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Case Report

Prosthetic hip infection with *Edwardsiella tarda* in sickle cell beta thalassemia disease: A case report

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ABSTRACT

Periprosthetic infection following total hip arthroplasty is a devastating complication that has been reported to occur in up to 1.6% of all primary total hip arthroplasties. We report a previously unrecognized gram-negative bacillus as the infecting agent in a patient with bilateral total hip arthroplasties for stage IV osteonecrosis. A 22-year-old male with combined sickle cell disease and beta thalassemia with a prior history of unknown hip surgeries and treatment for distal tibial osteomyelitis in Africa developed a periprosthetic joint infection; intra-operative cultures confirmed the infecting organism to be *Edwardsiella tarda* which was sensitive to late-generation cephalosporins and vancomycin. He was successfully treated with a staged revision total hip arthroplasty with an antibiotic spacer and has been infection-free since. *E. tarda* is a gram-negative bacillus which has not been previously associated with periprosthetic infection following TJA. This organism infects both humans and fish, and is particularly associated with commercial fishing and fish farming of freshwater and marine fish, potentially putting workers in these industries at risk. Little is known about antibacterial resistance in this organism. Infection by *E. tarda* presents a new organism which may affect individuals undergoing TJA, particularly if they have medical comorbidities that increase their risk for infection, or work in industries which put them at a higher risk of infection by this organism. Further study on the antimicrobial resistance patterns of this organism will be required to be able to treat potentially resistant organisms.

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1. Introduction

Avascular necrosis of the proximal femur is a common sequela of sickle cell disease that is usually treated with total hip arthroplasty at advanced stages.¹ Although improvements in

surgical technique and implant design have improved the prosthetic survivorship, periprosthetic infection continues as a leading cause for failure. For a variety of reasons, patients with hemoglobinopathies are at increased risk for infections.² *Edwardsiella tarda*, a member of the family Enterobacteriaceae, has been recognized as pathogenic, especially in patients with

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Fig. 1 – (A) Preoperative evaluation; (B) original post-total hip arthroplasty; (C) prosthetic removal, irrigation and debridement, and antibiotic spacer; and (D) 1-year follow-up post-revision total hip arthroplasty.

underlying illnesses.³ Although there are some sporadic cases highlighting the association between sickle cell disease and *E. tarda* infections, to the best of our knowledge, a periprosthetic hip infection has not been reported.

2. Case presentation

A 23-year-old African-American man with history of sickle beta thalassemia disease presented with worsening pain in bilateral hips, right more than left. He had undergone a procedure suggestive of incision and drainage of this right distal tibia and ankle for osteomyelitis at the age of 5 in Africa. He also underwent bilateral hip surgeries as a child through an anterior approach (details unknown). Five years prior to presentation, he underwent left hip core decompression for early-stage osteonecrosis. On examination, there was global restriction of hip motion and significant pain, right side worse than left. Radiographs showed bilateral Ficat-Arlet stage IV osteonecrosis (Fig. 1A). Due to functional limitation and pain refractory to conservative treatment, he was indicated for right THA. Preoperative workup did not reveal evidence of active infection. He underwent a right THA with a cementless modular stem, ceramic-on-ceramic bearing, and cementless cup (S-ROM modular implant with a Duraloc acetabular cup, DePuy Orthopaedics, Warsaw, IN; Fig. 1B). Intra-operatively, the bones were noted to be very sclerotic and the femoral head

was deformed. There was no clear femoral canal; hence, a canal was created by directing a 3.2 mm guide wire into the diaphysis under fluoroscopic guidance, and progressively hand reaming. During seating of the metaphyseal sleeve, an incomplete calcar fracture at the level of the lesser trochanter was discovered and fixed with two cerclage cables. Perioperative course was otherwise uneventful. He underwent routine protocol which included 24 h of intravenous antibiotics, removal of Foley catheter on first post-operative day, physical therapy, early mobilization, and aspirin and mechanical thrombo-prophylaxis. He was discharged to inpatient rehabilitation, then home uneventfully.

Two months post-operatively, he had a sickle cell crisis which was conservatively managed. At his four-month postoperative clinic visit, a superficial wound dehiscence was observed. He was otherwise asymptomatic, but because of his high-risk status, he was treated with one week of intravenous vancomycin and a two-week course of oral amoxicillin/clavulanic acid per infectious disease recommendations. His dehiscence closed but an area of subcutaneous abscess emerged, from which purulent material was aspirated. He was indicated for surgical exploration and debridement of the wound. During surgery, purulent drainage was noted from a sinus in the fascia lata, but the short external rotators and hip joint capsule were intact. Intra-operative cultures were negative. Per infectious disease recommendations, he was discharged on a two-week course of oral amoxicillin/clavulanic acid.

He was closely followed in our clinic with initial improvement. After 4 weeks, he reported increased pain and wound drainage and was indicated for irrigation and debridement. During surgery, the fascial sinus was observed to communicate with the hip joint. The acetabular component was well fixed, but the femoral component was loose, an antibiotic cement spacer with 6gm of vancomycin and 7.2gm of tobramycin was placed (16-hole LCP-plate, Stryker Orthopaedics, Mahwah, NJ; Fig. 1C). He was made 50% weight bearing. Intra-operative cultures grew pansusceptible *E. tarda*. Urine and stool cultures were negative. He was treated with intravenous cefepime and vancomycin for 3 weeks. He then refused intravenous treatment and was started on oral ciprofloxacin for 3 weeks, to complete a total course of 6 weeks. Eight weeks post-explant (2-week antibiotic holiday), his infectious markers were within normal limits and his hip aspiration cultures were negative.

He was then indicated for second-stage reimplantation; underwent irrigation and debridement, removal of cement spacer, and revision THA with a cementless modular femoral stem, ceramic-on-polyethylene bearing, and a cementless-acetabular component (Restoration-modular stem, BioloX head, Tritanium Cup, and Trident X3 polyethylene-insert; Stryker Orthopaedics, Mahwah, NJ; Fig. 1D). He was treated with IV-cefazolin for seven days until intra-operative cultures were finally interpreted as negative. He was allowed to bear weight as tolerated and followed standard post-operative protocol and was discharged to acute rehabilitation, then home. At thirty months, he reported excellent satisfaction and no activity restrictions.

3. Discussion

Prosthetic joint infection is a serious complication affecting less than one percent of total joint arthroplasties. The gold standard for chronic (type II) infections in the United States remains two-stage revision total hip arthroplasty with placement of a temporary antibiotic spacer and treatment with parenteral antibiotics. Eradication rates following two-stage revision arthroplasty vary between 85 and 100%.⁴

E. tarda is a motile, facultatively anaerobic, gram-negative rod, which is member of the family *Enterobacteriaceae*, and the only species within the *Edwardsiella* genus that is known to cause human infection.⁵ Most virulent strains of *E. tarda* are found in the gut flora of fresh water and marine fish, though other strains have also been found in the normal human flora.³

Serious infections with *E. tarda* have been shown to occur more commonly in patients with an underlying systemic illness.³ Though the correlation between *E. tarda* infection and hemoglobinopathies has not been investigated directly, multiple case reports of *E. tarda* bacteremia in the literature occur in patients with sickle cell disease. The exact pathophysiology behind this increased susceptibility is not currently known. However, it has been shown that *E. tarda* has a high affinity for red blood cells, primarily mediated by specific fimbriae it produces. Furthermore, *E. tarda* is very similar clinically and biochemically to *Salmonella*,³ and share same virulence factors (TS33).⁶ In humans, most *E. tarda* infections are intestinal, infections out of the gastrointestinal tract are rare, but when

they occur, these cause septicemia, meningitis, cholecystitis, and even osteomyelitis.^{6,7}

Patients with sickle cell disease are known to be increasingly susceptible to *Salmonella* and other gram-negative rods due to three main factors: functional asplenia, deficient levels of circulating antibodies, and impaired complement pathways leading to defects in opsonophagocytosis.² Intestinal micro-infarctions due to repetitive vaso-occlusive crises is thought to cause a transient bacteremia. Macrophage saturation will also enable seeding of the gram-negative bacteria to other susceptible areas (e.g. infarcted bone). Knowing that *E. tarda* can be found in normal human gut flora, this mechanism may explain the means of our patient's infection.

Patients in iron-overloaded states may be particularly susceptible to *E. tarda* septicemia.⁷ Increased iron availability promotes the replication of invasive gut flora, increases adherence and translocation, and suppresses host antimicrobial immune-effector pathways, causing worse infections.⁸ Hepcidin, a protein that lowers serum iron, has shown to have increased antimicrobial activity against *E. tarda* compared to other gram-negative bacteria.⁹ In high-iron states, *E. tarda* has increased activity and may become upregulated,⁷ and expresses the enzyme iron-cofactor superoxide dismutase (FeSOD), which inhibits macrophage-mediated immune responses in human hosts,¹⁰ and produces B-hemolysin (pathogenic *Edwardsiella*).⁷

4. Conclusion

To the best of our knowledge, *E. tarda* has not previously been reported as a cause of periprosthetic hip infection. A successful outcome in this case was achieved by following the principles of two-stage reimplantation and antibiotics. Patients with hemoglobinopathies should be counseled about this potentially rare infection.

Conflicts of interest

The authors have none to declare.

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