Spontaneous Gas Gangrene Due to Clostridium perfringens

The development of infections due to Clostridium species in persons with various malignancies, including leukemia, gastrointestinal carcinomas, and other solid tumors, has been reported previously [1–4]. In most cases, Clostridium septicum is the major cause of nontraumatic spontaneous gas gangrene in patients with malignancies [5]. Herein, we describe a pediatric patient who developed fulminant gas gangrene due to Clostridium perfringens.

In our review of the literature, we found only two pediatric cases of gas gangrene, neither of which was caused by C. perfringens [1, 6].

A 7-year-old boy presented with a 3-week history of generalized malaise, upper respiratory infection symptoms, nausea, emesis, and low-grade fever. Findings on physical examination were a grade 2 systolic murmur, hepatosplenomegaly (below the level of the umbilicus), and cervical and inguinal lymphadenopathy. A laboratory evaluation on admission revealed the following values: WBCs, 127,800/mm³ with 100% blasts; hemoglobin, 3.9 g/dL; hematocrit, 11.5%; and platelets, 25,000/mm³. After a bone marrow biopsy revealed lymphoblastic leukemia, chemotherapy was started.

On day 2 of chemotherapy, the patient developed a low-grade fever and was started on empirical therapy with parenteral cefazolin, ceftazidime, and gentamicin after blood for cultures was obtained. Therapy with these antibiotics was discontinued after he became febrile and results of blood cultures were negative for 48 hours. The patient became neutropenic on the fourth day of chemotherapy, and his WBC count was 4,001/mm³ with 100% neutrophils, 50% lymphocytes, 40% blasts, and 4% atypical lymphocytes. On day 7 of chemotherapy, the patient developed hyperglycemia requiring subcutaneous injections of insulin, given in the right and left thighs and in the deltoid areas.

On the 16th hospital day, the patient complained of leg pain in the left dorsal aspect of his thigh, where he had previously received an intramuscular injection of L-asparaginase. The leg showed no evidence of erythema or edema. Serial measurements performed every 2–4 hours did not reveal any increase in leg diameter. The pain was relieved temporarily with acetaminophen and codeine. The patient was transferred briefly to the intensive care unit, and piperacillin and clindamycin were added to the therapy regimen. He then was moved to the operating room because of suspicion of gas gangrene. Intraoperative findings revealed massive fulminant necrotizing fasciitis of the left thigh, necrosis and thrombosis of the femoral vessels, and myonecrosis of the quadriceps. Wide debridement was attempted, but the patient became hemodynamically unstable and died in the operating room. Cultures of specimens from the site later yielded spore-forming C. perfringens. Cultures of blood obtained that same day remained negative.

Clostridia are spore-forming anaerobic gram-positive bacilli found in the soil, and are part of the normal flora of the human gastrointestinal, biliary, and female genitourinary tracts [2] and the skin. Clostridial infections have been associated with traumatic wounds [1, 2, 7] and surgical procedures [1, 7]. The three most common species responsible for myonecrosis are C. perfringens, C. septicum, and Clostridium novyi [2]. However, the major cause of spontaneous nontraumatic gas gangrene is C. septicum [2, 4, 6, 8]. Risk factors for development of nontraumatic gas gangrene include intramuscular or subcutaneous injections [3, 4, 6–9], malignancy [1–4, 6–8], immunosuppression [6], and leukopenia or neutropenia.

The clinical presentation of gas gangrene usually starts with excruciating pain, not relieved by analgesics [2, 6, 8]. Other clinical findings include elevated temperature, tachycardia, hypertension, and changes in mental status [10]. The skin around the site of infection usually becomes tense and appears blanched initially and then quickly progresses to a dusky brown or reddish color [10]. The development of crepitus is usually a late finding that may be associated with the appearance of hemorrhagic bullae. This infection can rapidly progress to septicaemia and shock [8]. Pathogenesis of gas gangrene is due to toxin production at the site of the infection [2]. Treatment involves primarily antibiotic therapy and immediate surgical debridement [6, 8, 10]. Paramount to successful treatment is prompt suspicion of the diagnosis and initiation of treatment. The use of hyperbaric oxygen remains controversial.

Our case is unusual in two respects. First, the responsible organism, C. perfringens, is rarely associated with development of spontaneous gas gangrene. Second, gas gangrene rarely occurs in the pediatric population. The occurrence of gas gangrene in patients with leukemia may be due to the degree of immunosuppression. Leukemic infiltrates [1], necrotic ulcerations, and hemorrhage in the gastrointestinal tract [1, 2, 6] may predispose patients to infections by providing a route of access into the circulation. It is not clear exactly when or where our patient acquired the C. perfringens. He was noted to have loose stools 4 days before his death (the last 2 days, stools tested positive for occult blood). Cultures of stool were negative. On physical examination, there was no evidence of anal erythema or fissures. He received triple antimicrobial therapy for 5 days, which could have predisposed him to Clostridium overgrowth in his intestines. The development of diarrhea and possible denudation of his intestinal lining could account for a route of entry for hematogenous spread. This is not as likely since blood and stool cultures were negative. Another possible mechanism is stool contamination of the skin near or at the site of injection. (A bottle of L-asparaginase from the same lot that was injected in our patient did not yield C. perfringens.) Regardless, the progression of events leading to our patient’s very rapid death...
Successful Treatment of Rhinocerebral Zygomycosis: A Combined-Strategy Approach

Rhinocerebral zygomycosis is a life-threatening infection caused by different opportunistic fungi of the order Mucorales. Common predisposing conditions include hyperglycemia, acidosis, and profound neutropenia [1]. Neutrophils, the main defense against the development and progression of invasive fungal infection, have abnormal function in persons with poorly controlled diabetes [2]. We describe a diabetic patient with rhinocerebral zygomycosis whose brain involvement was successfully treated with prolonged medical therapy.

A 21-year-old noncompliant insulin-dependent diabetic man presented with left-eye blurred vision that rapidly progressed to left-eye blindness in 2 days. On admission the patient was in a state of diabetic ketoacidosis. Physical examination findings were remarkable for a fixed 6-mm left pupil; there was complete ophthalmpoplegia and blindness of the left eye. The right eye was normal. The left nasal turbinate appeared black, and the left palatal mucosa gray. A CT scan with angiography showed left-sided nasal mucosal thickening, opacification of the left maxillary and ethmoidal sinuses, and normal bilateral flow in the cavernous sinuses. The neutrophil count was 26,000/μL, and the glucose level was 317 mg/dL.

The patient underwent left total maxillectomy, sphenoidectomy, and left orbital exenteration. Examination of a frozen biopsy specimen showed nonseptate hyphae branching at right angles, compatible with Mucorales fungi, and a culture was positive for Mucor. Five days after the initial surgery, therapy with granulocyte colony-stimulating factor (G-CSF) at a dosage of 1.5 μg/(kg · d) (for 5 days initially) and hyperbaric oxygen treatments were started in an attempt to control this fungal infection. Follow-up MRI 3 days later showed residual thickening of the left skull base that prompted repeated debrideements. Frozen tissue sections and cultures were persistently positive for Mucor. Five days after the initial surgery, therapy with amphotericin B (AmB) at a dosage of 5 μg/(kg · d) (for 5 days initially) and hyperbaric oxygen treatments (6 times a week) were also started in an attempt to control this fungal infection.

A follow-up MRI 20 days after the initial surgery showed marked enhancement of the left frontal lobe and left cavernous sinus compatible with inflammatory changes.