First Report of Septic Arthritis Caused by *Klebsiella oxytoca*[▽]

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Received 15 February 2010/Returned for modification 9 April 2010/Accepted 11 June 2010

***Klebsiella oxytoca* is known to be a pathogen in immunodeficient adults and children. Here we report the first case of a *K. oxytoca* infection associated with spontaneous arthritis of the knee in a child with no history of immunosuppressive therapy or previous bacterial infections. Despite an initial antibiotic treatment failure, a second treatment led to a cure of the infection with no joint sequelae.**

CASE REPORT

The patient, a 30-month-old girl, was referred to the Pellegrin Children's Hospital of Bordeaux for febrile arthritis of the left knee. There was no previous medical history of bacterial infection, especially urinary tract infection, or recent hospitalization. Upon admission, the patient was febrile with a fever of 39°C and had presented arthritis of the left knee for 2 days. A mild nonsuppurative recurrent eczema was observed in the creases of the elbows, on the back of the hands, and on the back of the knees. Biological tests revealed a marked elevation of C-reactive protein (52 mg/liter) and fibrinogen (5.7 g/liter) and a white cell count of 17.5 g/liter with 37% polynuclear neutrophils. An articular puncture was performed and showed a purulent liquid with 5.1×10^4 cells/mm³, 100% of which were polymorphonuclear neutrophils. The patient had been vaccinated according to the French vaccination schedule, the last vaccine injection having been administered 1 year before the septic arthritis appeared. These vaccinations comprised four injections of seven-valent pneumococcal conjugate vaccine and four injections of a combined diphtheria, tetanus, acellular pertussis, inactivated polio, and *Haemophilus influenzae* type b vaccine. The pentavalent vaccine (diphtheria, tetanus, *H. influenzae* type b, inactivated poliovirus, and acellular pertussis) and seven-valent pneumococcal conjugate vaccine were administered at 2, 3, and 4 months of age. The patient received a booster dose of seven-valent pneumococcal conjugate vaccine at 12 months of age and a booster dose of pentavalent vaccine at 18 months of age. All of the vaccines were injected into the anterolateral thighs.

Septic arthritis in young children who have received all of the recommended vaccinations is due mainly to *Staphylococcus aureus* and *Kingella kingae* and more rarely to *Streptococcus pneumoniae* (3, 17, 21). *S. aureus* is a pathogen associated with a poorer prognosis, in contrast to *K. kingae*, which is easier to eradicate. Considering the likelihood of an *S. aureus* infection, the patient was treated with oxacillin (150 mg/kg/day) and gentamicin (3 mg/kg/day) immediately after the puncture (9),

knowing that *K. kingae* is also sensitive to oxacillin. After 3 days of this treatment, the patient remained febrile (38.8°C) with an inflamed knee, pain, and limited movement. The biological markers of inflammation continued to rise despite active (*in vitro*) antibiotic treatment (see below), as demonstrated by increased C-reactive protein (238 mg/liter) and fibrinogen (6.8 g/liter) levels. Then, on the 4th day of hospitalization, the antibiotic treatment was changed according to bacterial genotypic and phenotypic identifications.

K. kingae is now considered to be the main cause of osteoarticular infection in young children (3, 13, 17, 21), but its bacteriological diagnosis is difficult, making PCR an ideal tool for the diagnosis of this infection. Thus, a real-time PCR targeting *K. kingae* (3) was performed on the synovial fluid immediately after the puncture, as well as real-time PCR targeting *S. aureus* (16) and *S. pneumoniae* (8). Negative results were observed for these bacteria, while a universal 16S rRNA gene PCR used as the PCR control (15) gave an amplification, attesting to the presence of a bacterium. 16S rRNA gene amplification and sequencing (14) were then performed using synovial fluid. The 1,446-bp amplified primerless 16S rRNA genes sequence was compared to the GenBank database (2), which showed 99% identity in a 1,446-nucleotide overlap with *K. oxytoca* strain 5 (GenBank accession number AB353045). This species identification was also confirmed by using the bioinformatics bacterial identification tool BIBI (4).

With regard to phenotypic identification, the synovial fluid culture grew yellow mucoid colonies on a bromocresol purple lactose agar plate (bioMérieux, Marcy l'Etoile, France) after an 18-h period of incubation at 37°C. Identification of the bacteria to the species level was first carried out using the API 20E conventional biochemical identification system (bioMérieux), and susceptibility testing was performed by disk diffusion. The identification and susceptibility testing were both confirmed using the Phoenix automated microbiology system (BD Diagnostics, Le Pont-de-Claix, France). Both methods identified *K. oxytoca* harboring an intrinsic low-level resistance to ampicillin and ticarcillin. The isolate remained susceptible to other β -lactam antibiotics (amoxicillin-clavulanic acid, piperacillin-tazobactam, cephalothin, cefoxitin, cefotaxime, ceftriaxone, ceftazidime, cefepime, ceftiofur, aztreonam, imipenem), to aminoglycosides (gentamicin, tobramycin, amikacin, netilmicin), to fluoroquinolones (norfloxacin, ofloxacin,

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[▽] Published ahead of print on 23 June 2010.

ciprofloxacin), and to doxycycline, sulfamethoxazole/trimethoprim, and fosfomycin. Moreover, to confirm the identification to the species level, analysis using a matrix-assisted laser desorption ionization–time of flight mass spectrometer (Ultraflex III TOF/TOF version 3.0; Bruker Daltonics, Wissembourg, France) with the Bruker BioTyper database, version 2.0, identified *K. oxytoca* with a score of 2.212 compared to *K. oxytoca* ATCC 700324. The same identification was obtained by performing 16S rRNA gene amplification and sequencing on the mucoid colonies. In accordance with the antimicrobial susceptibility test results, the patient received ceftriaxone (50 mg/kg/day) and amikacin (15 mg/kg/day) for 2 days, followed by 13 days of ceftriaxone alone. She was nonfebrile 3 days after the administration of ceftriaxone and recovered her knee mobility at day 5. She was discharged from the hospital with ciprofloxacin antibiotic treatment (30 mg/kg/day) for 2 months. Three months later, the patient had completely recovered and an X-ray of the left knee showed no sequelae.

Acute forms of septic arthritis in adults are usually caused by bacteria such as *S. aureus*, *S. pneumoniae*, hemolytic streptococci, or gonococci, whereas in children they are caused mainly by *S. aureus* or *K. kingae* and more rarely by *S. pneumoniae*, *Streptococcus pyogenes*, coagulase-negative staphylococci, hemolytic streptococci, or *H. influenzae* type b (3, 17, 21). Septic arthritis in children is a serious infection that may be associated with long-term sequelae. Septic arthritis due to *Klebsiella* species is a rare event which occurs in patients with underlying predisposing conditions or treatments affecting the immune response (18). In these cases, *Klebsiella pneumoniae* is the most frequent pathogen incriminated. *K. oxytoca* is a member of the family *Enterobacteriaceae* known to be responsible for nosocomial infections and urinary tract infections (6, 7, 10), respiratory tract infections, surgical wound infections, and also colitis and diarrhea after antibiotic use (6, 7, 10). Lin et al. reported that the clinical syndromes associated with *K. oxytoca* infection include hepatobiliary infections (58% of patients), primary bacteremia (23%), intravascular device-associated infections (7%), urinary tract infections (5%), peritonitis (2%), and skin and soft tissue infections (5%) (12). Most (93%) of these patients had underlying diseases, including hepatobiliary diseases (53%), neoplastic diseases (42%), and diabetes mellitus (16%). *K. oxytoca* infection was also associated with active ankylosing spondylitis in adults (5, 19). *K. oxytoca* infections have been described in acute bacteremia in neonatal units. Numerous studies have assessed the etiological agents of septic arthritis in children, but *K. oxytoca* has never been identified (1, 17, 20). Here we report the first case of community-acquired *K. oxytoca* arthritis in a young child. In the present case, the persistence of arthritis and fever was due to treatment failure. Indeed, in septic arthritis in children, empirical antibiotic treatment with penicillin M (usually oxacillin), which targets the most frequently encountered bacteria, i.e., *S. aureus* and *K. kingae*, is recommended. In the absence of currently recommended vaccinations, septic arthritis due to *H. influenzae* type b or *S. pneumoniae* is also suspected and dual-antibiotic treatment with penicillin M and an expanded-spectrum cephalosporin is recommended. In the present case, the

patient had received all of the injections of the French recommended vaccination schedule. Hence, she was not initially treated with an expanded-spectrum cephalosporin. Moreover, it should be noted that the last vaccine was administered 1 year prior to the onset of arthritis and at a good distance from the area of arthritis, excluding the possibility of a relationship between vaccination and the onset of arthritis symptoms. The bacterial source was not found. No urinary tract analysis was performed after the culture results, since the patient had already received antibiotics. Nevertheless, the patient did not initially present symptoms of urinary tract infection. The patient presented eczema. Eczema is known to be a risk factor for *S. aureus* infections, but no case of eczema related to *Klebsiella* species infection has been reported in the literature (11). Moreover, it was a very mild nonsuppurative eczema. It is unlikely that this eczema was the source of the *K. oxytoca* infection. To the best of our knowledge, this is the first report of *K. oxytoca* septic arthritis reported in a child with no immunosuppressive therapy or history of bacterial infections.

Nucleotide sequence accession number. The sequence of the *K. oxytoca* 16S rRNA gene (1,446 bp) has been submitted to GenBank under accession number GU119910).

We are grateful to Christophe Hubert and Jean-William Dupuy from the Genomic Platform of the Bordeaux 2 University for their technical support in sequencing and mass spectrometry analyses.

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