Fatal *Clostridium septicum* infection in a patient with a hematological malignancy

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A 49-year-old woman with acute myeloid transformation of myelodysplastic syndrome was admitted with mild erythema and pain in the right thigh and left forearm. She was doing well and had been discharged the previous day after consolidation chemotherapy. Examination showed only mild erythema and tenderness of the right thigh. She was started on broad-spectrum antibiotics. Discoloration progressed rapidly, and within hours the right femoral and left brachial pulses were not palpable. She was taken to the operating room for a suspicion of embolic arterial occlusion. Surgical incision, however, revealed extensive necrosis of the tissues with the presence of gas. Her relatives did not want her to undergo amputation. The patient developed refractory hypotension and died within 15 hours of presentation. Blood samples later tested positive for *Clostridium septicum*. This case is presented to create awareness about the subtle presentation and rapid progression of this infection, which can lead to death in less than 24 hours.

C*lostridium septicum* is an anaerobic gram-positive bacillus that is ubiquitous in the environment and is a resident of normal intestinal flora. It is capable of causing gas gangrene in the absence of trauma but usually in the setting of colonic or hematological malignancy (1, 2). This case report highlights the subtle presentation of this infection, which progresses within hours with a high mortality rate without early treatment.

CASE REPORT

A 49-year-old woman with acute myeloid transformation of myelodysplastic syndrome was discharged home in an asymptomatic state after the first consolidation chemotherapy regimen with high-dose cytosine arabinoside. She was otherwise healthy, and her bone marrow aspirate was clear of blasts after the first induction chemotherapy. She was admitted the next day with pain in her right thigh and left forearm. Examination showed only minimal erythema and tenderness of the right thigh. Her blood pressure and heart rate were normal. Her abdomen was soft with normal bowel sounds, without organomegaly. Her white count was $1100/\text{mm}^3$ with an absolute neutrophil count of $500/\text{mm}^3$. The chest radiograph was normal. Half an hour later, however, the redness in her thigh had spread and the skin had turned blue. Blood cultures were obtained. She was started

empirically on cefepime and vancomycin. Three hours later, she had significant swelling of her right thigh and left forearm with feeble distal pulses. Embolic occlusion of the right femoral artery and left brachial artery with compartment syndrome or necrotizing fasciitis was suspected. An arterial Doppler showed only feeble flow beyond the right femoral artery and the left brachial artery, although no thrombus was visualized.

The vascular surgeon decided to do a manual thrombectomy. After incision of the groin, however, it was evident that she had necrotic thigh muscles extending posteriorly to the buttocks, and there was gas formation in the tissue. Exploration of the left cubital fossa also revealed the same findings. It was evident that she would require disarticulation of the right hip and amputation of her left arm since limb salvage was not thought to be possible. The family disagreed with this plan and wanted only conservative measures. She became profoundly hypotensive in spite of multiple vasopressors and died within 18 hours of admission. Blood samples were positive for *C. septicum*.

DISCUSSION

C. septicum (previously *Vibrio septique*) is historically important in microbiology, being the first pathogenic anaerobe cultured by Pasteur and Joubert in 1877 (3). Most of the gas gangrene in soldiers during the first and second world wars was attributed to this organism (4). Civilian infections due to this organism were thought to be extremely rare at that time, with only 11 cases reported from 1940 to 1967 (5). However, with better anaerobic culture techniques, this organism is being isolated in increasing numbers. Fortunately, this infection is still rare, but it is usually fatal. This infection has been associated with multiple medical problems including colonic malignancies (1), hematologic malignancies, peripheral vascular disease, cyclic neutropenia with enterocolitis, and diabetes mellitus. Most cases, however, are associated with malignancies. The infection might predate malignant tumors by several years. Hence, follow-up evaluation might be important in patients who survive (6). Early treatment is vital for this rapidly spreading infection,

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with a mortality rate close to 100% if not treated within 12 to 24 hours (7).

C. septicum is a normal commensal of the human intestinal tract and is ubiquitous in the environment. It is notorious for causing gas gangrene in the absence of trauma (8), which makes the diagnosis challenging without a high index of suspicion. It can produce several toxins including deoxyribonuclease, lecithinase, hyaluronidase, and hemolysins, which can lead to tissue necrosis, disseminated intravascular coagulation, intravascular thrombosis, and hemolysis.

Factors causing defective host immunity, such as steroids, diabetes, neutropenia, and alcohol abuse, might lead to translocation of the bacteria. This organism has been reported to cause several infections, including clostridial myonecrosis (8), osteomyelitis, septic arthritis, panophthalmitis, aortitis, intraabdominal abscess, intracranial infections, and abdominal wall cellulitis. Localized pain, inflammation, crepitation, gas production, disproportionate tachycardia, discolored edematous skin, and features of systemic toxicity are features that raise clinical suspicion (9). Gas may be seen in tissues on x-rays and computed tomography scans in cases of gas gangrene and is due to the production of nitrogen and hydrogen by the organism.

Even with effective treatment, including debridement and antibiotics, the mortality rate approaches 60% (10). The drug of choice for this infection is penicillin G. The extended-spectrum cephalosporins, carbapenems, and metronidazole are the usual alternatives in patients allergic to penicillins. Clindamycin, being a protein synthesis inhibitor, is believed to help reduce toxin production by the organism. Amputation might be needed when limb salvage is not possible. No controlled studies are available

regarding the use of hyperbaric oxygen therapy. Another concern regarding hyperbaric oxygen therapy is that compared with other clostridia, this organism has more tolerance to oxygen (11). Factors associated with poor prognosis are presentation with septic shock, immunosuppression, liver disease, and delay in initiation of treatment.

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