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Ralstonia pickettii infection in total knee arthroplasty: From isolation and identification to revision surgery

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Abstract:

Ralstonia pickettii remains a rare cause of periprosthetic joint infections, may therefore elude diagnosis, and causes a delay in optimal management. We describe our experience with a case of *R. pickettii* prosthetic knee joint infection to highlight key features in clinical presentation, isolation, identification, and optimal management.

Keywords:

Knee joint infection, *Ralstonia pickettii*, periprosthetic joint infection

Introduction

Periprosthetic joint infections (PJIs) are a devastating event that impacts significantly a patient's physical, psychological, and social well-being and imposes a substantial financial burden on global health-care systems. A variety of diseases causing microorganism are responsible for PJIs with the most common offender being staphylococci.[1] *Ralstonia* PJIs occur rarely. *Ralstonia pickettii*, an aerobic gram negative, non-fermentative rods. They are commonly found in the soil, water and are oxidative positive bacterium of the *Pseudomonas (Burkholderia)* group. Although these are generally of minor clinical significance; however, comorbidities, acquired or therapeutic immunosuppression, and cystic fibrosis have been identified as a significant risk factor for primary bacteremia.[2-4] While incidences of PJIs in hip and knee arthroplasties have increased over the past decades, there have been only infrequent case reports of *R. pickettii* PJIs.[5,6] Due to the rarity of these PJIs in knee arthroplasty, the optimal management remains controversial. Failure to treat PJIs effectively deteriorates joint function and can lead to joint fusion or amputation. In the present report, we aim to summarize the key features in clinical presentation, isolation, identification, and optimal management of *Ralstonia* PJIs. To the best of our knowledge, this is the first confirmed case of PJIs in knee arthroplasty due to *R. pickettii* in India. The authors have obtained the patient's informed written consent for print and electronic publication of the case report.

Case Report

An 87-year-old female patient presented to our outpatient department with pain, swelling, and discharging sinus right knee with restriction of movements for 5 months. She was unable to bear weight. She had undergone bilateral total knee arthroplasty in 2009 for osteoarthritis of both the knees. Two years after the index surgery, the patient had pain and swelling in the right knee. The initial laboratory profile was not suggestive of any infection; therefore, antibiotics were not started. The patient was responded to supportive treatment. Four years after the initial episode, the

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patient complained of continued pain and swelling in the right knee following minor trauma. She took symptomatic treatment. In mid-November 2015, she had noticed purplish skin discoloration over the right knee with itching and burning sensation. She was febrile. In December, patients complained of burning pain in joint, pus discharge, difficulty in walking, and occasional fever. Finally, she approached our institute for further investigation and management. On admission, the patient was febrile (38°C). She was on antihypertensive medications and antibiotic (tablet amoxicillin and potassium clavulanate 625 mg oral). She had no history of diabetes and other comorbidities. Physical examination revealed warmth, redness, pigmentation, and swelling in the region of right knee and a pus discharging sinus on anteromedial aspect [Figure 1]. The movements were painfully restricted. The remaining physical examination was unremarkable. Erythrocyte sedimentation rate (ESR) (90 mm/1 h) and C-reactive protein (CRP) (280 mg/dL) were elevated. The remaining laboratory parameters were within normal limits. The culture of knee aspiration was negative. Standardized anteroposterior and lateral X-ray of right knee showed prosthetic loosening with osteopenia and component migration (tibial tray) [Figure 1]. A two-stage revision of the total knee arthroplasty was decided. Informed consent for the surgical procedure was obtained. The revision surgery consisted of a two-stage approach. The first stage (DRICS: Debridement Implantation of Cement Spacer) was performed under spinal anesthesia through previous midline incision medial parapatellar arthrotomy. It comprised of resection arthroplasty (removal of prosthesis), thorough debridement, radical synovectomy, removal of cement, and irrigation of joint followed by implantation of a temporary custom-made antibiotic (0.55 g of gentamicin sulfate with additional 4 g vancomycin) laden polymethylmethacrylate spacer. Monofilament suture was used for wound closure in layers under negative suction (left for 48 h) [Figure 2]. Infected fluid, periprosthetic tissue (from five different sites) samples has been sent for microbiology, histopathology, and molecular evaluation. Removed prosthesis was sent for sonication. Infected samples and polymerase chain reaction (PCR) (16sDNA sequencing) were positive for *R. pickettii*. A bulky Jones dressing with a splint in extension was applied, and the patient was mobilized with walker support under the expert guidance. As per sensitive antibiogram, antibiotic therapy with intravenous cefoperazone + sulbactam (1.5 g BD) for 8 weeks and tablet trimethoprim/sulfamethoxazole 1 BD was continued for 10-week postprocedure. Prophylactic low molecular weight heparin (enoxaparin) was advised for 4 weeks. The patient was discharged on 15th day of surgery and was allowed guarded ambulation. A follow-up was done at the outpatient department first at 14 day after surgery for stitch removal and assessment of surgical wound, at 6 weeks with a new assessment of ESR and CRP, and finally at 12 weeks to assess the signs of infections (clinically, radiographically, and inflammatory markers) after the first stage. She responded well to the first stage. Fourteen weeks after the first stage, the patient's knee was free of any sign of clinical infection and she had normal inflammatory markers. The patient was readmitted for the second stage. It includes the removal of cement spacer, debridement, and reimplantation using THE PFC® SIGMA REVISION KNEE SYSTEM using the medial parapatellar approach under spinal anesthesia [Figure 3]. A deep perispacer tissue culture, after second stage procedure, yielded no bacterial growth. She received 1 week of intravenous cefoperazone + sulbactam (1.5 g BD), followed by 2 weeks of tablet trimethoprim/sulfamethoxazole 1 BD. She was mobilized on the 1st postoperative day under supervision of physiotherapists. Full weight-bearing was allowed at

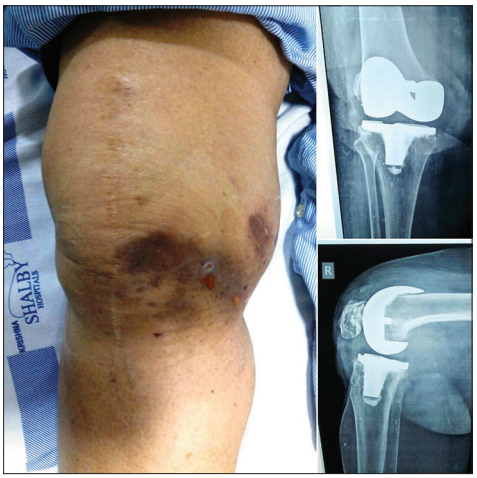

Figure 1: Clinical picture (redness, pigmentation, and swelling in the region of right knee and a pus discharging sinus). Standardized anteroposterior and lateral X-ray of right knee showed prosthetic loosening with osteopenia and component migration (tibial tray)

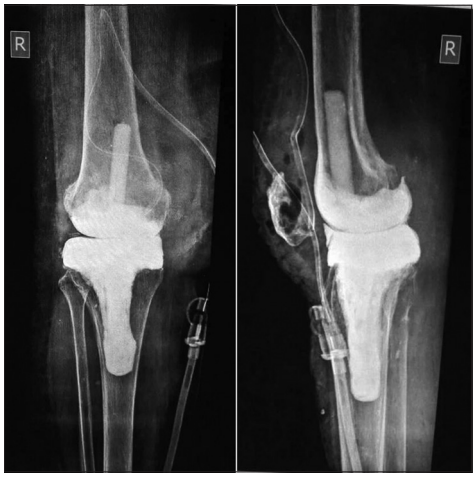

Figure 2: Standardized anteroposterior and lateral X-ray of right knee: Debridement Implantation of Cement Spacer

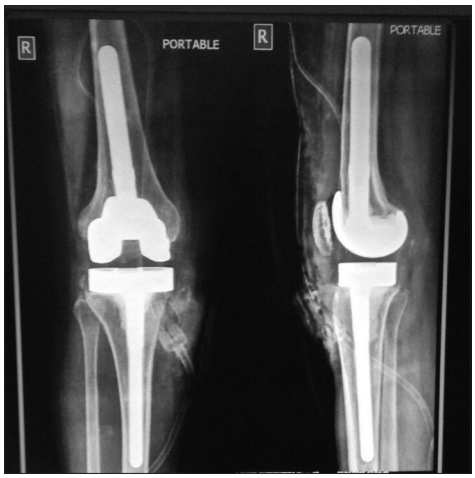

Figure 3: Standardized anteroposterior and lateral X-ray of right knee: THE PFC® SIGMA REVISION KNEE SYSTEM

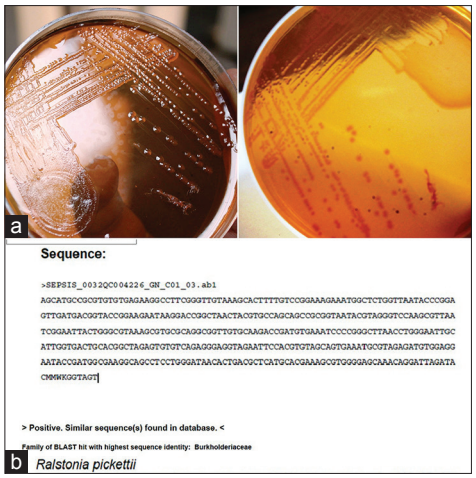

Figure 4: (a) Nonlactose fermenting, shiny colonies of *Ralstonia pickettii* on MacConkey agar; (b) 16S rRNA gene sequence analysis

the first follow-up. She returned to outpatient department for postoperative follow-up at 3, 8, and 20 weeks and then yearly for clinico-radiological evaluation of the operated knee. Twelve months postoperatively, her knee remains pain free and stable, without any signs of persistent or reinfection since the initial second-stage revision with good range of movements.

Microbiological procedure

Infected joint fluid has been aspirated in sterile syringe and 3 ml each inoculated into BACTEC Peds Plus and BACTEC Myco/F vials. Periprosthetic tissue specimens from five different sites have been taken in sterile container containing Stuart transport medium and sent for Culture. Tissue was vortexed, grinded, and cultured on Sheep Blood Agar, MacConkey agar with crystal violet, Nutrient Agar, and Sabouraud Dextrose Agar incubated at 37°C. The explanted orthopedic devices were sonicated.[7] After two overnight incubations from the tissue culture, and subculture of both positive BACTEC vials and sonication fluid, nonlactose fermenting, and oxidase-positive shiny colonies were identified [Figure 4a]. For identification and susceptibility testing, colonies were processed in Vitek2 compact instrument. Vitek2 compact has given identification as *R. pickettii*. As it is unusual organism, colony further processed for bacterial 16S rRNA gene sequence analysis for confirming the phenotypic method of identification by genotypic method. Gene sequencing was identified (as family Burkholderiaceae, species *R. pickettii*) [Figure 4b]. Susceptibility testing result showed resistant to most antibiotics. As the organism was unusual, the surveillance cultures were sent, but unfortunately, we were unable to determine the source of infection.

Discussion

PJIs are probably the most dreaded complication in patients with knee arthroplasty and it has been demonstrated as a microbial biofilm-associated infection with poor prognosis.[8] Although the most common offending organism for majority of PJIs are Gram-positive bacteria, Gram-negative PJIs account for a substantial percentage of all PJI episodes.[9] Although rarity has been regarded by some evidences as a cause of PJIs,[5,6] *R. pickettii* has been identified as the causative agent of several serious infectious conditions range from minor infections to more severe invasive infections.[10] The increasing incidence of nosocomial *Ralstonia* infections is of particular concern for immunocompromised and cystic fibrosis patient population, as these groups of patients are at high risk for complications associated with it.[2-4] It is an emerging global opportunistic pathogen usually found in a nosocomial setting in immunocompromised and/or immunosenescence patients, as seen in the present case. The elderly populations (as present case is 87-year-old female) are in an Immunosenescence[11], the state that contributes to the increased susceptibility to develop this infection. Currently, paucity exists of literatures that have comprehensively described the *Ralstonia* prosthetic knee joint infection. These organisms are well adapted to oligotrophic or low nutrient conditions. They have been recovered from numerous water sources/supply (including municipal drinking water supplies and hospital water supplies), from medicine vials, contaminated saline, irrigation system or from blood culture bottles.[12] Furthermore, *Ralstonia* species can cause catheter-associated bloodstream infections as these bacteria readily form biofilm. Cure often requires the removal of foreign material. Although the exact mode of transmission is unknown in the present case, it seems likely that it involves exposure to contaminated medical devices.

Sonication (ultrasound waves) dislodges biofilms from the surface of explanted arthroplasties, releases active microorganism, promotes microbiological

culture, enhances culture sensitivity, and improves the microbiological diagnosis of PJIs.[13] Sonication followed by PCR and sequencing imparts a high level of accuracy in organism identification in atypical PJIs[13] as in the present case. Being intrinsically resistant to many antimicrobial agents, it is often difficult to treat and eradicate *Ralstonia*.[4] Ryan *et al*. demonstrated that this could be attributed to the presence of mobile genetic elements.[14]

The primary objective in treating PJIs is to eradicate the infection, attainment of optimal pain relief, and restoration of function. The treatment of choice for PJI caused by *R. pickettii* has not yet been established. Several treatment options are available for the optimal management of PJIs.[15-18] At present, two-stage revision remains the gold standard for treatment of infected total knee arthroplasty.[19] We were aiming at eradication of the infection and preservation of the joint function in the present case. Authors felt that she had two available treatment options: debridement antibiotics and implant retention (DAIR)[20] or two-stage revision surgery. There are insufficient evidence-based literatures to claim clear benefit for DAIR versus revision surgery as a primary modality. Furthermore, DAIR has stringent indications.[20] The authors have deferred DAIR as the first option in the present case as factors, namely, immunosenescence status, loosened prosthesis (doubtful prosthesis-bone interface), and presence of sinus with purulent discharge has failed to yield the satisfactory long-term outcome. The patient underwent two-stage revision arthroplasty combined with organism-specific antibiotic therapy. After 12 months of follow-up, she has had no evidence of residual and/or recurrent infection and has stable knee with a good range of movements.

Ralstonia infections are usually uncommon, when clinical isolate of *R. pickettii* is detected, medical device contamination should be suspected, and an epidemiological investigation should promptly be initiated to elucidate the source of contamination. Nosocomial organisms are also commensal organism; therefore, it is imperative to determine whether the isolate recovered from the patient is a pathogenic strain responsible for infection or a commensal contaminant. Accurate and reliable taxonomic classification of pathogens is critical so that an early and appropriate treatment can be started. The integration of molecular typing with conventional culture and sonication process has been proven to diagnose these nonfermenters more precisely as in the present case.

Immunosenescence and/or immunocompromised population and patients with endovascular devices with a history of joint replacement, when presented to outpatient department with nonspecific infectious signs and bacteremia, should prompt special precautions and searches for infections by uncommon pathogen. Previously, being reported as *Burkholderia* species, establishing a diagnosis of *Ralstonia* PJIs is an arduous task and misdiagnosis is an issue. Delayed diagnosis and misinterpretation can be hazardous to patients of PJIs caused by *R. pickettii*. The authors concluded that early detection and diagnosis and prompt initiation of sensitive antimicrobial therapy combined with two-stage revision surgery for treatment of *Ralstonia* PJIs are associated with high rate of favorable outcomes. DAIR is an option in acute cases with a stable prosthesis and antibiotic-sensitive organisms.

Conclusion

With increasing in the susceptible population, a rise in incidence of *Ralstonia* as an emerging cause of prosthetic joint infection is to be expected in the future. Optimal treatment strategy has not been well studied; two-stage revision knee arthroplasty combined with antimicrobial therapy is likely the best treatment for this kind of infection. Broad-range bacterial 16S rRNA gene sequence analysis followed by sequencing is imperative for identification of unusual microorganisms.

Declaration of patient consent

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

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Conflicts of interest

There are no conflicts of interest.

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