Case report

First described case of prosthetic joint infection with *Clostridium disporicum*

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**Abstract**

An orthopedic hardware infection with *Clostridium disporicum* is described. *C. disporicum* is a gram-positive anaerobic bacillus which can contain two subterminal spores. *C. disporicum* had not previously been reported in musculoskeletal infections. Gram stains demonstrating gram positive bacilli with two subterminal spores should alert practitioners to the possibility of *C. disporicum* infection.

1. **Introduction**

Clostridium is a diverse genus that consists of over 150 species. Clostridial species are gram-positive, sporulating, anaerobic bacilli normally found among gut flora and soil. Spontaneous gas gangrene or clostridial myonecrosis are particularly serious infections and can be associated with contaminated wounds. *Clostridium disporicum* was first isolated from rat intestinal flora in 1987 [1]. Biochemical evaluation revealed *C. disporicum* to be a novel species distinct from *Clostridium oceanicum*, a previously described two-spore producing *Clostridium* species [1]. We report a case of *Clostridium disporicum* in a post-surgical hardware associated infection.

2. **Case report**

In 2016, a 70 year old male with a history of diabetes mellitus, chronic kidney disease, and metastatic renal cell carcinoma presented with an acute onset of fevers, chills, and right thigh pain 17 days after orthopedic surgery. He had recently undergone a radical resection of the right distal femur with placement of hinged total knee megaprosthesise for recurrent metastatic renal cell carcinoma of the femur.

The patient had been diagnosed with metastatic renal cell carcinoma two years earlier following discovery of a lytic lesion in his right femur. At that time he underwent removal of the soft tissue mass and prophylactic intramedullary nailing of the femur. His renal cell carcinoma was subsequently managed with laparoscopic nephrectomy and radiation therapy. Despite the surgery and radiation, he developed recurrent carcinoma surrounding the intramedullary rod.

The 2016 intraoperative course for femoral resection and megaprosthesise placement was uneventful. The original intramedullary rod was removed. He was placed on peri-operative parenteral cefuroxime for 72 h. His hospitalization was complicated by postoperative delirium and *Clostridium difficile* associated diarrhea. He was ultimately discharged home 11 days following surgery.

Following discharge, he remained asymptomatic over the first five days; however, on the sixth day he reported an abrupt onset of high fevers, chills, and excruciating pain in his right thigh. Upon presentation, he had a temperature of 40.3 °C, a heart rate of 115 beats per minute, a blood pressure of 148/85, and an oxygen saturation of 93%. There was no erythema, drainage, or discharge surrounding his surgical site. Laboratory evaluation yielded a white
blood cell count of 11.0 K/µL, an erythrocyte sedimentation rate (ESR) of 61 mm/h, and a C-reactive protein (CRP) of 20 mg/dL. Blood cultures were obtained and he was started on levofloxacin. Due to concern for necrotizing fasciitis, he was brought to the operating room where a large hematoma was encountered. The fascia appeared intact without evidence of necrosis. Cultures of the hematoma and fascia were obtained. Due to significant morbidity associated with prosthesis removal, the hardware was retained. Gram stain of both cultures revealed greater than 25 polymorphonuclear cells and many large gram positive rods; frequently treatment with piperacillin/tazobactam and parenteral vancomycin. Due to high suspicion of clostridial infection, clindamycin was added to decrease toxin production.

Within two days, intra-operative cultures revealed a Clostridium species growing at 37 °C on reducible blood agar in an anaerobic environment with 10% CO2. Matrix assisted laser desorption/ionization time of flight (MALDI-TOF) mass spectrometry identified the organism as Clostridium disporicum (Bruker biotyper, library v5989). 16S ribosomal RNA gene sequences, consisting of two overlapping PCR products targeted by two sets of primers (5' F: ATR GTT TGA TCC TGG CTC A, 5' C14 R: GGA CTA CCA GGG TAT CTA AT; 3' F: TGC CAG CCG CCG TAA, 3' R: GGY TAC CTT GTC ACG ACT T), were real-time amplified on a LightCycler® 480 using LightCycler® 480 High Resolution Master (HRM) Sybr reagents (Roche Applied Science, Indianapolis, IN). PCR products were treated with shrimp alkaline phosphatase and exonuclease I and subsequently bidirectionally sequenced on an Applied Biosystems 3500 (Thermo Fisher Scientific, Waltham, MA). The generated DNA sequences were aligned to databases of known bacterial sequences, such as Greengenes (http://greengenes.lbl.gov/cgi-bin/nph-index.cgi). Results confirmed identification of C. disporicum with a 99% match. Antimicrobial susceptibility testing characterized the isolate as pan susceptible with minimum inhibitory concentrations (MICs) of penicillin 0.5, clindamycin 0.064, ertapenem 0.064, metronidazole 0.25, moxifloxacine 0.5 and tetracycline of 0.125. His antibiotics were narrowed to penicillin G plus clindamycin. He was ultimately discharged on continuous penicillin G monotherapy dosed at 8 million units every 24 h due to underlying renal disease.

Five weeks later his symptoms had improved but his inflammatory markers remained elevated (ESR: 120, CRP: 10). At eight weeks, his inflammatory markers (ESR: 110, CRP: 6) continued to be high and oral metronidazole 750 mg q 12hrs was added to the penicillin. At ten weeks, his inflammatory makers decreased (ESR: 78, CRP: 1.4) allowing for discontinuation of parenteral penicillin. Due to his retained prosthesis, continued antimicrobial suppression was recommended. At follow up one month later, he reported dysgeusia and lower extremity neuropathy. Metronidazole suppression was discontinued in favor of amoxicillin 500 mg q 12hrs. At one year postoperatively, he remains on suppressive amoxicillin with no recurrence or post-infection complications.

3. Discussion

Clostridial infections produce a wide spectrum of clinical disease, many of which are can be life-threatening. While many Clostridium species are common intestinal anaerobic flora in humans, C. disporicum is rarely encountered. C. disporicum has been isolated from intestinal tract of Crohn's disease patients and contributes to their abnormal microflora when compared to healthy hosts [2]. Primary bacteremia from C. disporicum was described in a 75 year old diabetic female following insertion of a ring pessary for management of uterine prolapse [3]. Intra-abdominal infection caused by C. disporicum was reported in a 66 year old male following hemicolectomy for colon cancer [4]. Both reported cases required bacterial 16S rDNA sequencing for identification and neither documented the presence of two subterminal spores on gram stain [3,4]. In our case, identification was rapidly reached with the use of MALDI-TOF and later confirmed with 16S ribosomal RNA bacterial identification.

Clostridial musculoskeletal infections are most commonly associated with traumatic penetrating injury and can rapidly progress to fulminant necrotizing fasciitis [5]. Musculoskeletal infections attributed to clostridial species will often present with erythema, warmth, tenderness, joint effusion and limited range of movement. Infections can produce overt fascia necrosis and gross tissue destruction with or without subcutaneous gas. Our patient presented with high fevers alongside severe surgical site tenderness; however, he had no evidence of wound erythema nor frank fasciitis intraoperatively. The absence of our patient’s localized tissue destruction highlights the need for prompt evaluation, recognition and surgical management of Clostridium musculoskeletal infections.

Hardware associated infections with clostridial species have been reported in association with malignancies and
immunocompromised states [6,7]. The long term survival of clostridial spores makes eradication of hardware associated infections challenging. Our patient’s persistently elevated inflammatory markers, and improvement only after combining parenteral and oral treatments, underscore the difficulties in management of hardware associated clostridial infections. In most cases, the preferred treatment is a 2-stage exchange arthroplasty which includes debridement, prosthesis removal, placement of antibiotic-impregnated spacer, parenteral antimicrobial therapy, and ultimate revision [8]. In situations with high surgical morbidity, another potential option is prosthesis retention via surgical debridement in conjunction with chronic antibiotic suppression [8]. In our case, due to the femoral bone’s preexisting damage from metastasis and radiation, alongside the surgical complexity of megaprosthesis removal, retention of the hardware with chronic antibiotic suppression was selected. It is not clear why he failed penicillin monotherapy yet seemed to improve with the addition of metronidazole given the low MIC’s of the organism.

Previously, many Clostridium species were not identifiable in clinical laboratories [3]. With the advent of newer and more readily available identification techniques such as bacterial 16S rDNA and MALDI-TOF mass spectrometry, clinicians may become more familiar with rarer Clostridium species including C. disporicum.

Conflicts of interest

There are no conflicts of interest to disclose.

References