Symmetrical peripheral gangrene (SPG) is a rare condition in which symmetrical ischemia and dry gangrene of the acral areas occur. Body parts commonly affected include the toes, hands, scrotum, and earlobes, increasing the risk of limb amputation and affecting the quality of life [1].

The aetiology is multifactorial but has been linked to vasopressor’s use during the treatment of septic shock [1, 2]. There is consensus in the literature that early recognition of PSG, along with underlying conditions, can change significantly the treatment and the final evolution [2].

The vascular injury mechanism is disseminated intravascular coagulation (DIC) [3, 4]. Several infectious and noninfectious etiologic factors have been associated with SPG [2, 5–7]. It has been described in conditions associated with sepsis, low blood flow states, vasospastic conditions, hyperviscosity disorders, and myeloproliferative disorders [8]. The appearance of SPG related to the inappropriate use of vasopressor drugs also has been described [9].

Dopamine and norepinephrine are the first-choice drugs in septic shock cases due to their positive inotropic effects. SPG can occur with prolonged administration, especially at high infusion rates. SPG can cause catastrophic complications with high mortality rates and high frequencies of multiple limb amputations in up to 70% of surviving patients [8, 9]. We present the case of a patient with SPG associated with vasopressor use who required amputation of all fingers and toes.

2. Case Series

2.1. Case 1. A 46-year-old woman with history of uterine fibroids after elective hysterectomy presented with surgical wound infection evolving to septic shock that required admission to the intensive care unit (ICU).

During admission, the patient developed multiorgan failure, abdominal compartment syndrome, and DIC. Positive cultures for Pseudomonas aeruginosa, Enterococcus faecalis, and Candida tropicalis were obtained, for which intravenous antibiotics and antifungals were administered. Due to the hemodynamic instability, it was necessary to administer vasopressors to maintain systolic blood pressure and mean arterial pressure goals.

With increasing doses of 1.5 μg/kg/min of norepinephrine, the patient’s lactate was 6.6 mmol/L on the same day.
On the third day of admission to the ICU, the patient underwent surgery again due to suspected abdominal compartment syndrome; twenty-four hours later, the norepinephrine dose was decreased, and a lower lactate level of 4 mmol/L was observed. On the fifth day of ICU admission, norepinephrine was withdrawn, and that same day, the presence of greyish lesions was observed on both hands, finger pads that evolved into haemorrhagic blisters on the left hand and patchy purple lesions on both feet and toes and stayed cyanosis in the heels. Radial, ulnar, pedal, and posterior tibial pulses of all extremities were normal on Doppler examination. The lesions evolved into necrotic areas at the metacarpal and phalangeal levels in both hands and distal phalangeal levels in both feet (Figure 1).

The patient received ventilatory support treatment, dialysis, and antithrombotic treatment with low molecular weight heparin, remaining in the ICU for 54 days. During necrotic lesions’ delimiting time, wound care was performed with dry dressings and limbs covered with padded bandages. In gangrenous areas, surgical amputations were performed. In the right hand, the four triphalangeal finger stumps were regularized at F1 transphalangeal level, and bone coverage with deep plane and closure by second intention was performed. In the 3rd finger, a radial pedicled flap advancement was performed, and in the thumb, regularization of the second phalanx and coverage with a Moberg-type flap was performed, leaving the matrix and part of the nail bed. Transphalangeal amputation of the 2nd and 3rd fingers was performed on the left hand associated with deep plane coverage, fingers 4th and 5th were amputated at the level of the middle phalanx, and radial flap advancement was performed on the thumb to close the cutaneous defect, maintaining part of the matrix and the nail bed. Despite the aggressiveness of the amputation surgery, the patient retains a certain ability to grip both hands and an acceptable prehension of the thumb and index on the left hand. Result of the surgeries performed can be seen in Figure 2.

Transmetatarsal amputation of the second to the fifth finger and proximal transphalangeal amputation of the first finger were performed on the left foot. On the right foot, she required complete transmetatarsal amputation plus posterior grafting.

One year later, she continued her recovery as an outpatient, presenting with right thumb nail matrix discomfort, requiring matrix surgery and sterilization, with no reports of other complications.

2.2. Case 2. A 53-year-old man was in ICU after septic shock secondary to appendicitis that progressed rapidly to peritonitis and multiple organ failure with DIC.

During admission, norepinephrine administration was necessary to maintain hemodynamic stability. The patient underwent an urgent laparotomy and negative pressure therapy. Positive cultures for *E. coli* were obtained, which received targeted antibiotic treatment. Initial lactate was 6.8 mmol/L on the first day of admission. On the fourth day of admission, he presented ischemic skin lesions on the fingers of both hands and feet toes. On the left hand, nonsuppurative, dry, and well-defined necrosis stabilized at the distal level of the fingers 1st, 2nd, and 3rd with proximal interphalangeal joint involvement, 4th and 5th were only affected in the pad, and also, a superficial necrotic eschar at the left dorsal hand level and wrist on its radial face.
3. Discussion

Symmetrical peripheral gangrene or purpura fulminans [10, 11] is a rare syndrome characterized by an acute onset of ischemic damage in peripheral acral areas without obstruction or vasculitis of the supplying vessels [1, 6].

There are no large studies that provide scientific evidence about this rare condition [8], being in this article 3 cases reported.

Altered microcirculation and vasospastic conditions with poor peripheral perfusion are the main clinical scenarios associated with SPG [1, 6, 9].

Disseminated intravascular coagulation (DIC) could be the last cause of microvascular injury. This association was first described in 1970 by Strossel and Levy [6]. The possibility that SPG may be one special cutaneous variant of DIC has been described [2].

In patients with DIC and hypovolemia, the use of vasoconstrictor drugs like epinephrine, dopamine, and norepinephrine can cause SPG by decreasing tissue perfusion and exacerbating ischemia, leading to eventual tissue necrosis and gangrene [2, 12].

Some studies describe that the dose instead of the duration could be more important in the development of SPG and also have additive effects [2, 9, 12].

In this report, all 3 cases were caused by septic conditions [13] which lead to DIC and precise norepinephrine at curative levels developing SPG in a few days, 4 to 12.

The first suggestive sign is the presence of cold, erythematous extremities followed by dark discoloration of the skin. Ischemic changes progressing to cyanosis and hemorrhagic bullae may develop in symmetric acral distribution over the fingers and toes. In severe cases, involvement of the nose, earlobe, or scrotum can be observed [10]. Of the reported cases, two had both hands and feet involved and the 3rd only hands, no other body parts were involved.

In the first 12-24 hours, dry gangrene appears and progresses proximally with a demarcation line that develops in approximately two or three weeks [6, 8].

Laboratory tests like complete blood count with blood smear help to identify myeloproliferative or infectious alterations. D-dimer can indicate the presence of DIC. Blood biochemistry helps detect chronic pathologies. In patients with septic shock, high levels of serum lactate can be observed just before the appearance of SPG [2, 6]. In all cases, reported serum lactate was elevated from 6.6 to 11.2 mmol/L.

The initial management is hemodynamic stabilization. Early recognition of cyanosis, reversal of DIC, and
correction of hypovolemia are essential to prevent the progression to gangrene. Effective treatment of underlying pathologies like antibiotic treatment for sepsis will determine the outcome in individual cases. The use of heparin in the treatment of DIC remains controversial, although it may be useful in patients with clinically evident thromboembolism and extensive fibrin deposition. Antithrombin III alone or in association with heparin appears to be a promising agent [6].

The only definitive treatment established for gangrene of acral areas is amputation. It should be considered after the development of a clear line of demarcation, until this moment emphasis should be placed on local wound care [2]. Also, self-amputation of the gangrenous digits on very distal lesions could be seen [2, 6].

The level of amputation must be decided during surgery. Separate bone and soft tissue reconstruction leads to good results in terms of wound healing and ambulatory status [2]. In most cases of fingers, a V-Y advancement flap can be performed in either volar or a double lateral flap trying to maintain the maximum finger length, especially in thumb and index fingers used for pinch grip. Treatment in our case was amputation using different flap types like Moberg, Atasoy, or fish mouth were performed with acceptable functional results.

For the lower extremities, microsurgical techniques and the use of free flaps have been described with good functional results [14, 15]. In case one, foot amputations were performed using a skin graft in the right foot with no other complications.

4. Conclusions

SPG is a rare condition that mainly affects critical patients who require the use of inotropes such as norepinephrine. In these patients, strict surveillance of the acral areas is necessary during treatment to detect ischemic signs in time and correct the already existing DIC since the development of SPG can lead to limb amputation with serious impairment of quality of life. Treatment, once dry gangrene is established, consists of amputation of necrotic areas when they are demarcated trying to preserve functionality if possible. Clinical suspicion and early diagnosis is key improve its management.

Data Availability

The data that support the findings of this study are available from the corresponding author, upon reasonable request. Sensible information that could lead to personal patient identification will not be provided.

Conflicts of Interest

The authors declare that there is no conflict of interest.

Acknowledgments

The APC charges were covered by the Institut de Recerca Biomèdica de Lleida (IRB Lleida), Av. Alcalde Rovira Roure, 80, 25198, Lleida, Spain.

References


