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Case report

Moraxella nonliquefaciens septic arthritis in an immunocompetent child: A case report

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ABSTRACT

A 2-year-old, previously healthy, male presented with an insidious history of intermittent left knee pain and edema who had been evaluated in the emergency department on multiple occasions with unremarkable imaging and normal laboratory results. On the day of presentation, he had mild edema of the left knee and inability to bear weight. Synovial fluid analysis showed an elevated white cell count with neutrophil predominance and mildly elevated inflammatory markers, consistent with septic arthritis. He underwent knee arthrotomy with irrigation and debridement and was initiated on broad spectrum antibiotics. Cultures were negative, polymerase chain reaction for MRSA and *Kingella kingae* were negative. He was started on a fifth-generation cephalosporin with resolution of symptoms, marked clinical improvement and normalization of inflammatory markers. The identification of the etiologic agent was possible due to detection of bacterial 16S rRNA gene amplification by PCR for *Moraxella nonliquefaciens* in the synovial fluid. He completed a course of 3 weeks of parenteral antibiotics at home with full recovery.

Introduction

Septic arthritis (SA) is an uncommon but urgent infection among children of industrialized countries, affecting nearly 1 in 100,000 children annually, with devastating sequelae if not identified and treated in a timely manner [1,2]. Most affected patients are male, frequently infants or toddlers, or have predisposing factors such as lines, prematurity, sickle-cell disease, among others [1]. These infections are most commonly caused by hematogenous spread of bacteria but can also be secondary to direct inoculation or contiguous infection. The most common pathogens vary by age and include *Staphylococcus aureus,* group A Streptococci*, Streptococcus pneumoniae, Haemophilus influenzae*, *Kingella kingae*, Salmonella species and *N gonorrhea* [1,2]. Synovial fluid analysis is required to confirm the diagnosis of septic arthritis, to identify the etiologic agent to narrow down antibiotic selection and to optimize therapy duration [1].

However, a pathogen is not always detected by standard culture methods as they may fail to identify the etiologic agent in up to 70 % of cases [3], making culture-negative SA challenging to treat. Patients with culture-negative SA tend to have longer hospital stays, longer antibiotic use, and higher treatment failure rates than their counterparts [3]. Recent literature supports the utilization of molecular diagnostic techniques such as polymerase chain reaction (PCR) or nucleic acid amplification tests (NAAT) in synovial fluid samples, to help with the detection of pathogens not usually detected by standard methods [1,3,4]. Among these, *Kingella kingae* is by far the most common pathogen detected by these methods [2,4,5]. *Moraxella sp*., in the other hand, is not a frequent finding [6]. Thus, we present the first reported case of *Moraxella nonliquefaciens* septic arthritis in an immunocompetent child detected by 16S rRNA gene amplification by PCR (16S rRNA PCR).

Case

A 2-year-old male presented to the Rheumatology office with 3 weeks of intermittent left knee pain and swelling, and one day of refusal to bear weight on the left lower extremity. He had no significant past medical history and was fully vaccinated. His mother denied any history of trauma, recent travel, recent respiratory or gastrointestinal tract infections, nor fevers. He had been evaluated in the ER on two occasions, as well as, at the Orthopedics office since the onset of symptoms. During those

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visits, physical examination was only remarkable for mild edema of the medial aspect of the left knee; and workup had been grossly unremarkable, including normal complete blood count (CBC), C-reactive protein (CRP), procalcitonin and erythrocyte sedimentation rate (ESR). Radiograph of the left knee showed no osteoarticular abnormalities. Comparative hip and pelvis radiographs showed no abnormalities. Left knee ultrasonography showed no soft tissue edema or effusions. Orthopedic surgeon had recommended management with as-needed NSAIDs for symptomatic relief and close follow-up as outpatient. However, symptoms lingered, and further investigation was deemed necessary. An MRI of the left knee showed moderate joint effusion with synovial enhancement, compatible with toxic synovitis versus juvenile idiopathic arthritis (JIA), as well as mild nonspecific edema along the medial collateral ligament without bone compromise. He was, then, started on scheduled Ibuprofen with mild symptomatic improvement until the day of presentation, when he awoke with severe left knee pain and refusal to bear weight on that limb.

On the day of presentation, his vital signs were within normal limits except for a heart rate of 120bpm. His physical exam showed worsening left knee edema, mild erythema, and limited range of motion to passive extension of the joint. Arthrocentesis was performed and synovial fluid analysis showed a white cell count of 57,618 cells, with 90 % of segmented neutrophils and 1 % of bands. Repeat CBC was unremarkable with 8800 white blood cells/uL, CRP mildly elevated at 1.9 mg/dL and ESR at 60 mm/hr. He was initiated on parenteral ceftriaxone and vancomycin and was admitted to the hospital for management of septic arthritis.

During admission, the patient underwent left knee arthrotomy with irrigation and debridement without complications. He developed a fever for the first time on post-operative day 1 with a maximum temperature of 101.2 F which subsided within the same day. MRSA PCR of the synovial fluid was negative, and vancomycin was discontinued after completing 3 days. 24 h after discontinuation of vancomycin, patient developed another fever, with maximum temperature of 101.9 F, and a rash surrounding surgical dressings. Repeat inflammatory markers upraised, with a CRP of 3 mg/dL and ESR of 72 mm/min. Antibiotic was switched to ceftaroline on day 5 of hospitalization to cover for gram positive cocci and *Kingella kingae*. Fevers resolved the following day. *Kingella kingae* PCR of the synovial fluid resulted negative. Acid fast bacilli, aerobic and anaerobic cultures of synovial fluid were also negative. Blood cultures remained negative. Autoimmune workup including Anti-Nuclear antibodies, rheumatoid factor, HLA-B27, and complement resulted negative. The rest of his hospital course went uneventfully. He showed remarkable clinical improvement and the patient was eventually discharged on IV ceftaroline to complete 21 days of parenteral antibiotics. Within one week of discharge from the hospital, 16S rRNA PCR resulted positive for *Moraxella nonliquefaciens*. After completion of antibiotics, his inflammatory markers had normalized, and he remained asymptomatic and ambulating as usual.

Discussion

The diagnosis of septic arthritis in our patient was challenging, as he presented with a lengthy and indolent course, very mild symptoms, and a near-normal physical exam for virtually the entirety of his course. Laboratory and imaging tests were grossly unremarkable or inconclusive, which made other diagnoses like JIA or toxic synovitis more probable. When SA was finally confirmed with synovial fluid analysis, gram stain and cultures failed to identify a pathogen. Due to concerns for the possibility of uncommon pathogens and/or culture-negative septic arthritis, 16 rRNA PCR of the synovial fluid was obtained, which lastly identified *Moraxella nonliquefaciens* as the causative agent.

Moraxella spp. have been rarely described as causative agents of septic arthritis. A recent literature review found only 19 cases reported from 1969 to 2019; most of which were among adult patients with comorbid conditions and/or immunosuppression [6]. *Moraxella nonliquefaciens* SA is even rarer, with this report being the first case described in an immunocompetent child [6–8]. These bacteria are gram-negative diplobacilli considered non-pathogenic microorganisms that are part of the upper respiratory tract flora [9,10]. Most species are nutritionally fastidious, and growth may be deterred on standard culture media [9], making identification difficult and possibly underestimating the pathogenic ability of these microorganisms. Reports have shown that these bacteria can spread hematogenously and cause invasive and fatal disease in immunocompromised patients [11–13]; however, when causing septic arthritis, *Moraxella spp*. seem to produce mild to moderate disease with a good prognosis, as seen in our patient [6].

Current literature recommends molecular testing, in addition to standard cultures, in cases of septic arthritis in children to increase the likelihood of accurately identifying an etiologic agent, mostly oriented toward MRSA and *Kingella kingae* [1,3,[4]]. Even then, a pathogen may go unrecognized in more than a third of SA cases in children [4]; and more sensitive tests may be warranted. The role of 16S rRNA gene amplification by PCR for diagnosing slow-growing or fastidious bacteria in bone and joint infections in children is yet to be determined. Some authors have found additional diagnostic yield in performing 16S rRNA PCR among children with culture-negative septic arthritis, even when *Kingella kingae*-specific PCR was available [4,15]. However, studies in adults have failed to identify such benefit, most likely due to the different causative microorganisms involved [16–18]. Further studies comparing these methods, as well as the clinical benefit of additional testing are needed.

Moraxella spp. are susceptible to penicillins and other betalactams, quinolones and macrolides [19], which are usually contemplated in the empirical treatment of SA. Despite the increasing rates of inducible beta-lactamase production described among *Moraxella* spp. in recent years [19], ceftriaxone remains the antibiotic of choice. In our patient, antibiotic susceptibility could not be determined due to inability to isolate the microorganism by conventional methods, and no MIC breakpoints have been determined by CLSI standards for *M nonliquefaciens,* but it is assumed that these breakpoints are similar, if not the same, to *M. catarrhalis* [20]. In our case, the delayed response to ceftriaxone and the development of fever after discontinuation of vancomycin without a clear etiologic agent, made it reasonable to broaden coverage with ceftaroline.

In summary, *Moraxella nonliquefaciens*, although rarely, can cause septic arthritis in immunocompetent children. It may be seen in indolent subacute cases of septic arthritis with negative cultures and may require molecular testing of the synovial fluid for its detection. Empiric therapy with betalactams should be effective against these bacteria and prognosis is generally favorable.

Declaration of Competing Interest

The authors disclose no conflict of interest.

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Consent

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Author contribution

Giancarlo Giovannini-Sanguineti, MD: contributed to study design, data collections, data analysis, and writing of the manuscript.

Karen Hanze-Villavicencio, MD: contributed to study design, data collections, data analysis, and writing of the manuscript.

Carolina Sanchez-Vegas, MD: contributed to study design, data collections, data analysis, supervision and writing of the manuscript.

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