

Right Knee Ureaplasma Septic Arthritis in an Immunocompromised Host, Requiring Right Hip Disarticulation for Definitive Source Control

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Learning Point of the Article:

Refractory culture-negative septic arthritis in immunocompromised patients warrants early 16S rRNA PCR testing to detect atypical organisms like *Ureaplasma urealyticum*.

Abstract

Introduction: *Ureaplasma urealyticum* is a fastidious, urease-producing bacterium typically responsible for urogenital infections. In immunocompromised hosts, a full-thickness mucosal breach may be complicated by hematogenous spread, leading to septic arthritis in distant joints. *U. urealyticum* is difficult to isolate on routine culture and requires special media or 16S rRNA polymerase chain reaction for detection.

Case Report: We report a 26-year-old immunocompromised female with neuromyelitis optica on long-term cyclosporine and Grave's disease, who developed chronic right knee *U. urealyticum* septic arthritis. She presented with the right calf pain; knee aspiration was turbid but culture-negative on routine testing. Despite 6 weeks of empirical antibiotics, symptoms persisted, and arthroscopic biopsy with 16S molecular testing eventually identified *U. urealyticum*. She was treated with multiple antibiotic regimens, including intravenous (IV) aztreonam, vancomycin, oral levofloxacin, and IV azithromycin, and her immunosuppression was reduced. Despite this, she developed medial tibial plateau osteomyelitis, an intra-articular abscess, and a sinus tract, requiring multiple debridements, cement spacer insertion, external fixation, and eventually two-stage revision knee replacement with flap reconstruction. Cultures remained persistently positive for *U. urealyticum* despite prolonged therapy and repeated surgery. One year after the index revision attempt, she underwent above-knee amputation for source control, followed by hip disarticulation 1 month later due to persistent stump infection. With aggressive wound care, including negative pressure wound therapy and staged dressing de-escalation, the wound achieved complete healing. She was discharged 180 days after hip disarticulation and, at 2-year follow-up, was ambulant with a hip prosthesis, independent in activities of daily living, and had returned to work.

Conclusion: This case highlights the diagnostic challenge and potential severity of *U. urealyticum* septic arthritis in immunocompromised hosts, which may progress to refractory osteomyelitis and necessitate radical surgical measures, including amputation, for definitive source control despite prolonged targeted antibiotic therapy.

Keywords: Septic arthritis, *Ureaplasma urealyticum*, immunocompromised.

Introduction

Ureaplasma urealyticum is a fastidious, urease-producing bacterium typically responsible for urogenital infection [1]. In unusual circumstances, such as in an immunocompromised host, a full thickness breach in the mucosal surfaces may be

complicated by hematogenous spread of the microbe, leading to septic arthritis in distant joints [2]. Septic arthritis caused by *Ureaplasma* species has previously been reported in patients with common variable immunodeficiency and X-linked agammaglobulinemia, as well as in patients on

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Author's Photo Gallery



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immunosuppressive agents with resultant hypogammaglobulinemia states [3].

U. urealyticum is difficult to isolate in culture and requires special culture media. It is not an organism that may be detected on routine microbiological cultures and requires a specific 16S RNA gene polymerase chain reaction for detection.

The authors report a case of an immunocompromised 26-year-old female with the right knee chronic *U. urealyticum* septic arthritis, which demonstrated poor response to multiple debridements and aggressive intravenous (IV) antibiotics over 2 years.

Case Report

A 26-year-old Chinese female with a background of neuromyelitis optica on long-term cyclosporine and Grave's disease first presented to a tertiary hospital in Singapore for right calf pain. A magnetic resonance imaging done for her showed non-specific muscle edema in the posterior compartment of the calf with no collections. Initial knee aspiration, while turbid with a white cell count of 12,300 cell/L, did not grow any microbes on routine cultures. Despite completing 6 weeks of antibiotic therapy, she had persistent

knee swelling and worsening knee pain. A right knee arthroscopic biopsy and washout was performed. Synovium samples were sent for 16 s molecular test on top of routine investigations, which finally yielded *U. urealyticum*. She was initially started on IV aztreonam and vancomycin, although later developed severe drug exanthem and switched to oral levofloxacin and IV azithromycin. Her ciclosporin was switched to oral prednisolone.

She later developed medial tibial plateau osteomyelitis and an intra-articular abscess with anteromedial knee subcutaneous sinus tract. Multiple right knee debridements and washouts were performed, with later insertion of cement spacer and external fixation. Intraoperative samples persistently isolated *U. urealyticum* isolates despite her antibiotic regime.

Seven months later, the patient underwent a right knee washout, first stage revision knee replacement with antibiotic cement spacer and reconstruction with gastrocnemius flap and split skin graft (SSG) (Fig. 1). This wound demonstrated poor healing, requiring application of negative pressure wound therapy with instillation and dwell time (NPWTi-d) (3M™ Veraflo™ Therapy, USA). Nonetheless, despite a second attempt at first stage revision total knee replacement and an interval removal of cement spacer, osteotomy of osteomyelitic bone with insertion of a new cement spacer, there was minimal improvement with persistent *U. urealyticum* isolates.

One year after the index attempt at first stage total knee revision, the patient underwent an above-knee amputation (AKA) for definitive source control. Even so, the right AKA stump wound demonstrated poor healing, which failed to improve despite aggressive debridements and NPWTi-d. She underwent a right hip disarticulation 1 month later, from which there was purulent discharge expressed from the disarticulated hip joint and a sinus tract extending to the superior aspect of the acetabulum (Fig.

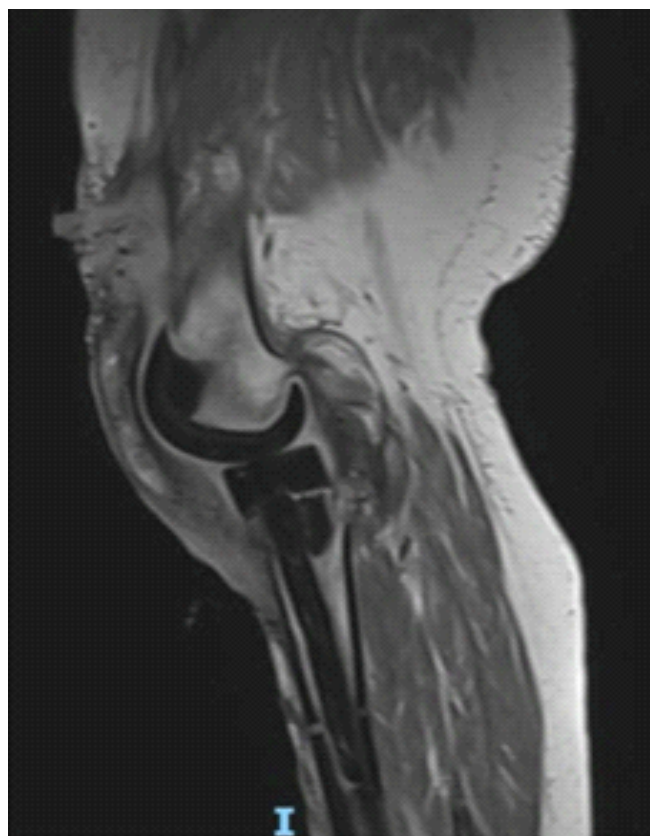


Figure 1: Lateral suprapatellar collection in communication with the joint space and femoral implant, with cutaneous sinus tract after a repeat Stage I revision right total knee replacement.



Figure 2: Remnant sinus tract extending into the right acetabular fossa after hip disarticulation.

2). An SSG was applied over the hip wound 1 month later, which took well after 2 months of debridements and negative pressure wound therapy (Vacuum-assisted closure therapy, KCI USA). The dressing was eventually de-escalated to silver hydrofiber foam dressing (Aquacel Ag, Convatec, USA) for 1 month, and switched over to lipodo-colloid with silver dressing (UrgoTul Ag, Urgo Medical, North America).

Her wound gradually granulated well with complete healing after 1 month. She was successfully discharged on 180 days after her hip disarticulation. At 2 years follow-up post-hip disarticulation, the patient was ambulant with a hip prosthesis, the SSG had healed well with no issues, was independent in her activities of daily living, and had returned to work.

Discussion

Septic arthritis caused by *U. urealyticum* is an rare and challenging condition to diagnose and treat. Due to its unique structure in lacking a peptidoglycan cell wall, *Ureaplasma* is undetectable by routine Gram staining [4], and intrinsically resistant to all beta-lactams [5]; meanwhile, as cells do not undergo de novo synthesis of folic acid, sulfonamides and diaminopyrimidines are rendered ineffective as well [6]. This limits treatment options to macrolides, tetracyclines, and fluoroquinolones, although resistance is an emerging concern necessitating susceptibility testing to guide treatment.

U. urealyticum may cause locoregional infection by attaching to mucosal surfaces through the presence of cytoadherence proteins, with virulence through expression of surface lipoproteins, phospholipases A and C, immunoglobulin A1 proteases, and urease activity [7]. This allows it to mitigate the immune defenses and facilitates the bacterial colonization. The virulence and persistence of *Ureaplasma* may also be attributed to their ability to build biofilms, encouraging microbial survival and persistent inflammation. This presents a therapeutic challenge in systemic eradication of *Ureaplasma*, especially so in this case where antibiotic susceptibility testing for *Ureaplasma* was not readily available. As such, akin to previous reports, this patient received prolonged duration of non-specific broad-spectrum antimicrobial agents, which proved ineffective due to the lack of *Ureaplasma*-specific activity [8-10].

An additional hurdle was the patient's allergy to multiple antibiotics, limiting her antibiotic options. As such, her

prescribed antibiotic therapy was insufficient in containing the infection, which resulted in progressive joint destruction and necessitated increasingly radical surgical management.

The decision to proceed with an AKA and later a right hip disarticulation was undoubtedly a difficult one. A multidisciplinary approach involving orthopedic surgeons, infectious disease specialists, rehabilitation professionals, and psychosocial support would have been essential to weigh the risks and benefits of such extensive surgical interventions in this complex case. In addition, patient's outcome may have been influenced by the delayed diagnosis of chronic *U. urealyticum* septic arthritis. This condition is often insidious and may mimic other causes of chronic joint inflammation. Increased awareness among healthcare providers, especially in the context of immunocompromised patients with atypical presentations, is crucial for early recognition and appropriate management.

Despite the extensive surgical burden, this case demonstrates the potential for meaningful functional recovery even after major limb loss. The patient was successfully fitted with a hip prosthesis post-disarticulation, allowing independent ambulation and reintegration into the workforce. Once again, the involvement of a multidisciplinary team is cardinal to coordinate long-term care of these complex patients as part of a broader strategy to restore function and quality of life.

Conclusion

The presented case emphasizes the challenges encountered in managing chronic *U. urealyticum* septic arthritis in an immunocompromised with multiple antibiotic allergies. The poor response to antibiotic therapy and subsequent need for extensive surgical interventions highlight the importance of early recognition, appropriate antibiotic selection, and a multidisciplinary approach to optimize patient outcomes. Further research and case reports are warranted to guide clinicians in effectively managing similar complex cases in the future.

Clinical Message

In immunocompromised patients with treatment-refractory septic arthritis, early molecular testing and a low threshold for radical surgical debridement are key to preventing progressive, limb-threatening infection.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given the consent for his/ her images and other clinical information to be reported in the journal. The patient understands that his/ her names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Conflict of interest: Nil **Source of support:** None

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