, myeloproliferative disorders, and hyperviscosity syndromes.[6,7] SPG related to inappropriate use of vasoactive drugs has been also described.[8–11]

Dopamine and norepinephrine have positive inotropic effects, and so are frequently used in the management of severe ill patients with cardiogenic or septic shock. SPG can occur with prolonged administration, especially at high infusion rates. While rare, SPG may lead to a catastrophic complications with high mortality rate and high frequency of multiple limb amputations

Editor: N/A.

Funding/support: This work was supported by the Soonchunhyang University Research Fund.

This article does not contain any studies with human participants or animals performed by any of the authors.

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article. All authors of this article declare that we have no conflict of interest.

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Medicine (2018) 97:5(e9800)

Received: 29 November 2017 / Received in final form: 6 January 2018 / Accepted: 16 January 2018

http://dx.doi.org/10.1097/MD.0000000000009800

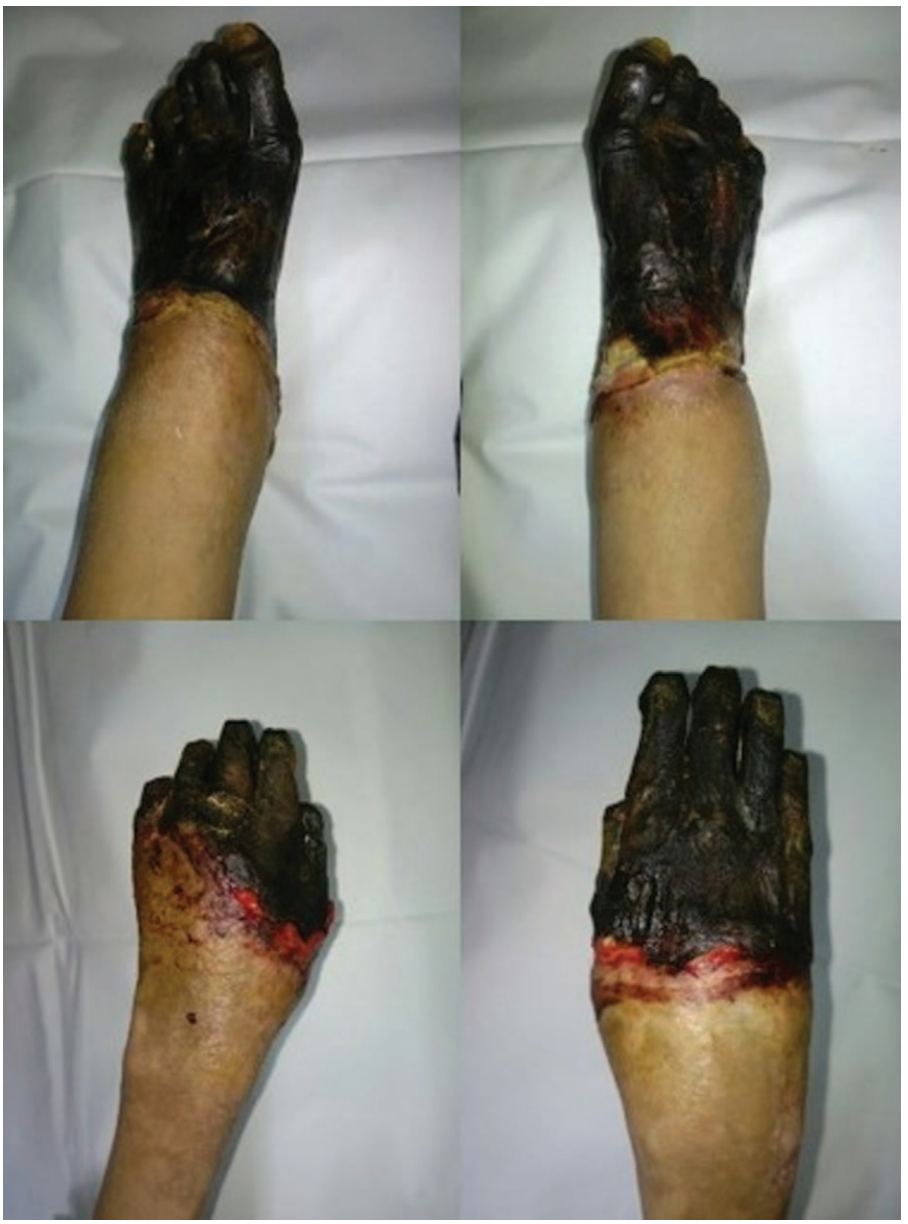

Figure 1. Ischemic changes in 4 limbs after use of the inotropic agent.

in up to 70% of surviving patients.[6] We present 4 cases of SPG associated with use of vasoactive drugs.

2. Case 1

A 46-year-old woman came to our hospital because of high fever. In the emergency room, she was diagnosed with urinary tract infection and was admitted to our nephrology department. On the admission day, septic shock, hypotension (80/40), and tachycardia of 120 beats per min developed. Our nephrologist decided to use inotropic therapy comprising norepinephrine 32 mg every 24 hours in the intensive care unit (ICU). On day 8 following admission, multiple bullae formation was found. A dermatology consultation was done initially for clinical evaluation. On day 11 following admission, necrotic gangrene advanced in the hands and feet (Fig. 1) necessitating consultation with the orthopedic department. In ICU care, vital signs were unstable and her general condition made her unfit for surgery. After 3 months treatment in the nephrology department, her general condition was recovered, but gangrene had advanced to the wrists and ankles. Amputation surgery was done 4 weeks later to remove the septic sources. After demarcation, disarticulation of both wrists and 2 below knee amputations were done (Figs. 2 and 3). She was recovered 8 weeks of surgery. She was observed in our out-patient department and participated in a rehabilitation program using orthosis.

3. Case 2

A 28-year-old man came to our hospital because of abdominal pain. He was diagnosed with colitis and known end stage renal disease, and was admitted to our gastroenterology department. On the day of admission, he had fever (38.8°C) and hypotension (80/60 mm Hg); the hospital gastroenterologist decided to transfer the patient to

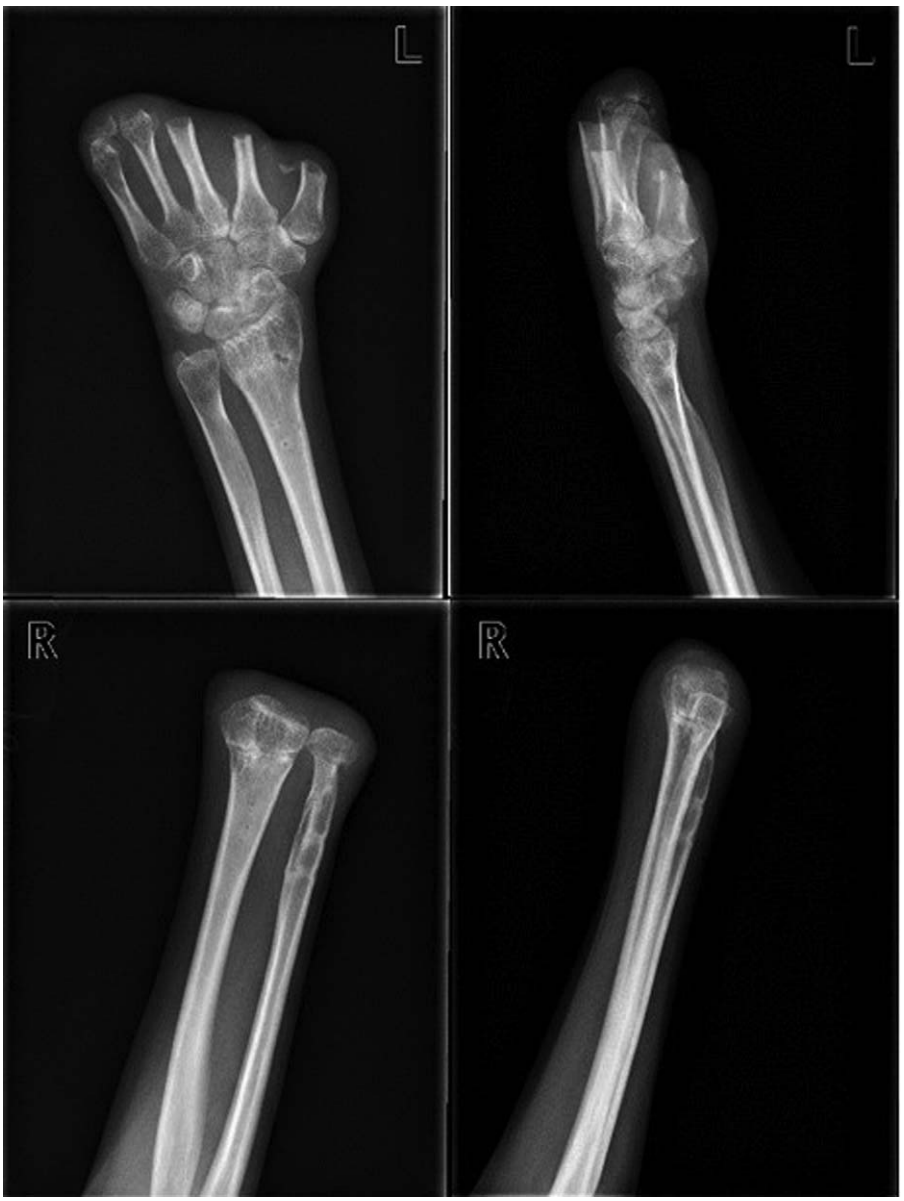

Figure 2. Postoperative radiographs of both wrists.

ICU because of septic condition and to use inotropic therapy consisting of norephinephrine (32 mg every 24 h). On post-admission day 3, necrotic gangrene was found on the distal end of the extremities. On day 12 following admission, the patient had recovered from the septic condition, but the necrotic gangrene had advanced in both feet (Fig. 4). The orthopedic department was consulted. After 2 months treatment in the gastroenterology and nephrology department, both legs were operated on using below the knee amputation (Fig. 5). He was observed in our outpatient department and underwent a rehabilitation program using orthosis.

4. Case 3

A 72-year-old woman came to our hospital because of dyspnea and tachycardia. She was diagnosed with sepsis and admitted to our pulmonology department. On the day of admission, she was moved to the ICU and inotropic therapy involving norephinephrine (32 mg every 24 hours) was begun to maintain her blood pressure. On day 3 following admission, necrotic gangrene was found on the distal end of the extremities (Fig. 6) and the orthopedic department was consulted for management of the infection. Seven days after admission, wound curettage and anti-bead insertion surgery was done for management of the infection. However, the necrotic gangrene advanced. After a 3-week treatment in the pulmonology department, below the knee and ray amputation surgeries were done (Fig. 7). She was carefully treated in the pulmonology department, but her general condition worsened because of pneumonia. Two months after admission, she expired due to acute respiratory distress syndrome.

5. Case 4

A 76-year-old woman came to our hospital because of fever and metabolic acidosis. She was diagnosed with sepsis and admitted to the nephrology department. Before transfer to our hospital, she was treated for traumatic intracerebral hemorrhage and

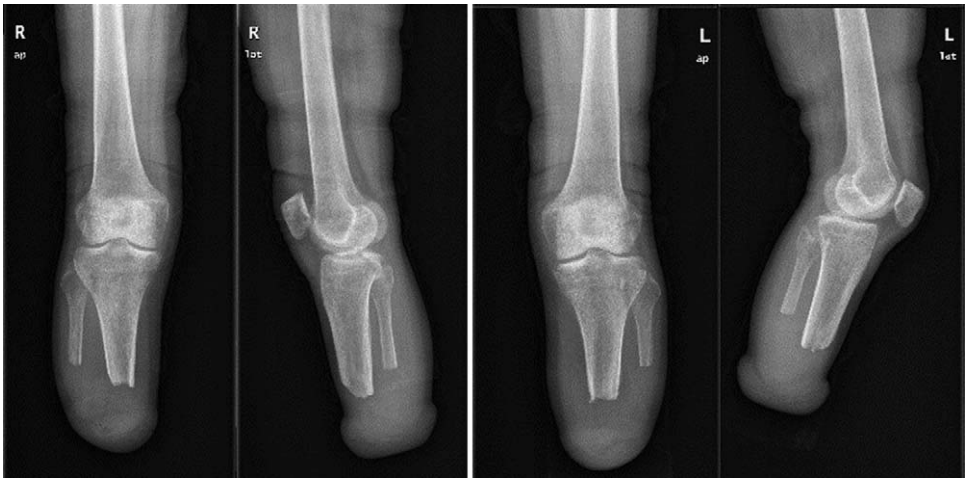

Figure 3. Postoperative radiographs of both knees.

traumatic subarachnoid hemorrhage, and was bedridden. On the day of admission, she was moved to the ICU and received continuous renal replacement therapy because of anuria, and inotropic therapy with norephinephrine (80 mg every 24 hours) was initiated to maintain her blood pressure. On day 3 following admission, necrotic gangrene was found on the distal end of the extremities and the orthopedic department was consulted for management of the infection (Fig. 8). Surgery was recommended but was opposed by a family member. Instead, the wounds were dressed. After 3 months of treatment in the nephrology department, amputation surgery was done. This involved disarticulation of both wrists and below the knee amputation (Fig. 9). She was observed in the physical medicine and rehabilitation department and participated in a rehabilitation program using orthosis.

6. Discussion

SPG is a relatively rare phenomenon characterized by symmetrical distal ischemic damage that leads to gangrene of 2 or more sites in the absence of large blood vessel obstruction, where vasoconstriction rather than thrombosis is implicated as the underlying pathophysiology.[4,12]

Inotropic drugs including dopamine and norepinephrine are frequently used in the treatment of hypotension, and its effectiveness in treating shock is firmly established. However, it can cause peripheral gangrene with prolonged administration of high doses and was first reported as a complication about 25 years ago.[5]

Dopamine and norepinephrine are also frequently used in septic shock because of their positive inotropic effects. When

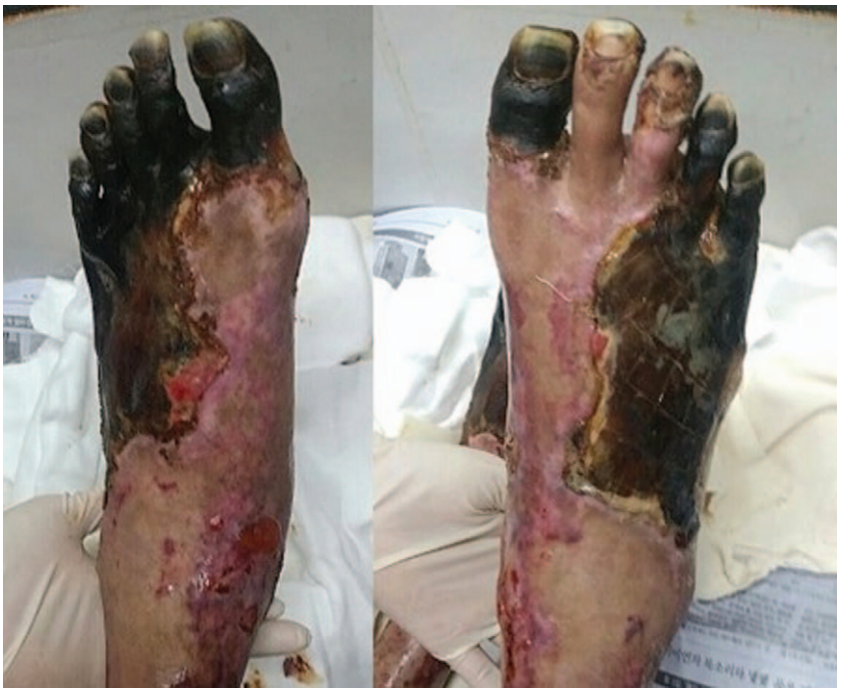

Figure 4. Ischemic changes in both fee after use of the inotropic agent.

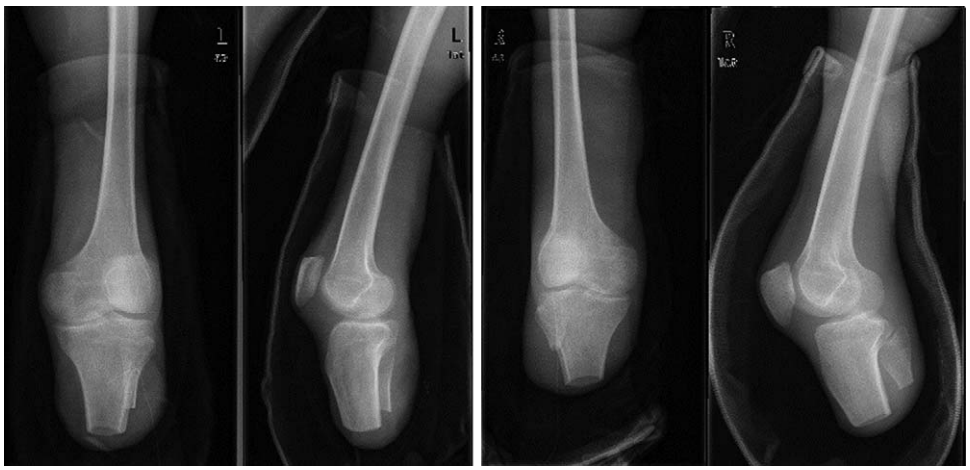

Figure 5. Postoperative radiographs of both knees.

dopamine is administered in low doses of 2 to 5 μg/kg/min, it causes vasodilatation of the coronary, renal, and mesenteric vessels. In moderate doses of 5 to 20 μg/kg/min, it brings about the desired outcome of enhanced cardiac contractility caused by a direct action on beta-adrenergic receptors and by the release of phenylpropanolamine from tissue storage sites. However, in higher doses of up to 20 to 50 μg/kg/min, vasoconstriction may occur due to alpha-receptor stimulation. The use of the alpha-receptor stimulator noradrenaline is frequent in patients with septic shock, but their vasospastic effects may be more intense in the digital vascular beds. As a result, peripheral gangrene is not unexpected following high doses of dopamine or noradrenaline.[3]

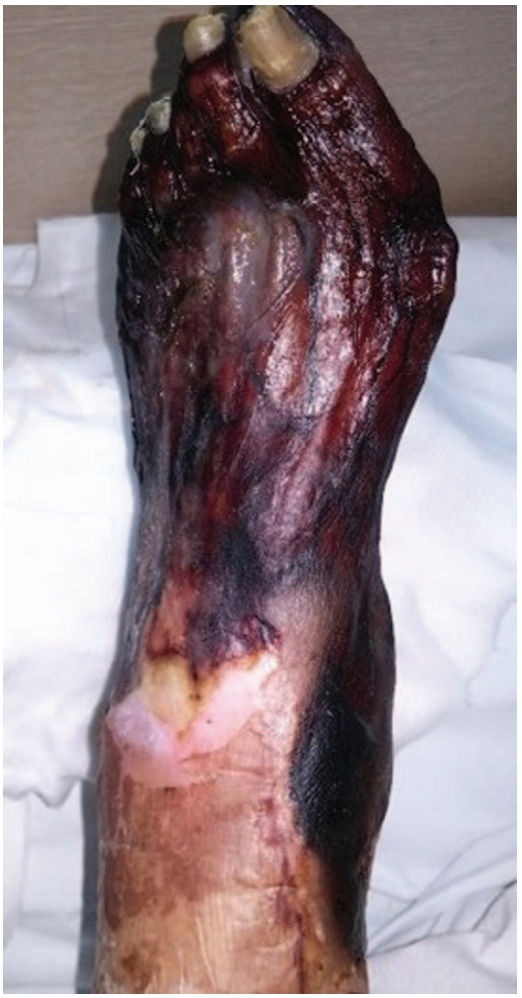

Figure 6. Ischemic changes in foot after use of the inotropic agent.

The 4 cases presented here had different clinical histories and background factors, but each experienced sepsis; about 80% of SPG is related to sepsis.[13] Inotropics were applied to maintain blood pressure. After a few days of inotropic therapy, necrotic gangrene was evident at the distal end of the extremities where the blood supply was poor.

In internal medicine, epoprostenol sodium, tissue plasminogen activator, aspirin, vasodilators, and sympathetic blockade have been suggested as treatment modalities for SPG.[14] These options were unsuccessful for our patients. After medical treatment, we decided on surgical intervention when gangrene had demarcated, as suppuration is rarely complicated and the outcome of surgery is usually good.[14]

The 4 cases of SPG within 6 months indicate to us that SPG may not be as rare as assumed. The possibility of SPG should be considered during inotropic therapy; proper dosage and duration

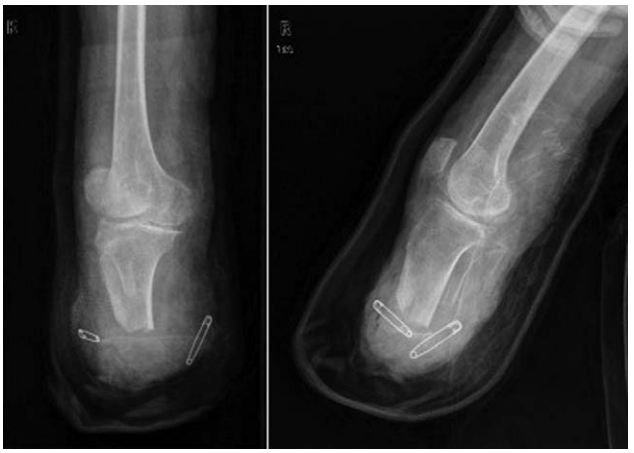

Figure 7. Postoperative radiographs of both knees.

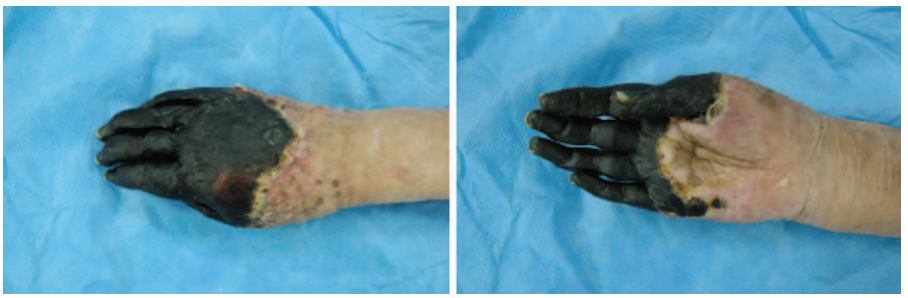

Figure 8. Ischemic changes in hand after use of the inotropic agent.

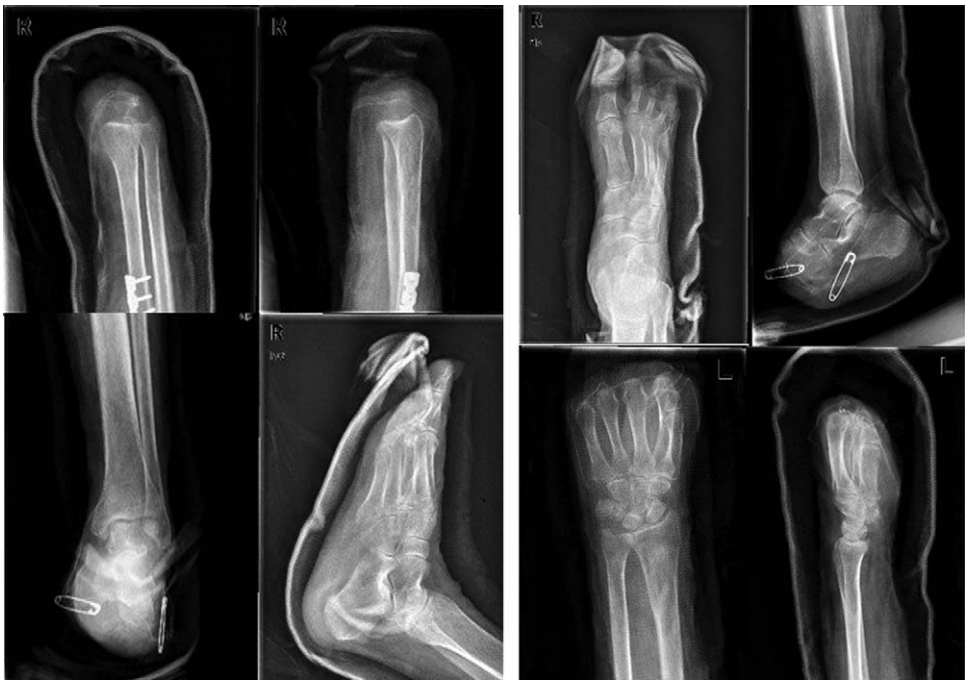

Figure 9. Postoperative radiographs of 4 limbs.

of inotropics in patients with sepsis are important to treat shock effectively and prevent SPG.

Suggested first-line measures when SPG is identified early include discontinuation of vasopressors, reversal of DIC by cautious anticoagulation, and aggressive treatment of shock and sepsis. Adjuvant therapy with tissue plasminogen activator, plasmapheresis, sympathetic blockade, and aspirin has been recognized to contribute to a favorable outcome. Amputation remains the final treatment option available to the patient for established gangrene. The level of amputation is determined by the line of demarcation in concert with considerations of the biomechanics of stump stability, weight bearing, and ambulation.[10]

7. Conclusion

We presented 4 cases of amputations due to use of inotropics for sepsis. Microvessel spasm is an extremely rare but critical complication in patients. When a patient is treated by inotropics (dopamine or norepinephrine), close observation of the distal end of the extremities, which have the poorest vascular supply, and control of the drug dose are prudent step to prevent tissue necrosis. It is important to alert the possibility of amputations according to the use of inevitable inotropic agents, and we recommended the careful use of the inotropic agents.

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