Symmetrical Peripheral Gangrene and Tuberculosis: A Rare Kinship

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Abstract

Symmetrical peripheral gangrene (SPG) is a rare clinical syndrome characterized by ischemic necrosis of 2 or more limbs, without involvement of large vessels. It is often associated with disseminated intravascular coagulation and septic shock. Usually caused by Gram-positive and Gram-negative organisms, tuberculosis as a cause is extremely rare. We present the case of a 46-year-old man, who initially presented with signs and symptoms suggestive of tuberculosis but later developed SPG along with septic shock after his initial visit. The case highlights the progression of this dreaded complication and touches upon recent developments in its etiology as well as pathogenesis.

Keywords: Disseminated intravascular coagulation, limb gangrene, miliary tuberculosis, purpura fulminans, septic shock, symmetrical peripheral gangrene, tuberculosis

INTRODUCTION

Symmetrical peripheral gangrene is a vascular emergency associated with disseminated intravascular coagulation and sepsis. Although well described in nature, its dramatic presentation, high mortality rate and relative rarity makes it an enigmatic disease process. Recent developments have furthered our understanding of the pathogenesis of the syndrome. Previous descriptions of the syndrome and Tuberculosis are infrequent and do not describe the disease process with respect to newer pathophysiological concepts. We present a case of symmetrical peripheral gangrene and Tuberculosis, followed by a brief review of recent literature on the topic.

CASE REPORT

A 46-year-old man presented to the department of emergency medicine with the chief complaints of progressive discoloration of his limbs for the past 3 days accompanied by high-grade fever. The patient was a known smoker with a 35-year pack-year history. Twelve years back, he had been treated for pulmonary tuberculosis but discontinued treatment after 3 months. The patient was initially taken to a primary health center, where blood investigations revealed anemia and thrombocytopenia. Owing to the worsening and progression of the limb discoloration, the patient was referred to our hospital 2 days after the onset of these symptoms. At arrival in the emergency, the patient had bluish-black discoloration of both feet and hands, beginning at the tip of the toes and fingers with proximal extension. On examination, the patient was pale, drowsy, and febrile (101 F). The patient had cold peripheries, with a dry tongue and sunken eyes. Pulse rate was 126/min and blood pressure was 80/60 mm of Hg in the right arm in supine position. The radial, brachial, femoral, and dorsalis pedis pulses were palpable, but the patient had developed isolated gangrene of digits of the hand and the feet [Figure 1].

On laboratory investigations, hemoglobin was 11.6 g/dl and the white cell count was 28,000 with neutrophils 82% and lymphocytes 16%. Platelet count was 42,000/mm³. The chest X-ray showed miliary mottling. International normalized ratio (INR) was 2.2 and accelerated partial thromboplastin time (APTT) was 50 s. D-dimer levels were 1450 µg/ml. Renal function tests, blood glucose levels, and bilirubin levels were normal. Liver enzymes were grossly deranged (>1000 IU/L),

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and lactate was 5.2 mmol/L. Abdominal sonography and Doppler study of the limb vessels were within normal limits. Peripheral smear for malaria and tests for HIV, hepatitis B, hepatitis C, antinuclear antibodies, and antiphospholipid antibodies were negative. Blood cultures were sterile. A biopsy from a discolored patch over the left leg revealed multiple small thrombi within small vessels with ischemic necrosis. Sputum was positive for acid-fast bacilli (AFB). A line probe assay (LPA) was positive for Mycobacterium at 48 h, and the organism was sensitive to rifampicin and isoniazid. The patient was treated with intravenous (IV) fluids, antitubercular treatment, and steroids. By day 5 of admission, the patient stabilized. By this time, all the digits of the hand except for both thumbs were lost as were the 4th and 5th digits of the left foot. Histopathology of the severed digits revealed coagulative necrosis with diffuse microthrombi at the point of severance. The patient was eventually discharged on day 12 and put on thrice weekly short-course treatment for tuberculosis with isoniazid, rifampicin, ethambutol, and pyrazinamide.

**Discussion**

Our patient was diagnosed with symmetrical peripheral gangrene (SPG) based on clinical features, laboratory investigations, histopathological features, and exclusion of other entities presenting in similar fashion. SPG was first described by Hutchison in 1891. It is defined as ischemic necrosis simultaneously affecting the distal part of two or more extremities, without evidence of large vessel obstruction. A term often misused synonym, “purpura fulminans,” should only be used when there is extensive, multicentric, nonacral skin necrosis with or without limb necrosis.

The exact pathogenesis of SPG is still unknown. Disseminated intravascular coagulation (DIC) is found in 85%–100% of all cases. SPG is often accompanied by shock but may occur in a patient with normal blood pressure even in the absence of DIC. Proposed mechanisms include the Shwartzman reaction, bacterial endotoxin release, arteriolar platelet plugging, vascular wall infection, and a preceding event of acute ischemic hepatitis.

Ischemic limb necrosis usually begins 2–5 days after initial transaminitis. This period reflects the time that is required for the development of critically low levels of protein C as its synthesis is impaired in the “shock liver.” A more rapid fall in the concentration of protein C compared to other Vitamin K-dependent procoagulant factors leads to a temporary hypercoagulable state.

Etiology for SPG is multifactorial [Table 1]. It can be arbitrarily divided into primary and secondary causes. Primary SPG occurs without any known trigger or occurs a few weeks after a varicella infection. Whereas, Gram-positive sepsis is the most common cause for secondary SPG. Aggravating factors include asplenia, immunosuppression, cold injury to extremities, diabetes, renal failure, increased sympathetic tone, use of vasopressors, and arterial cannulation. Clinically, the patient may have fever and pain in the extremities. Coagulopathy, shock, purpuric patches, and necrotic areas over extremities are common and may rapidly progress to acrocyanosis and dry gangrene. Involvement is symmetric, with the feet being involved more than the hands. Large vessels are characteristically spared. Apart from the extremities, other areas of the body may be involved, including the tip of the nose, the ears, genitalia, and the scalp. Although necrosis is usually limited to the dermal and subdermal areas, in some patients, the bone may be involved as well. Investigations are required to confirm diagnosis and to search for the precipitating factor. Blood investigations may reveal evidence of hemocoagulation, leukocytosis or leukopenia (the latter being a poor prognostic factor), thrombocytopenia, elevated liver enzymes, raised INR and APTT, increased D-dimer, and lactate.

A biopsy helps to support DIC if changes are seen. It also helps to rule out vasculitis and other causes of limb gangrene. Typical changes associated with DIC are diffuse intraluminal microthrombi in the capillaries of the superficial and deep vascular plexus along with intraluminal deposition of fibrin.

Differential diagnosis of SPG includes atherosclerosis, Buerger’s disease, thromboembolic gangrene, Raynaud’s phenomenon, frostbite, ergotism, calciphylaxis, postoperative thrombotic thrombocytopenic purpura, myeloproliferative disorders, and vasculitis, among others.

Treatment is based on anecdotal evidence. No guidelines exist for the management of SPG. In general, reduction or stoppage of vasopressors, appropriate antibiotics, IV fluids, and correction of any metabolic abnormality are standard measures. DIC should be managed as per presentation. In case of thrombosis, heparin should be used. The use of heparin is known to reduce mortality by 12% in sepsis with DIC. Transfusion in the form of fresh frozen plasma/platelet-rich plasma or factor-specific concentrates may be
used as per the clinical setting and availability. Treatments such as activated protein C, plasmapheresis, trimethaphan, nitroprusside, topical nitroglycerin, and epoprostenol have all been used sporadically in literature. Given the high mortality of SPG (33%-50%), surgery might seem like an attractive option but should be avoided whenever possible. A fasciotomy can worsen the already compromised blood flow and leads to unnecessary delay in anticoagulation. Amputation, if required, should be done once a clear line of demarcation has appeared, else autoamputation often suffices. In some cases, the patient may need skin grafting as well. Preservation of joint mobility and range of motion is best achieved by physiotherapy.\[^{3,4}\]

**Conclusion**

SPG in association with tuberculosis has rarely been reported.\[^{8,10}\] Vasculitis can be associated with tuberculosis, but our case did not fit into any of the vasculitis syndromes. Moreover, apart from a positive sputum for AFB and military mottling on X-ray chest, the LPA was also positive, confirming our diagnosis of miliary tuberculosis.

**Conflicts of interest**

There are no conflicts of interest.

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