

Case Report

Non-clostridial gas gangrene of a diabetic foot with COVID-19 infection

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ABSTRACT

Gas gangrene is a manifestation of soft tissue infection by clostridial group of bacteria. Non-clostridial gas gangrene is uncommon and seen rarely in diabetics. In the era of COVID-19 pandemic where COVID-19 itself induces hyperglycemia non clostridial gas gangrene may arise due to altered immunity. We present a case of non clostridial gas gangrene of lower limb in a middle aged person who was not a known diabetic. A brief case report with review of literature is presented.

Keywords: Gas gangrene, Diabetic foot, COVID-19

INTRODUCTION

Gas gangrene is the term used to describe necrotising skin and soft tissue infection by gas forming organisms. This type of infection is prone to occur in wounds of the extremities. When compared to infection with non-gas forming organisms, gas gangrene prognosticates a worse outcome. It is usually characterized by early onset toxemia and multi-organ dysfunction unless aggressive antibiotic therapy and radical surgical debridement is undertaken.¹ Non-clostridial gas gangrene is reported rarely. Here we present a case of a middle aged male with diabetes with lower limb non clostridial gas gangrene with COVID-19 infection.

CASE REPORT

A 47-year-old male presented to the emergency department with swelling and blackish discoloration of left lower limb since four days and drowsiness since two days. Patient had history of trauma over the left foot fifteen days ago which was managed conservatively. However, swelling and pain progressed and the patient started developing blackening of the foot gradually increasing proximally. There was history of low grade fever responding to antipyretics. Patient had no known co-

morbidities, surgical or drug history. He had no history of smoking, tobacco chewing or alcohol abuse.

Clinical examination revealed the patient to be drowsy but responsive to commands and oriented with a glasgow coma scale score of 14/15. Patient had pulse 110/min and blood pressure of 110/60 mmHg and was tachypneic. He was febrile and pale.

On examination of the left lower limb, there was wet gangrene of the foot extending up to mid-calf (Figure 1). The limb was foul-smelling, tender, with areas of fluctuation, blebs and crepitus extending up to upper calf. The dorsalis pedis artery, the posterior tibial artery were not palpable. The popliteal and femoral artery were palpable and equal on both sides. There was no significant inguinal lymphadenopathy. The right lower limb was unremarkable and pulses were well felt. Other peripheral pulses were well felt. Systemic examination was unremarkable. Blood glucose levels via glucometer were 560 mg/dL and urine ketones via dipstick was positive.

Biochemical and haematological investigations revealed a haemoglobin level of 8.4 g%, raised white cell count of 17,200/mm³, platelet count was normal, serum creatinine of 1.1 mg%, blood urea of 98 mg%, serum ketones were

negative, and international normalized ratio (INR) was 2.14. Serum sodium and potassium were 149 mEq/l and 2.9 mEq/l respectively. Liver function tests were within normal limits. Arterial blood gas analysis (ABG) was suggestive of compensated metabolic acidosis. Nasopharyngeal swab was sent for COVID-19 RT-PCR.



Figure 1: Image showing wet gangrene of the foot.

X-ray of the affected limb was suggestive of extensive subcutaneous gas shadows extending from the foot up to upper calf (Figure 2 and 3). An arterial doppler study of the left lower limb showed monophasic flow in the dorsalis pedis and the posterior tibial arteries, biphasic flow in the anterior tibial arteries and triphasic flow in the popliteal artery and femoral artery.



Figure 2: X-ray of the affected limb.



Figure 3: X-ray of the affected limb.

In view of crepitus and air shadows on X-ray, diagnosis of gas gangrene of the left lower limb was made along with diabetic ketoacidosis. Patient was resuscitated with IV fluids and human insulin via infusion. Serial blood glucose monitoring was done till glucose levels dropped below 250 mg% and urine ketones were negative. Broad spectrum antibiotic therapy was initiated. Fresh frozen plasma (FFP) was transfused at the rate of 10ml per kg body weight. However even after the transfusion, INR was 1.9. Patient and his relatives were counselled regarding the need for urgent below knee amputation of the affected limb as a life saving measure.

As the patient was in septicemia, he was taken up for emergency surgery without waiting for results of COVID-19 RT-PCR test. Patient was resuscitated and due consents were obtained. Patient was taken for surgery under general anaesthesia. Regional anaesthesia could not be given due to raised INR. A guillotine below knee amputation was performed and the tissue was sent for bacterial culture and sensitivity and anaerobic culture in Robert-son's cooked meat medium.

Post-operatively, patient was not extubated in view of septic shock and continued on synchronous intermittent minute ventilation. The bacterial culture was negative for clostridial species, but was positive for *E. coli*. COVID-19 RT-PCR was positive. The patient's white cell count continued on a decreasing trend. However, the patient continued to remain drowsy and disoriented and showed no clinical signs of improvement with increasing respiratory acidosis. On post-operative day three, patient succumbed to respiratory failure.

DISCUSSION

Gas gangrene is regarded as a disease associated with war or other mass casualty situations and is rarely seen in day to day medical practice.¹ Non-clostridial gas gangrene is relatively rare, and diagnosis is frequently delayed and often missed.² Although infection of extremities with gas forming organisms with wet gangrene makes one think about clostridial infections this may not be true in diabetic limbs. The syndrome of non-clostridial gas gangrene occurring in the lower limbs of diabetics was first described by Chiari in 1893 and subsequently con-firmed by Hirschmann and Lindenthal.^{3,4} Bessmann et al demonstrated in their study of 278 admissions of diabetic patients with limb infections in which 17% had non-clostridial gas infections and 3% had clostridial gas gangrene.⁵ This relative frequency of non clostridial gas forming infection in diabetics was further confirmed by Darke et al.¹

Non-clostridial gas gangrene is due to anaerobic fermentation of sugar by various streptococci and gram negative bacilli releasing carbon dioxide as a by-product.⁶

Patients with clostridial gas gangrene show symptoms, on an average, after four days after the initiating event and the

non clostridial type presents after an average of nine days.¹ In the present case the patient suffered blackening of skin and swelling over the affected limb after nine days of trauma. He was not a known diabetic and was diagnosed after admission. Binding of SARS coronavirus to ACE-2 receptors in the islet cells in the pancreas has been shown to cause acute onset diabetes. There are also several precedents for a viral cause of ketosis-prone diabetes, including other coronaviruses that bind to ACE-2 receptors.⁷ Present case might be a manifestation of the same as he was COVID-19 positive.

Gas gangrene is characterized by fever, sudden onset of prominent pain, massive local edema, severe extensive myonecrosis, and the accumulation of gas at the site of infection. As the infection progresses, myonecrosis is accompanied by necrotizing fasciitis. The appearance of the skin around the site of infection usually becomes tense and changes from pale to bronze initially and then to purplish red, and multiple hemorrhagic bullae develop. Shock and organ failure are present in 50% of patients and, among these, 40% die. Non clostridial gas gangrene presents in the same way albeit these patients are more likely to be drowsy at presentation. Mortality associated with non-clostridial gas gangrene is higher than that of its clostridial counterpart. Both subset of patients presents with uremia and hypotension however uremia is more common in the non clostridial variety.¹ In the present case, the patient who was diagnosed with hyperglycemia on admission, presented with drowsiness, hypotension and dehydration. Blood urea levels were elevated (98 mg%) and serum creatinine was 1.1 mg%.

Enterococcus fecalis, *Escherichia coli*, *Staphylococcus aureus*, group G *Streptococcus*, *Klebsiella pneumoniae*, *Proteus vulgaris* and *Citrobacter diversus* are the most common bacteria associated with non-clostridial gas gangrene.² In our patient, *E. coli* was isolated from wound swabs. Successful treatment for gas gangrene involves prompt recognition of the diagnosis and initiation of multi-prolonged therapy including supportive measures, antimicrobial therapy, and timely surgical intervention. In this case the patient underwent a below knee amputation of the affected limb with adequate personal protective equipment without waiting for COVID-19 RT-PCR test results as the patient showed signs of sepsis. There is increased risk of transmission of COVID infection with surgery and also increased risk of post-operative morbidity and mortality. As per guide-lines for performing surgery in the post COVID era, general anesthesia must be avoided to prevent the risk of aerosolisation of the virus.⁸ This patient however failed to achieve stable disease and was taken up for emergency surgery to avoid toxemia. Due to deranged coagulation profile, regional anesthesia could not be given, and the patient was operated under GA. This contributed to respiratory complications in the post-operative period. This goes to show that even though guidelines and precautions for operating a patient in the post COVID era are laid down, they need to be customized for every case. Postoperatively the patient was on

ventilatory support and showed a decrease in white cell count and an improving metabolic panel. Clinically however, he continued to remain drowsy and disoriented with increasing respiratory acidosis. Hypotension ensued and inotropic support was started. In the meantime, COVID-19 RT-PCR test was positive. The decrease in white cell count could be attributed to resolution of sepsis or could be a manifestation of COVID-19 infection. The patient succumbed to respiratory failure on the third post-operative day.

Patients infected with COVID-19 have decreased white cell count and show a pauci-inflammatory thrombogenic vasculopathy associated with complement activation and a procoagulant state. This underlying pathophysiology taking place in the lungs and skin was documented by Magro et al.⁹ Despite eliminating the source of infection, patient continued to deteriorate and succumbed to respiratory failure.

CONCLUSION

Immune system derangements along with hyperglycaemia caused by COVID-19 infection might predispose a person to acquire bacterial infections. These infections might also show increased pathogenicity, and contribute to worse outcomes. The complex pathophysiology of COVID-19 infection along with uncontrolled diabetes and gas gangrene poses a challenge in the clinical management of these patients. These observations support the hypothesis that COVID-19 infection might increase the number and severity of soft tissue infections. However, further studies are needed to confirm this.

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