Case Report

A Life- and Limb-Threatening Case of Clostridium septicum in a Total Hip Arthroplasty

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ABSTRACT

A 46-year-old male with bilateral metal-on-metal hip prostheses presented with a left periprosthetic hip infection, as well as chronic, progressive osteolysis of the proximal femur and acetabulum with pelvic erosion. Three years before, the bearing surface was changed to metal-on-polyethylene prosthesis during an attempted revision but was complicated by extensive blood loss. At our institution, gross inspection demonstrated a soft-tissue hip mass of unknown etiology. Open biopsy and culture were performed, but extensive hemorrhaging required interventional radiology. Cultures revealed Clostridium septicum infection—known for its associations with gastrointestinal malignancy. Workup in the hospital was negative for malignancy, and definitive management was left hip disarticulation and intravenous antibiotics. The patient developed a chronic wound on the left hip incision but was ultimately lost to follow-up.

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Introduction

Total hip arthroplasty (THA) can be complicated by periprosthetic infections, which are most likely to occur within the first 2 postoperative years [1]. Although gram-positive organisms from the Staphylococcus genus are most common, the Clostridium genus is also known to infect prosthetic joints. Clostridium septicum is a member of the normal gut flora in humans but can be found in an anaerobic environment. Unlike other Clostridium infections, trauma is not necessary for infection to begin. It is believed that C. septicum infection (CSI) occurs via hematogenous spread from the gastrointestinal tract [2,3]. So far, CSI has not been reported in a THA, and most prior reported cases discovered gastrointestinal malignancies. Previous CSI cases have been reported in the prosthetic knee [2,4], native shoulder [5], traumatic native knee [6], and atraumatic native knee [7,8]. Four of 6 case reports were associated with a gastrointestinal malignancy, and one of the other 2 was never worked up for malignancy as shown in Table 1. This case in a 46-year-old man is the first reported CSI in a THA.

The patient was informed and consented for publication of case data.

Case history

A 46-year-old male presented as a transfer from an outside facility with concern for sepsis secondary to an acute left hip periprosthetic infection. Over the previous 24 hours, there had been increased pain in the left hip with drainage of blood and purulence noted from an open wound. There was no history of trauma in the left hip and no preceding fevers or chills. Past medical history was significant for severe psoriatic arthritis treated in the past with steroids and recently treated with methotrexate. Past surgical history was significant for a left metal-on-metal THA performed 18 years before and a right metal-on-metal THA 9 years before.

On admission to our institution, the patient had an elevated white blood cell count of 24,000/mm³, decreased hemoglobin of 7 mg/dL, and hematocrit of 21%, elevated C-reactive protein of 257 mg/dL, and erythrocyte sedimentation rate of 96 mm/hr, and decreased albumin of 1.8 g/dL. Blood cultures were drawn, and a radiograph of the pelvis, left hip, and left femur was taken (Fig. 1a-c). The patient remained hemodynamically stable with signs of end-organ perfusion; therefore, the team did not feel the patient was in sepsis.

The patient had a negative deep vein thrombosis ultrasound and normal electrocardiogram and was started on vancomycin and Zosyn by the emergency department for presumed infection. Physical examination was significant for a chronically ill—appearing
patient with temporal wasting and severe bilateral lower extremity psoriasis with plaques creating woody edematous changes. There were no neurovascular deficits. A $12 \times 10 \times 4$-cm fungating mass protruded from the left lateral thigh.

**Prior history**

Further review of medical records revealed that the patient had reported to another hospital 8 years before, with 9 months of left hip pain. At that time, radiographs of the pelvis and left hip were taken (Fig. 2).

A computed tomography (CT) of the abdomen and pelvis was also performed at that time, which showed mild particle wear and a left hip fluid collection concerning for a left hip periprosthetic infection. The fluid collection was aspirated by interventional radiology (IR), and the patient was admitted to the hospital for further workup, initiation of intravenous (IV) vancomycin and Zosyn, and an orthopaedic consultation. After 5 days, the aspirated culture was negative for infection, antibiotics were stopped, and the patient was discharged without further treatment and slight resolution of the left hip pain.

The patient presented to the same hospital again 3 years before with function-limiting left hip pain. Another series of hip and pelvis radiographs were taken (Fig. 3a and b). An outside MRI and CT were reviewed by the treating surgeon and described as “loss of the left hemipelvis due to bubbling osteolysis.” In addition, there was “a massive pseudotumor about this left hip and an incredible amount of bone loss about the acetabulum and hemipelvis.” The patient was worked up for infection and metallosis. His serum chromium was <0.2 mcg/L and serum cobalt was 0.5 mcg/L both under the reference range. His erythrocyte sedimentation rate was elevated at 34 mm/hr and C-reactive protein was elevated at 3.12 mg/dL. He was again sent for aspiration of his left hip and a three-dimensional (3D) reconstruction CT scan of his pelvis. We were unable to obtain the 3D reconstruction CT scan images. The treating surgeon at that time planned for reconstruction with cup-cage construct vs custom triflange vs an allograft hemipelvis reconstruction. The aspiration results were again negative after being held for 2 weeks, no antibiotics were started, and the 3D scans were sent to DePuy Synthes for modeling of the pelvis. He returned to the clinic after modeling was completed with plans for revision of failed left THA, secondary to metallosis, with a cup-cage construct and debridement of the pseudotumor.

On the day of surgery, the previous anterolateral approach was used to access the hip. There was minimal extracapsular bleeding encountered. Once the capsule was incised and the hip exposed, 500 mL of “gross blood” was evacuated and engorged capsular vessels were encountered, which was thought to be a result of pressure from intracapsular fluid. During exposure of the femoral and acetabular components, “copious” amounts of coagulated blood were scooped out of the left hip surrounding the implants. The femoral head was disimpacted revealing mild trunnion wear, but during further exposure of the acetabular component, significant bleeding was encountered from multiple engorged vessels within the capsule. After discussion with the anesthesiologists and transfusion of 2 units of blood, the team decided to abort the reconstruction surgery. From the operative report, “the metal liner was disimpacted from the Pinnacle shell” and replaced with a polyethylene “10-degree +4 face changing liner.” The trunnion and inside of the original femoral head were cleaned, and the original head was impacted back onto the stem. There was no mention of stability of the acetabulum or femoral component. There was also no mention of the location of the acetabular component within the pelvis. Tissue samples obtained during surgery were sent for biopsy and culture. Layered closure was performed with absorbable sutures over 2 drains. Total blood loss was 3500 mL, and multiple blood products were transfused. IR colleagues, 4 days later, performed angiography to localize the source of bleeding. Medical records stated no intrapelvic arterial bleeding was visualized or amenable to intervention. A CT abdomen and pelvis was also obtained (Fig. 4a-c), but no additional bleeding was found, and the patient stabilized.

On the 6th hospital day, intraoperative biopsy results returned negative for malignancy but reported acute-on-chronic

| Authors            | Year published | Location of infection                     | Results of cancer workup                          |
|--------------------|----------------|------------------------------------------|--------------------------------------------------|
| Goon et al. [5]    | 2005           | The shoulder                             | No malignancy                                    |
| Harris [6]         | 1983           | The knee, associated with trauma         | Malignancy workup not performed                  |
| Hovenden et al. [7]| 1992           | The knee, nontraumatic                    | Cecal malignancy on autopsy                      |
| Macy et al. [8]    | 1986           | The knee, nontraumatic                    | Colonic adenocarcinoma                           |
| Burnell et al. [2] | 2011           | TKA                                      | Cecal malignancy                                 |
| Economides et al. [4]| 2021         | TKA                                      | Colonic malignancy                               |

Table 1
Reported *Clostridium septicum* infections and their malignancy findings.
inflammation. Cultures also returned negative for infection. The patient was downgraded from the intensive care unit and completed a 7-day course of IV vancomycin and Zosyn. Before discharge, the treating surgeon noted that the intraoperative finding was not consistent with bearing surface wear. The patient returned to the clinic 4 weeks later, and the record reports he had significant relief of his left hip pain and his wound was healing routinely. Radiographs were taken at that time (Fig. 5). The patient returned for one additional follow-up and self-reported he was better than before the surgery. He was subsequently lost to follow-up.

Recent history

After a detailed history was obtained, the patient was admitted by the orthopaedic service. Consultation with the faculty orthopaedic oncologist was made for surgical planning. With elevated inflammatory markers and an open wound draining purulent fluid, aspiration was bypassed because the patient met Musculoskeletal Infection Society definitions for prosthetic joint infection. The patient was taken to the operating room 2 days after admission for an open biopsy and culture of the left thigh mass (Fig. 6). During the operation, the same anterolateral approach was used to take an elliptical approach around the mass. The mass was a large collection of necrotic tissue combined with what appeared to be coagulated blood. There was a foul smell coming from the wound after the incision was made. After incising what remained of the fascia, extensive coagulated blood and necrotic tissue was evacuated from the extracapsular left hip. The proximal femur had extensive bone loss, and the prosthesis was visible through the necrotic tissue. It remained grossly fixed in the diaphysis, but the metaphyseal bone was eroded away with thin wafers overlying the lateral prosthesis that were easily removed by hand. There was also an extensive amount of bleeding once the capsule was incised, likely from the previous engorged intracapsular vessels. The acetabular component was easily exposed as the surrounding tissue was necrotic and removed by hand. There was a friable bone surrounding the cup that was easily removed using rongeurs. The cup itself appeared to be closely engaged to tissue inside the pelvis, and it was unclear precisely what it was stuck to at that time. An estimated 1500 mL of blood loss occurred in 5 minutes once inside the capsule. Continuous communication with the anesthesiologist and circulating nurse ensured appropriate delivery of blood products. A biopsy and culture specimen were taken, and hemostasis was achieved temporarily through use of thrombin spray, argon laser, gel foam sponges, and Bovie electrocautery. With concerns about patient stability and achieving control of blood loss, we decided not to pursue removing the cup during this operation. The wound was not closed, and instead, negative-pressure wound therapy was used to achieve a quick seal, allowing the patient to be taken to the IR suite. The IR team was able to embolize branches of the profunda femoris and medial femoral circumflex arteries to assist in hemostasis. The patient was transferred to intensive care unit and intubated for close monitoring. He was extubated on postoperative day 1. Preliminary biopsy results returned 2 days later with acute-on-chronic inflammation but negative for malignancy. Cultures this time returned positive for *C. septicum* within 36 hours. Infectious disease consultation was made for antibiotic regimen recommendations. Admitting blood cultures remained negative and were finalized.
Extensive discussion of the patient at a tumor board conference led to the differential diagnosis of chronic infection, particle-associated periprosthetic osteolysis, Gorham vanishing bone disease, lymphangioma, vascular tumor, and paraneoplastic abdominal tumor. The left hemipelvis was deemed nonreconstructable, and the patient was counseled on the risks and benefits of left hip disarticulation. The team felt left hip disarticulation in combination with antibiotics gave the patient the best chance to clear the infection, while preserving sitting function. A left hemipelvectomy was considered but thought to be too aggressive at that time. Ultimately, the patient agreed to a left hip disarticulation. The patient was then taken back to the operating room 4 days after initial biopsy. The acetabular component was grossly loose inside the pelvis abutting, but not eroding into the colon or any other organs. The acetabular component was removed with blunt dissection of the serosa off the cup. Rongeurs and curettes were used to debride all appreciable necrotic tissue. The gluteus maximus was healthy appearing and tacked down over a drain with polydioxanone suture into what little bone remained inside the dissociated acetabulum. The anterior and posterior skin was approximated with polydioxanone suture (J and J medical devices, New Brunswick, NJ) and staple closure. An incisional wound vacuum was used to aid in wound healing. A CT abdomen and pelvis after the procedure did not find evidence of gastrointestinal malignancy but found left inguinal, pelvic sidewall, and para-aortic and retroperitoneal lymphadenopathy. Once cultures were finalized, *C. septicum* remained the only organism, and recommendation was for 6 weeks of IV cefepime 2 g twice a day and oral Flagyl 500 mg 3 times a day.

The patient’s postoperative course started as routine healing and completion of antibiotic regimen. After the 6 weeks of IV antibiotics, he was switched to oral chronic suppression therapy with linezolid 600 mg twice a day and cefpodoxime 200 mg twice a day. At 4 months postoperatively, the patient developed a draining wound at the posterolateral aspect of his incision. This was treated with wet-to-dry dressing changes twice daily, and oral antibiotic suppression was continued. At his last postoperative visit 7 months out from surgery, the patient continued to have a draining wound at the posterolateral aspect of his incision that was slightly larger. After a thorough discussion of the risks and benefits of continued wet-to-dry dressings and antibiotics vs further surgical intervention, the patient expressed desire to proceed with conservative chronic antibiotic suppression and wound care. The team counseled the patient on obtaining a colonoscopy to rule out an occult gastrointestinal malignancy and placed a consult for him to see outpatient gastroenterology, but he never made his appointment. The patient was lost to follow-up despite multiple attempts by clinic staff to contact him. At 18 months postoperatively, the patient presented to the emergency room (ER) with continued wound drainage from his hip incision. The ER staff obtained new imaging (Fig. 7 and 8), but the patient left against medical advice before the orthopaedics team could see him. He has yet to follow up since.

**Discussion**

This case is believed to be the first report of a CSI in a THA. In the current literature, there are 6 cases of CSI in a native or prosthetic joint (Table 1). One case is a spontaneous CSI of the shoulder not
associated with malignancy [5]. Three cases involve infection in the native knee—one of which was traumatic, whereas the other 2 were atraumatic [6-8].

CSI is known for its associations with gastrointestinal and hematologic malignancies. The first report of a C. septicum intra-articular infection was published in 1983 and described a traumatic laceration of the knee in a 5-year-old who did not undergo a malignancy evaluation as the inoculation was related to trauma [5]. The second report was a 71-year-old female with atraumatic septic arthritis of the knee who had a colonic adenocarcinoma [8]. The third report was an 85-year-old female who died in the hospital shortly after presentation with septic arthritis of the knee but had an autopsy showing cecal malignancy [7]. The remaining 2 cases involve infection in a total knee arthroplasty (TKA). Burnell et al. [2] presented the first case of a prosthetic knee infected with C. septicum, which was ultimately found to have a colonic malignancy [5]. The second case of a prosthetic knee infection due to C. septicum was reported by Economedes et al. [4] on a patient who underwent simultaneous bilateral TKA. Their patient presented 2 weeks postoperatively with an acute left periprosthetic joint infection due to C. septicum, and Workup revealed a colonic malignancy. In this small cohort, 66% (n = 6) of reports of an infected joint with C. septicum also had an internal malignancy.

There are 9 other cases of infected joints with various other Clostridium species (Table 2) [4,9-16]. One case is Clostridium cadaveris in a patient with breast cancer who underwent THA [11]. Another case was Clostridioides (formerly Clostridium) difficile in a 16-year-old patient who underwent TKA treated for osteosarcoma [13]. The C. difficile infection was not believed to be associated with an underlying malignancy or the osteosarcoma itself. The remaining 7 cases are of Clostridium perfringens, and there is no mention of malignancy in these patients [5,10,12,14-16]. Of note, one patient with C. perfringens had bilateral prosthetic hips infected [9]. Therefore, infections with any Clostridium species are unusual and should alert clinicians to search for a source such as malignancy.

Overall, C. septicum is the second most common infectious species of the Clostridium genus, accounting for 40% (6/14) of reported Clostridium-infected joints in our analysis—second only to C. perfringens at 50% (7/14). Clostridium are aggressive, anaerobic, and spore-forming bacteria that produce a toxin capable of causing tissue destruction and myonecrosis [2-20].

There are 4 published case series describing the association of CSI with malignancy. Kornbluth et al. reported on a series of 162 cases of CSI, in which 81% had an associated malignancy [18]. In particular, they reported that 34% had a colonic malignancy, 40% had a hematologic malignancy and that the malignancy was occult in 37% of cases [4,18]. A salient point from Kornbluth et al. is that patients with CSI should undergo a thorough search for malignancy after acute therapy because the survival rate is only 35% [18].

Larson et al. reviewed patient records from 1966 to 1993 for necrotizing CSI at a single institution. They found 281 patients with a Clostridium infection diagnosed by culture, of which 32 had a CSI. They found a 56% mortality rate and a 50% malignancy rate in those with a CSI, compared with a 26% mortality rate of all Clostridium infections and an 11% malignancy rate in other types of Clostridium infections [2,20]. Arriving at the same conclusion as Kornbluth et al., Larson et al. recommended that the clinician must search for associated malignancies in patients with CSI [20].

Alpern et al. in 1969 also reported on a series of 28 patients with CSI. They found 27 patients with hospital records available for review, and 23 of these had a malignancy [17]. Of the 27 patients, 15 were treated with antibiotics and 13 died. Of the remaining 12 patients not treated with antibiotics, 11 died. Alpern et al. theorized that the patient’s gut was the likely source of bacteria [17]. Finally, Chew and Lubowski reported in 2001 on a series of 31 patients with Clostridium infections at a single institution between 1990 and

![Figure 7](image-url) Radiograph of the abdomen status after left hip disarticulation demonstrating continued erosion of the left hemipelvis.

![Figure 8](image-url) (a-c) Various coronal sections of a pelvic CT scan demonstrating osteomyelitis of the left hemipelvis, a soft-tissue mass, and bony erosion.

| Species                | Authors          | Year published | Location of infection |
|------------------------|------------------|----------------|-----------------------|
| C. cadaveris           | Morshed et al.   | 2007           | THA                   |
| C. difficile *Recently reassigned to the Clostridoides genus | Pron et al. | 1995 | THA, comorbid osteosarcoma |
| C. perfringens          | Kibbler et al.   | 1991           | THA, bilateral         |
| C. perfringens          | Maniolo et al.   | 1987           | Prosthetic joint, unknown |
| C. perfringens          | Pearle et al.    | 2003           | Knee extensor allograft |
| C. perfringens          | Rush             | 1976           | THA *Report on 2 different cases |
| C. perfringens          | Stern, Sculco    | 1988           | TKA                   |
| C. perfringens          | Wilde, Ruth      | 1988           | TKA                   |
2000. There were 5 patients with culture-proven C. septicum bacteremia, and 4 (80%) of these had malignancies (2 colon cancer and 2 hematologic) [3].

Although workup for our patient was negative for malignancy, our patient never underwent a colonoscopy, so the possibility of an occult gastrointestinal malignancy cannot be ruled out. One of the prior treating surgeons assumed that the process in the left hip was related to particle wear disease, as all other workup had been unrevealing. Given that the labs at that time were not consistent with metallosis, another possibility is that the infection occurred from direct inoculation as the acetabular component was in direct contact with the large bowel. Although there was no obvious perforation of the serosa, it is possible that the close proximity led to inflammation of the large bowel and allowed direct inoculation of the acetabular component.

While C. septicum infections are associated with a risk for malignancy, the patient in this case had a negative workup to date, as evidenced by his CT abdomen and pelvis and a tissue biopsy of the resected mass. It is our recommendation that patients with C. septicum infections, both intra-articular and extra-articular, undergo extensive workup to rule out both obvious and occult gastrointestinal malignancy. Future studies should evaluate the association between CSI and vascular and osteolytic symptoms like what was seen in this case.

Summary

Infection with C. septicum is rare, and there are no previous reports of a patient who underwent THA. We recommend screening for gastrointestinal malignancy in periprosthetic joint infections with C. septicum and the possible need for long-term antibiotic therapy with surgical intervention for those associated with chronic infection.

Conflict of interest

The authors declare there are no conflicts of interest.

References

[1] Pulido L, Ghanem E, Joshi A, Purtill JJ, Parvizi J. Periprosthetic joint infection: the incidence, timing, and predisposing factors. Clin Orthop Relat Res 2008;466(7):1710.
[2] Burnell CD, Turgeon TR, Hedden DR, Bohm ER. Paraneoplastic clostridium septicum infection of a total knee arthroplasty. J Arthroplasty 2011;26(4):666.e9.
[3] Chew SS, Lubowski DZ. Clostridium septicum and malignancy. ANZ J Surg 2001;71(11):647.
[4] Economedes DM, Santoro J, Deirmengian CA. Clostridium septicum growth from a total knee arthroplasty associated with intestinal malignancy: a case report. BMC Infect Dis 2012;12:235.
[5] Goon PK, O’Brien M, Titley OG. Spontaneous clostridium septicum septic arthritis of the shoulder and gas gangrene. a case report. J Bone Joint Surg Am 2005;87(4):874.
[6] Harris LF. Clostridium septicum arthritis. South Med J 1983;76(3):415.
[7] Hovenden JL, Murdoch GE, Evans AT. Non-traumatic clostridium septicum arthritis in a patient with caecal carcinoma. Br J Rheumatol 1992;31(8):571.
[8] Macy NJ, Lieber L, Habermann ET. Arthritis caused by clostridium septicum. A case report and review of the literature. J Bone Joint Surg Am 1986;68(3):465.
[9] Kibbler CC, Jackson AM, Gruneberg RN. Successful antibiotic therapy of clostridial septic arthritis in a patient with bilateral total hip prostheses. J Infect 1991;23(3):293.
[10] Maniloff G, Greenwald R, Laskin R, Singer C. Delayed postbacteremic prosthetic joint infection. Clin Orthop Relat Res 1987:194.
[11] Morshed S, Malek F, Silverstein RM, O’Donnell RJ. Clostridium cadaveris septic arthritis after total hip arthroplasty in a metastatic breast cancer patient. J Arthroplasty 2007;22(2):289.
[12] Pearle AD, Bates JE, Tolo ET, Windsor RE. Clostridium infection in a knee extensor mechanism allograft: case report and review. Knee 2003;10(2):149.
[13] Pron B, Merckx J, Touzet P, et al. Chronic septic arthritis and osteomyelitis in a prosthetic knee joint due to clostridium difficile. Eur J Clin Microbiol Infect Dis 1995;14(7):599.
[14] Rush JH. Clostridial infection in total hip joint replacement: a report of two cases. Aust N Z J Surg 1976;46(1):45.
[15] Stern SH, Sculco TP. Clostridium perfringens infection in a total knee arthroplasty. A case report. J Arthroplasty 1988;3(Suppl):S37.
[16] Wilde AH, Ruth JT. Two-stage reimplantation in infected total knee arthroplasty. Clin Orthop Relat Res 1988:23.
[17] Alpern RJ, Dowell Jr VR. Clostridium septicum infections and malignancy. JAMA 1969;209(3):385.
[18] Kornbluth AA, Danzig JB, Bernstein LH. Clostridium septicum infection and associated malignancy. Report of 2 cases and review of the literature. Medicine (Baltimore) 1989;68(1):30.
[19] Kurilo JC, Schmidt AH. Images in clinical medicine: gas gangrene of a prosthesis hip. N Engl J Med 2014;371(20):1917.
[20] Larson CM, Bubrick MP, Jacobs DM, West MA. Malignancy, mortality, and medicosurgical management of Clostridium septicum infection. Surgery 1995;118(4):592. discussion 7-8.