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Title: Septic Arthritis due to *Cellulosimicrobium cellulans*

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Septic Arthritis due to *Cellulosimicrobium cellulans*

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Abstract

*Cellulosimicrobium cellulans* has been reported as a rare cause of human pathogen. Infections mainly occur in immunocompromised patients and very often associated with foreign body. We report the first case of septic arthritis caused by *C. cellulans* in an immunocompetent patient. Our patient suffered a penetrating palm tree thorn injury in his left knee eight weeks before admission. Although no foreign objects were found they were suspected because previous reports suggest a frequent association with this microorganism, and open debridement was performed. Removal of foreign bodies related with this organism must be considered a high priority treatment in these patients to achieve a complete recovery.

CASE REPORT

An 81-year-old man was admitted to our department with a 6-day history of pain, loss of motion, erythema and swelling in his left knee. His past medical history was significant for gout, mild mitral regurgitation, hypertension and moderate chronic renal insufficiency, and eight weeks before he was admitted in our department with a septic
arthritis of the same knee caused by *Pantoea agglomerans* after suffering a penetrating injury in his left knee with a palm tree thorn, with good response to treatment with intravenous Ceftriaxone, 1 g per day for 15 days and Levofloxacin, 250 mg per day for 15 days).

Physical examination showed an afebrile patient with a painful, warm, swollen and tender left knee. Limitation of active and passive range of motion was also noted. Otherwise, the examination was unremarkable. Laboratory tests showed an elevated serum C-reactive protein (CRP) level (17 mg/dl; normal <0.5) with a normal blood cell count. Arthrocentesis yielded 30 ml of yellowish fluid. Direct microscopic examination of the synovial fluid revealed many leucocytes and crystal analysis with compensated polarized light was negative. Gram stain was negative and empiric treatment with Levofloxacin (500 mg initial dose, then 250 mg every 24 hours, because of renal failure, creatinine clearance 40 ml/min) intravenously was started. Three days after admission, a gram-positive rod grew in synovial cultures and was subsequently identified as *Cellulosimicrobium cellulans*. Identification was initially made by MALDI-TOF MS® (Bruker Daltonics) and lately confirmed by semiautomatic culture system (VITEK-II). The microorganism recovered was fully susceptible to vancomycin (MCI = 1 µg/ml) and linezolid (MCI = 1 µg/ml), and showed intermediate susceptibility to tetracyclines (MCI = 4 µg/ml), and levofloxacin (MCI = 3 µg/ml). The isolate was interpreted as a contamination, so we continued therapy with Levofloxacin.

Three days later, due to the persistence of symptoms and the high levels of CRP (23,49 mg/dl) and Erythrocyte Sedimentation Rate (ESR) (99 mm/hr; normal < 13 mm/hr), a new arthrocentesis was performed and *C. cellulans* was again isolated. Linezolid was added based on the lack of response to treatment and suspicion of antibiotic-resistant
gram-positive cocci infection as a causative agent, especially MRSA. However arthritis symptoms worsen and a new joint fluid aspiration was performed 7 days after admission showing this organism in the synovial cultures. Susceptibility pattern was unchanged with respect to the first isolated. A 16 rRNA sequencing was carried out, which confirmed the pathogen as *C. cellulans* (GenBank accession number JN695266). A new laboratory evaluation showed persistence of raised CRP levels (22.51 mg/dl) and high D-dimer levels (4.55 mg/L; normal <0.5 mg/L).

A colour doppler ultrasound of the left leg was negative and a magnetic resonance imaging of the left knee showed a 20 x 1.7 x 3.2 cm sized abscess along the inner portion of the lower thigh, located from the outer surface of the *gracilis* muscle to the internal lateral ligament and articular capsule of the knee, and other abscess posterior to the superior tibio-fibular joint of 18 mm in diameter, bone erosions, a Baker’s cyst and synovitis (Figure 1). An ultrasound examination confirmed the presence of both abscesses but foreign bodies were not found. Treatment with levofloxacin was stopped and we add oral rifampin to linezolid. The patient subsequently underwent surgery with debridement and drainage of the abscesses.

After surgery we saw an important reduction of CRP (22.51 mg/dl to 3.15 mg/dl) and ESR levels (99 mm/hr to 21 mm/hr), improvement of arthritis symptoms and general condition and he was discharged to complete a six-week antibiotic regimen with rifampin and linezolid. At the follow-up visits three and six months later our patient was symptom free and the acute-phase reactants were negative.

**Discussion**

Septic arthritis is defined as a joint infection caused by pathogenic inoculation of the joint either directly or more commonly by haematogenous spread [11]. Plant thorn
penetration after injury and the remaining parts of the thorn as a foreign body have been described as a rare cause of microorganism inoculation and, subsequently, septic arthritis [3]. In these cases *Pantoea agglomerans*, a gram-negative bacterium, is the most frequently isolated microorganism from synovial fluid specimens and blood cultures [3, 20]. Other bacteria, such as *Serratia fonticola*, have been also related with this mechanism of infection [6].

We report the first case described of septic arthritis caused by *Cellulosimicrobium cellulans* (equivalent name *Oerskavia xanthineolytica*) in an immunocompetent patient after a palm tree thorn injury. The genus *Cellulosimicrobium* is composed of three species, namely, *C. cellulans*, *C. funguei* and *C. terreum*. *Cellulosimicrobium* are non-acid fast, catalase positive, gram-positive bacilli. This genus belongs to the suborder Micrococcineae, order Actinomycetales and class Actinobacteria [1, 16, 17, 24]. *C. cellulans* is an uncommon human pathogen that has been rarely related with human infection that inhabits soil, grass cuttings, water, decaying plant material and brewery sewage [1, 24]. It has been mostly reported in immunocompromised hosts and associated with the presence of a foreign body including plant thorns [19]. Isolation of this organism from sterile fluids as synovial fluid should be interpreted with caution. There have been 27 case reports published so far describing infection due to *Cellulosimicrobium* including bacteraemia, peritonitis, meningitis, endocarditis, gangrenous colicistitis, keratitis, pyonephrosis, soft tissue infection and associated to bone marrow transplantation among them [4, 5, 13, 16]. Prosthetic joint infection and pyogenic flexor tenosynovitis, both foreign-body-associated infections, have also been reported [13, 16], but a case of septic arthritis due this microorganisms has never been describe. In most of the cases already reported involving *C. cellulans* (14 of 21 cases),
infection was secondary to a medical device and removal of the device was required for resolution of the infection in the majority of them. [4, 7, 9, 10, 14, 16, 18, 19, 21]. In other two cases, infection was related with an invasive procedure, such as cholangio-pancreatic endoscopy and steroid injections [16]. Our patient reported that eight weeks prior to admission he had been injured by a palm tree thorn on the medial side of his left knee. The patient was then also admitted to our department for further investigation and 

*P. agglomerans* was isolated on synovial fluid, with a complete resolution after two weeks of successful antibiotic therapy. The possible presence of a foreign body seems to be related with the first episode of arthritis after the palm tree thorn injury. We believe that *C. cellulans* might have been present since the moment of the injury but the relatively non-virulent and smoldering course of this pathogen [7, 13] and the use of levofloxacin to treat the *P. agglomerans* infection, could have delayed the presence of symptoms 8 weeks after pathogen inoculation. Involvement of direct intra-articular inoculation during arthrocentesis after careful aseptic and any source other than a foreign body were considered highly unlikely. 

Although antibiotic susceptibility testing demonstrated intermediate susceptibility to levofloxacin, because of high penetration of levofloxacin in joint fluid exceeding serum levels we believe the inadequate response to therapy was due to biofilm formation of foreign body-associated infection [15, 22]. However, we can not rule out that persistence of the clinical picture was secondary to a delay in the initiation of appropriate therapy. In addition to susceptibility pattern, the absence of previous reports of arthritis caused by this microorganism prompted us to consider *C. cellulans* as a contamination and that the responsible pathogen for the infection was *P. agglomerans*. 

Two cases of previously healthy patients have been reported [2, 19], however, *C. cellulans* has been described as an opportunistic pathogen in humans and as a cause of
infection in immunocompromised patients in the context of HIV infection, tumor-induced immunosuppression and post-transplant patients [4, 8, 19]. Furthermore, several patients presented end-stage renal disease as the most frequent underlying condition [14]. Our patient was not immunocompromised but he related history of moderate chronic renal insufficiency. 

*C. cellulans* has been reported as resistant to erythromycin and other macrolids [7, 18] but is considered vancomycin susceptible in vitro, being the therapy of choice in most of the cases reported. However, removal or early debridement has been indispensable in most of the cases when infection was related with a foreign body. [7, 10]. In nine of the fourteen cases related with foreign bodies, monotherapy or a prolonged course of combined antibiotic therapy were not enough to eradicate the pathogen completely [16], and patients only improved after the foreign body had been removed. This lack of antibiotics efficacy has been related with an inadequate penetrance in the infected area, which inhibits but not eradicates the microorganism [4, 12]. 

In our case, although no foreign objects were found, they were highly suspected as this microorganism has been often related to foreign body-associated infection and resolution was not achieved until debridement and drainage of the abscess were performed. Association of prolonged course of combined antibiotic therapy with linezolid and rifampin was needed for a complete resolution of the infection, after not improving with Levofloxacin and linezolid after antibiotic susceptibility testing. The association of Rifampin to other antibiotic has been described in three cases with good response [10, 16, 23].

To our knowledge, our patient represents the first documented case of a septic arthritis due to *C. cellulans*, a human opportunistic pathogen with increasing relevance in the last years. Furthermore, if history of previous penetrating skin injury is reported by the
patient and this microorganism is isolated from sterile fluids, the presence of foreign bodies must be investigated and a prolonged course of combined antibiotic therapy must be started after a comprehensive microbiologic evaluation. The presence of a foreign body requires a removal and early invasive surgical debridement is essential in cases where foreign body is not found. A prompt intervention in these cases improves the prognosis and maximizes the possibility of cure reducing the long-term functional problems associated with arthritis.
References


Legends:

**Figure 1.** Magnetic resonance imaging of the left knee. (a) Axial T2-weighted fat suppressed shows a 20 x 1.7 x 3.2 cm sized abscess along the inner portion of the lower thigh (narrow arrow), bone erosions and synovitis (b) coronal T1-weighted shows the same abscess (narrow arrow) and other abscess posterior to the superior *tibio-fibular* joint of 18 mm in diameter (large arrows).