



Clostridium perfringens as an unusual cause of a prosthetic joint infection following total knee arthroplasty



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ABSTRACT

Prosthetic joint infections are a serious complication of prosthetic joint implantations. These infections are generally caused by gram-positive, aerobic pathogens, however anaerobic organisms have been rarely implicated. We describe the case of an adult male who developed a *Clostridium perfringens* prosthetic joint infection four weeks following a right total knee arthroplasty. The patient had recently had a revision of a vascular graft, and there was initial concern for infectious graft involvement. Our case highlights a successful management pathway that included staged surgical revisions and extended courses of clindamycin and metronidazole, which ultimately spared any vascular complications.

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Introduction

Prosthetic joint infections are one of the more serious complications that can occur from prosthetic joint implantation [1]. Despite a relatively low lifetime infection rate of a prosthetic joint (1–2% depending on a number of variables), prosthetic joint infections are a relatively common occurrence due to the number of prosthetic joint replacements performed (estimated to near 4 million in the United States alone by 2030) [1,2]. Management of prosthetic joint infections often necessitates use of prolonged courses of intravenous antimicrobials, as well as surgical revisions [1]. When prosthetic joint infections do occur, they typically are a result of aerobic gram-positive pathogens, with staphylococcal infections being the most common [1]. Anaerobic pathogens are not commonly seen in prosthetic joint infections [3].

Clostridium perfringens is a gram-positive, rod-shaped, spore-forming, anaerobic organism that can be isolated from a variety of environments, notably soil and the gastrointestinal tracts of humans and animals [4]. It is a rapidly-growing pathogen that is hardy enough to spread across environments due to its relative aero-tolerance and its sporulation properties [4]. When pathogenic, it is generally associated with gastrointestinal disease, including enterocolitis and foodborne illness, however, it can be associated with more systemic infections in humans as well. It is capable of

profuse gas production that can lead to clostridial myonecrosis (gas gangrene), and it can produce a variety of toxins and virulent enzymes that can cause cellular necrosis [4].

Cases of involvement of *Clostridium perfringens* in prosthetic joint infections have only been described infrequently in medical literature [3]. The following is a case report of a *Clostridium perfringens* prosthetic joint infection shortly after a total knee arthroplasty, complicated by pre-existing endovascular grafts in place.

Case report

A 64-year-old male with a history of hypertension, hyperlipidemia, and severe peripheral arterial disease underwent an uncomplicated right total knee arthroplasty for osteoarthritis. Two weeks later, he developed critical arterial ischemia of his right leg due to thrombosis of an existing femoral-popliteal graft (original graft procedure performed slightly more than 2 years prior). He underwent a right femoral cut-down and Fogarty embolectomy of his graft. He felt well for two weeks and then presented for acute onset of severe pain and swelling of his right knee. He was tachycardic with heart rate in the 110 s, and was found to have white blood cell count of 23.2×10^3 cells/uL and a lactate of 3.1 mmol/L. Physical exam of the right knee was significant for erythema, edema, severe tenderness to palpation, and pain with movement. X-ray of the right knee showed swelling and gas within the soft tissue of the anterior aspect of the knee (Fig. 1). It was noted by the radiologist that the gas could potentially be related to infection with a gas-forming organism or possibly represent postoperative air. The prosthesis was noted to

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Fig. 1. Right knee radiograph on day of admission.

be in normal position and alignment. Knee aspiration was performed in the emergency department and revealed grossly purulent fluid with 93,000 neutrophils/uL.

The patient was taken to the operating room for urgent irrigation and debridement later that same day, and was started empirically on intravenous (IV) vancomycin 1000 mg every 12 h and ceftriaxone 1 g every 24 h. Lactate quickly normalized to 1.0 mmol/L the day of admission. Orthopedic surgery took the patient for a second debridement the following day. Aspirate gram stain originally showed gram positive and negative rods, and approximately 48 h later, the culture was resulted as moderate amounts of *Clostridium perfringens*. Surgical cultures from the joint also grew many *Clostridium perfringens*. Antimicrobial sensitivities for the *Clostridium perfringens* were not performed.

Infectious disease specialists were consulted once the cultures were resulted, and the patient was transitioned to combination therapy with IV clindamycin 900 mg every 8 h and IV metronidazole 500 mg every 8 h. Blood cultures were obtained prior to the start of antimicrobials, and were finalized as negative. WBC normalized to 9.0×10^3 cells/uL within 72 h. Given the rarity and potential severity of *Clostridium perfringens* in the setting of the patient with a recently revised vascular graft, infectious disease specialists at the institution felt there was a high risk for worsening complications, and therefore, recommended transfer to a limb preservation institute to explant the prosthesis.

After 3 days in the hospital, the patient was transferred to a more specialized facility in the area. He underwent further knee irrigation and debridement, removal of right total knee arthroplasty, synovectomy of right knee, and placement of an antimicrobial spacer impregnated with vancomycin and tobramycin. He had an uncomplicated post-operative course and was discharged after 7 days on IV clindamycin 900 mg TID and oral metronidazole 500 mg TID for a 6 week total antimicrobial course.

The patient remained stable but was unable to walk due to the explant and spacer. Two weeks after discontinuation of clindamycin and metronidazole, repeat knee aspirate was obtained and no organisms were identified. At that time, he underwent a right total knee revision and spacer removal. The decision was made to place him on chronic suppressive therapy with oral penicillin VK 500 mg four times daily for one year. There were no vascular complications throughout this medical course, and vascular surgery noted graft patency and good Doppler signals on exam.

Discussion

Clostridium perfringens is a rare pathogen for infections that arise outside the gastrointestinal tract, and it is exceedingly rare for

joint infections [3]. While there have been nearly 40 published case reports of joint infections related to *Clostridium* species, less than half of these have been due to *Clostridium perfringens* [5]. In addition, most cases of joint infections due to *Clostridium perfringens* have been septic arthritis of native joints, and typically due to either traumatic forces or hematogenous spread from bacteremia or gastrointestinal sources [5]. To the author's knowledge, there are only eight other published case reports of prosthetic joint infections due to *Clostridium perfringens* [6–12]. Among these eight, five were related to hip prostheses, and three related to knee prostheses [6–12]. Timing of infection onset relative to joint replacement/revision varied widely, from as little as 3 days, to as long as 4 years [6–12]. The majority did not have concurrent bacteremia (bacteremia in only two of the eight cases), or a clear source of infection [6–12]. Of note, when a clear source of infection was present (in three cases), infection arising from the biliary system was common (all three cases), and concurrent bacteremia was more likely (two of the three) [7,9,11]. Treatment in these case series were all fairly similar. Staged surgical revisions, with prosthetic explantation, were common, being performed in four of the eight cases [8,9,11,12]. All of the cases also utilized extended courses of IV penicillin over 4–6 weeks [6–12]. The combination of extended courses of antimicrobials and staged surgical revisions resulted in clinical cure in all eight cases [6–12].

The case presented here highlights that prosthetic joint infections due to *Clostridium perfringens* can occur, even without a clear source or concurrent bacteremia. This patient had negative blood cultures, and there was no suspicion for a gastrointestinal source based on the patient's lack of symptoms. The patient did undergo two surgical procedures in the preceding 4 weeks, so it is possible that perioperative contamination was the source, although this would be an unusual pathogen even in that context. The case also highlights that standard therapeutic approaches are effective, even in a patient with a very high risk for complications. Similar to other published case reports, this patient received staged surgical revisions, with prosthetic removal and subsequent reimplantation once the synovial fluid cultures became negative. Four to six weeks of intravenous penicillin has been an effective treatment option in other published reports [6–12]. This case is unique in that it supports the efficacy of a six-week course of IV clindamycin in combination with oral metronidazole. This may be useful for patients with penicillin allergies, or when culture sensitivity data is not readily available. While published literature indicates that *Clostridium perfringens* is generally sensitive to penicillin, clindamycin, and metronidazole, it is possible for resistance to occur [13]. As a result, combination therapy may be warranted when sensitivity data is not available. Another added advantage of using clindamycin and metronidazole relative to penicillin is that these agents have the ability to suppress *Clostridium perfringens* alpha-toxin activity [14].

This case, alongside other case reports of clostridial joint infections highlights several things. (1) While rare, prosthetic joint infections secondary to anaerobic pathogens can occur unexpectedly. Guideline recommendations should be followed in obtaining aerobic and anaerobic cultures from synovial fluid and blood [1]. (2) When *Clostridium perfringens* joint infections are identified, consideration should be made for ruling out biliary involvement as a potential source of infection. (3) Explantation of the infected prosthetic joint should be a goal for most patients, and it appears that re-implantation can be done successfully in most cases. (4) Extended courses of IV (or highly bioavailable oral) antimicrobials (4–6 weeks) are likely necessary. This could include IV penicillin, IV clindamycin, or oral metronidazole, and combination therapy might be most appropriate if sensitivities are not available to guide therapy.

Conclusion

This patient case highlights a pathway that was ultimately successful in managing a *Clostridium perfringens* prosthetic joint infection in a patient at high risk for further infectious complications due having an arterial graft in place. This pathway included staged surgical revisions, including multiple incision and drainages, prosthesis explantation, antimicrobial-impregnated spacer placement, and ultimately total knee revision. Extended courses of clindamycin and metronidazole were effective in sterilizing the joint to safely facilitate these surgical procedures.

Consent

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Declaration of Competing Interest

Neither Dr. Stroud, nor Dr. Vandiver have any financial or personal relationships to disclose that would inappropriately bias this manuscript.

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