

Case Report

Polymicrobial infection presenting as non-clostridial gas gangrene in a non-diabetic trauma patient. A case report and review of literature

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Abstract: Background: Clostridium species are known to be the primary causative organism of gas gangrene. Non-clostridial gas gangrene (NCGG) is another rare necrotizing entity often associated with an underlying disease, particularly diabetes mellitus, and has a high mortality rate. Case report: A 16-year-old, immunocompetent male was referred to us after four days, following a roadside accident, with a degloving injury over the thigh and knee along with fractures around the knee. Although clinico-radiologically suspicious of gas gangrene, the initial smear report was negative for any Gram-positive bacilli. On the same day, he underwent aggressive debridement with an external fixator spanning the knee to salvage the limb. On post-operative day one, due to deteriorating general clinical condition and a strong clinical suspicion of gas gangrene, he underwent above-knee amputation (open stump) after discussion with microbiologists and physicians. Results: Polymicrobial non-clostridial infection was seen in culture reports taken serially at different stages of management. The latest follow-up showed a healed amputation stump following split skin grafting. Conclusion: Although rare, polymicrobial infections can present as non-clostridial gas gangrene even in an immunocompetent patient. A high index of clinical suspicion with a multi-disciplinary approach helps in early decision-making to avoid a devastating outcome.

Keywords: Gas gangrene, non-clostridial gas gangrene, necrotizing fasciitis, myonecrosis, amputation, polymicrobial

Introduction

Gas gangrene is an acute, life-threatening infection characterized by sudden onset of pain, fever, massive local edema, severe, extensive myonecrosis, and the accumulation of gas at the site of infection [1]. Clostridium species are known to be the primary causative organism of gas gangrene. Clostridial myonecrosis, also known as true gas gangrene, is a destructive kind of clostridial infection requiring aggressive and early surgical intervention.

Infectious gangrene is a rapidly progressive cellulitis with extensive necrosis of subcutaneous tissues and the overlying skin. Various clinical pictures could be observed depending on the causative organism, anatomic location of the infection, and predisposing conditions. Such clinical entities include the following: (a)

necrotizing fasciitis (type I, or polymicrobial, often including Enterobacteriaceae and anaerobes; type II, or streptococcal gangrene caused by *S. pyogenes*); (b) gas gangrene (clostridial myonecrosis) and anaerobic cellulitis; (c) progressive bacterial synergistic gangrene; (d) synergistic necrotizing cellulitis, perineal phlegmon, and gangrenous balanitis; (e) gangrenous cellulitis in an immunosuppressed patient and (f) very localized areas of skin necrosis complicating conventional cellulitis [2].

Diabetic patients are more prone to peripheral neuropathy and microangiopathy, which can delay tissue healing and encourage opportunist infections. Phagocytosis and intracellular bactericidal activity are affected by the control of glycemia, and there may be some immunological impairment independent of glycemic control. The presence of pre-existing tissue necro-



Figure 1. Clinical presentation of the patient at the time of admission to our level 1 trauma centre.

sis in a hyperglycemic condition would provide an excellent environment for bacterial proliferation [3].

Early diagnosis is the most crucial part of the successful management of gas gangrene. A diagnosis of gas gangrene can be suspected until proven otherwise when the following features are present: history of prior trauma or surgery, muscle swelling, severe pain, edema (swelling due to accumulation of fluid), wound discoloration, watery discharge, hemorrhagic bullae (elevated blisters, usually exceeding 5 mm in diameter, filled with blood); malodor (unpleasant smell) and crepitus (a crackling sound).

Early surgical intervention is the cornerstone of treatment for gas gangrene. Once gas gangrene is suspected, aggressive debridement of all tissues involved should be done immediately. This includes multiple incisions, fasciotomy, and removal of all compromised tissue, foreign material, and hematoma to allow decompression and drainage [4].

Non-clostridial gas gangrene (NCGG) is another rare necrotizing entity that is associated with high mortality (42.9-64.5%) [5-7]. NCGG is often associated with an underlying disease, particularly diabetes mellitus [6]. NCGG requires an intense clinical as well as microbiological

evaluation and an emergency surgical treatment to prevent a devastating, life-threatening outcome [7].

Here we report an interesting case of NCGG of polymicrobial etiology in an adolescent immunocompetent (non-diabetic) male presenting with a degloving injury over the left knee and thigh following a roadside trauma. The rationale for reporting this case is to sensitize the primary clinicians regarding the possible occurrence of a rare entity following trauma known as NCGG and the need for an urgent diagnosis and aggressive surgical intervention to prevent morbidity and mortality associated with it. To the best of our knowledge, the polymicrobial infection presenting as an NCGG in an immunocompetent adolescent following trauma is not reported previously in the literature.

Case presentation

A 16-year-old male presented as a hit-and-run case by a truck while standing on the roadside sustained a degloving injury over his left knee and thigh. There were associated lacerated wounds over the bilateral ankles. The patient was initially taken to a nearby private hospital, where wound debridement of the thigh for degloving injury and wound stitches for lacerated wounds around ankles were applied. Then, the patient was further referred to our level 1 trauma centre for further management after four days of injury. He was oriented to time, place, and person on presentation to us. There was no history of loss of consciousness or vomiting/ear, nose, or throat bleeding. The patient had a high-grade fever and tachycardia at the time of admission. On local examination, there was blackening of the skin over the proximal tibia with visible devitalized tissue overlying the skin extending from the middle thigh up to the knee joint with the underlying deep muscle as well as a part of the visible comminuted femur bone. There was a presence of foul-smelling discharge. A sutured lacerated wound was present on the left ankle (15×4 cm) and right ankle (12×3×0.5 cm), respectively. The patient was diagnosed with an intraarticular left-sided distal femur and proximal tibia fracture (floating knee), an open knee joint with degloving injury over thigh and knee with a foul-smelling open Grade 3-B wound according to Gustilo Anderson classification (**Figure 1**). There was no distal neurovascular deficit.



Figure 2. X-ray (A) AP view and (B) Lateral view: Left knee showing intra-articular fracture of the distal femur with a proximal tibia fracture.

Radiograph image of the left knee anteroposterior and lateral view showed an intra-articular fracture of the distal femur with a proximal shaft tibia fracture (**Figure 2A and 2B**). CT scan of the distal femur with proximal tibia revealed multiple gas pockets (**Figure 3A-C**). Clinical suspicion of gas gangrene was made, and a wound swab from the foul-smelling discharge was sent immediately for Gram staining. However, Gram stain revealed pus cells with no microorganisms. Since it is a 4-day-old open fracture with an extensive degloving injury with foul-smelling discharge, obvious clinical signs of infection, and CT scan evidence of gas pockets, we suggested amputation surgery. But the patient/parents gave negative consent for primary amputation. In view of this, the patient underwent limb salvage surgery on the same day of admission during which aggressive debridement and a knee spanning external fixator was applied. An intraoperative pus sample was also sent for culture and sensitivity.

Meanwhile, the patient was started on intravenous antibiotic therapy consisting of clindamycin 600 mg TDS, piperacillin-tazobactam 4.5 gm TDS, and analgesics. The wound swab sent before the surgery from the triage area of emergency showed the growth of *Klebsiella pneumoniae* (resistant to all antibiotics except minocycline and colistin to which it was intermediate sensitive), *Acinetobacter baumannii* (resis-

tant to all antibiotics except tigecycline and colistin to which it was intermediate sensitive) and *Pseudomonas aeruginosa* (sensitive to aminoglycosides and cefoperzone-sulbactam, resistant to all other antibiotics). The intraoperative pus sample culture showed the growth of *Proteus mirabilis* (sensitive to all first-line antibiotics) and *Pseudomonas aeruginosa* with the previous sensitivity pattern (**Table 1**).

On day one post-operative period, the vitals of the patient was found to be unstable with high-grade fever (103.1° F) not subsiding with medication, tachycardia (120 beats/min), high respiratory rate (>18/min), and persistent hy-

potension after which he was shifted to High Dependency Unit (HDU) for further observation. He had persistent high-grade fever with soakage at the debridement site and a foul-smelling serous discharge from the wound. Because of the deteriorating clinical condition and after discussion with the microbiology and physician team, and also after obtaining consent for amputation, the patient underwent left-sided above-knee amputation (open stump) (**Figure 4**). Post-operatively, intravenous injections of vancomycin 1 gm BD, clindamycin 600 mg BD and amikacin 1 gm OD were started. The intraoperative culture sensitivity report indicated the growth of *Acinetobacter baumannii*. After two days, culture-specific antibiotic tigecycline was intravenously started 100 mg loading dose followed by 50 mg BD in view of the intermediate sensitivity of tigecycline to *Acinetobacter baumannii*. Subsequently, after five days, amputation stump debridement with split skin grafting aided by vacuum-assisted closure therapy (VAC) was done (**Figure 5**).

A preoperative sample was sent from the left knee amputation stump before VAC, for culture and sensitivity showed growth of *Proteus mirabilis*. The culture showed no growth of anaerobic bacteria. Based on culture and sensitivity reports, specific antibiotic cefoperazone-sulbactam 1.5 gm BD intravenously was started

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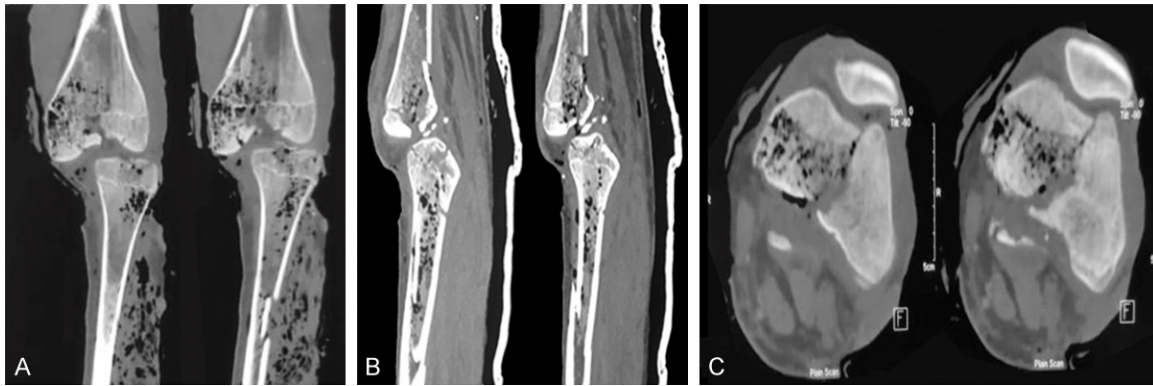


Figure 3. (A) Coronal, (B) Sagittal and (C) Axial sections - CT Scan image showing intraarticular distal femur and proximal tibia fracture with multiple gas shadows.

Table 1. Antibiotic susceptibility testing of various isolates

Date	Sample	Organism	Sensitive	Intermediate sensitive	Resistant
At the time of presentation, prior to surgery-sample taken from triage area	Wound swab	<i>Acinetobacter baumannii</i>	Nil	Tigecycline, Colistin	Amikacin, Ceftazidime, Cefepime, Imipenem, Meropenem, Ciprofloxacin, Cefoperazone + Sulbactam, Gentamicin, Levofloxacin, Piperacillin + Tazobactam
Prior to surgery	Wound swab	<i>Klebsiella pneumoniae</i>	Nil	Minocycline, Colistin	Cefotaxime, Amikacin, Ceftazidime, Imipenem, Meropenem, Ciprofloxacin, Cefoperazone + Sulbactam, Tigecycline, Piperacillin + Tazobactam, Ertapenem
Prior to surgery	Pus	<i>Pseudomonas aeruginosa</i>	Amikacin, Cefoperazone + Sulbactam, Gentamicin	Levofloxacin, Ciprofloxacin, Colistin	Ceftazidime, Cefepime, Meropenem, Aztreonam, Piperacillin + Tazobactam
Intra-operative sample	Tissue	<i>Proteus mirabilis</i>	Amikacin, Ceftazidime, Meropenem, Ciprofloxacin, Cefoperazone + Sulbactam, Gentamicin, Levofloxacin, Piperacillin + Tazobactam	Imipenam	Minocycline, Tigecycline
Intra-operative sample	Tissue	<i>Pseudomonas aeruginosa</i>	Amikacin, Cefoperazone + Sulbactam, Gentamicin		Ceftazidime, Cefepime, Imipenam, Meropenem, Ciprofloxacin, Levofloxacin, Aztreonam
Post-operative ward sample	Pus	<i>Proteus mirabilis</i>	Amikacin, Ceftazidime, Cefepime, Meropenem, Cefoperazone + Sulbactam, Gentamicin, Piperacillin + Tazobactam	Imipenam, Levofloxacin	Minocycline, Tigecycline
Intra-operative stump debridement sample	Tissue	<i>Proteus mirabilis</i>	Cefotaxime, Amikacin, Cefepime, Meropenem, Cefoperazone + Sulbactam, Gentamicin, Piperacillin + Tazobactam, Ertapenem	Imipenam	Ciprofloxacin, Tigecycline

post debridement. Vacuum-assisted closure therapy was removed after five days, and the patient was planned for discharge. Walking with the assistance of crutches, stump physiotherapy, and wheelchair mobilization was started at the time of discharge. The patient was advised for antiseptic dressings on alternate days with cefoperazone-sulbactam 1.5 gm BD intravenously to be continued for further two weeks.

At a four-month follow-up, the amputation stump healed well (Figure 6). At the 6-month

follow-up, the patient started bearing weight with the help of an above-knee prosthesis. In the final one-year follow-up, the patient's amputation stump was healthy and ambulatory with an above-knee prosthesis.

Discussion

Necrotizing fasciitis, synergistic necrotizing cellulitis, streptococcal myonecrosis, and gas gangrene are the various terms that have been used to describe necrotizing infections of the skin and subcutaneous tissue [8]. Gas gan-

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Figure 4. Post-debridement and above-knee amputation (open stump).



Figure 5. Split skin grafting (SSG) followed by Vacuum-assisted closure (VAC) therapy.

grene is most often seen in cases of trauma, injury by a foreign body, ischemia, use of illicit drugs, malignancy, and surgery [1]. The typical manifestations of the disease usually start with immense pain, which is not relieved by analgesics. As the infection progresses, mus-



Figure 6. After 4 months of VAC therapy with split skin grafting.

cular inflammation is followed by necrotizing fasciitis, and cutaneous and muscle necrosis [8]. Clostridium species are responsible for causing highly lethal infection of soft tissues such as gas gangrene, with Clostridium perfringens being the most common agent in 80-90% of the cases [9].

Microbiologically, necrotizing fasciitis has been classified as either type 1 (polymicrobial) or type 2 (monomicrobial) [10]. Polymicrobial infections are a mixture of aerobic and anaerobic organisms; they are also the most common infections in causing gas gangrene [11]. The perineum and trunk are the most common sites involved in these polymicrobial infections reflecting the normal skin commensalism found adjacent to the site of infection. These infections occur in immunocompromised individuals, such as patients suffering from diabetes mellitus or chronic renal failure. Monomicrobial infections are not very common as the polymicrobial variety. These infections typically occur in healthy patients with no associated comorbidities and there is often a history of trauma [8].

Recently, a few cases of non-clostridial infections have been reported [12-14]. Microbes such as *Escherichia coli*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae* have been isolated [14, 15]. The present case report highlights a rare presentation of NCGG in a young immunocompetent (non-diabetic) male associated with trauma at the roadside. In this patient, the clinical presentation of the wound showed blackening of the skin over the proximal tibia with visible necrosis of the overlying muscles with the comminuted distal femur and proximal tibia fracture. The culture of the pus demonstrated polymicrobial and non-clostridial etiology. *Acinetobacter baumannii*, *Klebsiella pneumoniae*, *Proteus mirabilis*, and *Pseudomonas aeruginosa* were isolated from the pus. No anaerobes were grown in any of the cultures. Also, the CT scan image showed multiple gas pockets at distal femur fracture open grade 3 B with a proximal tibia fracture. This clinical picture was suggestive of nonclostridial gas gangrene etiology.

As expected in a case of trauma, these pathogens could have been carried from the roadside, contaminated dressing of the affected site, or the patient's skin flora. The seeding of bacteria to the skin surface associated with trauma starts in the deep tissue planes. The clinical findings manifest when the infective organism spreads through the tissue along the deep fascia. Bacteria rapidly multiply within the viable tissues; however, fibrous attachments between subcutaneous tissues and fasciae limit the spread of the infection. The lack of fibrous attachments in the trunk and limbs can lead to widespread infection and tissue destruction. Involvement of venous and lymphatic channels leads to edema and the thrombosis of the blood vessels in the dermal papilla due to bacterial spread resulting in ischemia and gangrene of subcutaneous fat and dermis [16]. Infection can also spread to the muscle leading to myositis if the fascia is breached. Gas-producing organisms can give rise to subcutaneous gas formation.

This patient's possible etiology of gas gangrene could be clostridial or non-clostridial. Based on the patient's clinical presentation, it was thought to be clostridial gas gangrene initially, which is common. However, further microbiological investigations revealed the case to be non-clostridial gas gangrene caused

by polymicrobial organisms. Other causes could be implicated such as infection caused by *S. pyogenes* resulting in streptococcal gangrene, progressive bacterial synergistic gangrene, synergistic necrotizing cellulitis, and localized skin necrosis complicating conventional cellulitis [2].

A PubMed® search was conducted in February 2022 using the keywords non-clostridial gas gangrene, synergistic non-clostridial anaerobic myonecrosis, gas gangrene due to *Escherichia coli*, gas gangrene due to *Klebsiella pneumoniae*, in which we could find eleven papers in the last ten years [5, 12, 15, 17-24] (Table 2).

However, to the best of our knowledge, we could not find any case of non-clostridial gas gangrene reported in the last ten years in the pediatric and adolescent age group. Similarly, we could not find any immunocompetent (non-diabetic) trauma case with non-clostridial etiology. Thus, this report aims to highlight the role of non-clostridial organisms responsible for causing gas gangrene in a young immunocompetent (non-diabetic) trauma case.

Gas gangrene of the limbs is a rare infection due to facultative anaerobic bacteria associated with high morbidity and mortality. Gas gangrene has been seen mainly in patients with systemic pathologies such as immunosuppressive states and hematological illnesses [13, 15, 19]. Gas gangrene is rapidly progressive and is not only limb-threatening but also life-threatening. Furthermore, prompt and extensive surgery is clearly indicated [25].

In this case, the initial injury is due to a high-energy injury mechanism to the left lower extremity with extensive degloving injury and open fractures of the distal femur and proximal tibia, also called "floating knee". This typically happens with 'run-over' accidents and requires aggressive debridement and skeletal stabilization on day one of the injury. Unfortunately, it was addressed only by wound debridement of the thigh for degloving injury and wound stitches for lacerated wounds. Early, aggressive debridement on day one of presentation with skeletal stabilization using external fixators along with appropriate antibiotics covering both aerobes and anaerobes might prevent gas gangrene in this patient.

Non-clostridial gas gangrene

Table 2. Cases of non-clostridial gas gangrene published in the last 10 years

Case no	Year	Age	Gender	Risk factors	Location	Bacteriology	Treatment	Paper	Outcome
1 [24]	2015	78	Female	Diabetes Mellitus	Soft tissue swelling anterolaterally at intervertebral disc level T11/12	<i>Clostridium perfringens</i> and <i>Escherichia coli</i> .	Hemilaminectomy was done from T10 to T12, and an epidural abscess was removed. Fusion surgery 6 weeks after the initial operation	Vertebral osteomyelitis and epidural abscess caused by gas gangrene presenting with complete paraplegia: a case report (Japan)	Discharged 2 months later - At 18 months - normal gait without cane
2 [18]	2015	NA	NA	Diabetes mellitus Retroperitoneal infection, hyperlactatemia, and DIC	Neck in 4.2%, Thora-coabdominal wall and retroperitoneum in 12.5% each, the back in 33.3%, the buttocks in 25.0%, the perineum in 20.8%, and the extremities in 45.8%	<i>Klebsiella pneumoniae</i> in 8.3% and mixed infection in 91.7%	Managed by surgical debridement and culture specific antibiotics	Clinical Features of Non-clostridial Gas Gangrene and Risk Factors for In-hospital Mortality 10 year data showed 24 patients with NC Gas gangrene (Japan)	Mortality of 6 patients
3 [5]	2016	34	Male	History of intra-muscular injection of paracetamol	Left thigh and Gluteal region	<i>Klebsiella pneumoniae</i>	NA	Iatrogenic non-clostridial gas gangrene - a case report (India)	Patient was declared dead after 3 days of intramuscular injection
4 [19]	2016	53	Female	The patient was Schizophrenic and trapped for 4 months at home	Two large open wounds on both thighs and in sacral region	<i>Proteus mirabilis</i> and <i>Enterococcus fecalis</i>	Negative pressure wound therapy assisted dermatotraction	Negative pressure wound therapy-assisted dermatotraction for the closure of large open wounds in a patient with non-clostridial gas gangrene (Japan)	Patient was transferred to a rehabilitation hospital
5 [21]	2016	68	Male	Diabetes mellitus with multiple end-organ complications. Immunosuppressed on cyclophosphamide for immune negative glomerulonephritis	Lower left leg	<i>Escherichia coli</i>	Extensive debridement followed by vacuum dressings with antibiotics	<i>Escherichia coli</i> gas gangrene in an immunosuppressed diabetic man (Australia)	Patient was successfully discharged to inpatient rehabilitation on day 27
6 [26]	2017	51	Male	Diabetes mellitus and Hypertension	Submandibular region	<i>Pseudomonas aeruginosa</i> and <i>Klebsiella pneumoniae</i>	The offending tooth 38 was extracted. Meropenem 1 gm 8 hourly, InjAmikacin 1.5 g, and InjMetrogyl 100 ml	<i>Gas Gangrene in the Neck Caused by an Odontogenic Infection-A Case Report</i> (India)	The swelling reduced and clinical signs subsided within 2 weeks
7 [17]	2018	52	Male	The patient was immunocompromised with a history of Diabetes mellitus	Right foot	<i>Arcanobacterium haemolytic</i> , group G β -streptococcus, <i>peptostreptococcus</i> sp., <i>prevotella intermedia/disiens</i> , and Gram-negative anaerobic bacteria	Debridement and Meropenem hydrate 3 mg/day	Non-clostridial gas gangrene in a patient with poorly controlled type 2 diabetes mellitus on hemodialysis (Japan)	General condition improved

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8 [12]	2018	82	Male	Hilar cholangiocarcinoma, diabetes mellitus, hypertension, atrial fibrillation, and angina pectoris	Liver	<i>Enterococcus faecium</i> , <i>Klebsiella pneumoniae</i> and <i>Proteus mirabilis</i>	Surgical debridement of the liver surface, saline lavage in the abdominal cavity, and insertion of drainage tubes. Hyperbaric oxygen therapy with broad-spectrum antibiotics	Successful treatment of hepatic gas gangrene by open drainage: A case report and review of the Japanese literature (Japan)	The patient was discharged on the 28th post-operative day. No complications were detected, one year after the treatment
9 [22]	2020	72	Female	NA	Pancreas	<i>Klebsiella pneumonia</i>	NA	Pancreas Gas Gangrene Caused by <i>Klebsiella pneumonia</i> (Japan)	NA
10 [20]	2020	52	Male	Diabetes mellitus	Left foot	<i>Streptococcus agalactiae</i> , coagulase-negative staphylococci, and <i>Corynebacterium</i> species	Intravenous meropenem, clindamycin, and insulin and left below-the-knee amputation	Diabetes-associated Necrotizing Fasciitis of the Foot (Japan)	Able to walk with a prosthesis after eight months of gait rehabilitation
11 [15]	2021	53	Male	NA	Perianal area	<i>Clostridium perfringens</i> and <i>Escherichia coli</i>	Ceftizoxime, Ornidazole, Meropenem, and Vancomycin and debridement and drainage	Coinfection of <i>Clostridium perfringens</i> and <i>Escherichia coli</i> in gas-producing perianal abscess diagnosed by 16S rDNA sequencing: a case report (China)	The patient was discharged after 27 days of admission

Limitations of this paper could be that we are unsure if the fractures were recognized at the initial treatment facility and whether the debridement was adequate. There has been a tremendous delay (4 days) in providing appropriate treatment, leading to a serious gas-gangrene complication despite the patient being young and immunocompetent. The initial clinical picture of the wound on day one was not known, in addition, the patient reached our centre after four days which could lead to a serious complication of gas gangrene. On receiving in our centre, we suggested amputation and explained the prognosis, but with negative consent by the parents for primary amputation, emergency surgical debridement and skeletal stabilization were done immediately. On the next day, after obtaining proper consent, above-knee amputation was done due to deteriorating clinical signs and based on microbiological data. Further, split skin grafting with vacuum-assisted closure therapy was done to give stump coverage. A prompt but accurate institution of appropriate antibiotic therapy covering aerobic and anaerobic organisms is required based on discussion and coordination with the microbiology team. In this case, earlier vancomycin, clindamycin, and amikacin were instituted, followed by pathogen-specific antibiotic tigecycline and cefoperazone-sulbactam.

The patient responded with this appropriate treatment, and the amputated stump wound healed well. Later, the patient received an above-knee prosthetic fitting for ambulation. Along with this, a multi-disciplinary training approach for the appropriate use of the prosthesis and physiotherapy helped the patient carry out near normal day-to-day life activities.

Conclusion

- Nonclostridial gas gangrene (NCCG) is less recognized and reported than clostridial gas gangrene.
- NCCG, although rare, can be seen even in immunocompetent patients following a road-side trauma.
- A high index of clinical suspicion with a multi-disciplinary approach helps in early decision-making to avoid a devastating outcome like death.

- Appropriate antibiotic therapy in conjunction with early, aggressive surgical intervention is the cornerstone of treatment for desirable results to follow.

Disclosure of conflict of interest

None.

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