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Moraxella nonliquefaciens septic arthritis in a hematopoietic stem cell transplant patient a case report and review of the literature

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ABSTRACT

Background: Septic arthritis is a common rheumatologic condition with myriad microbiological causative agents. Moraxella is one of the very rare causes of septic arthritis. We hereby present the third case of *Moraxella nonliquefaciens* septic arthritis and the first case in a hematopoietic stem cell transplant patient (HSCT) along with a brief review of the literature.
Methods: We used PubMed with google search engine to search the literature for reported cases of moraxella septic arthritis.
Results: Information on 19 other cases of moraxella infectious arthritis was found. *M. catarrhalis* was the most common species isolated. Only 2 reports on *M. nonliquefaciens* were found; the first one in a multiple myeloma patient and the second one in a diabetic patient on hemodialysis. Predisposing conditions included inflammatory arthritis, prosthetic joints, diabetes, Human Immunodeficiency Virus (HIV) infection, Hepatitis C, hemodialysis, esophageal cancer, valve replacements, alcoholism and Intravenous (IV) drug use. The age group of the reported cases ranged from 3 months to 78 years.
Conclusion: Infectious arthritis with *Moraxella spp.* is a very rare entity which can occur in any age group and in the setting of various underlying medical conditions.
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Introduction

Septic arthritis is a medical emergency with high burden of morbidity and mortality (ranging from 11 to 50%). It is usually a diagnostic riddle especially with the non-specific clinical presentation that fits with a long list of differential diagnosis. Delayed diagnosis and treatment might lead to irreversible damage to the joint [1]. Many risk factors are recognized for the development of septic arthritis: underlying joint pathology, joint prosthesis, low socioeconomic status, hemodialysis, immunosuppression, intravenous drug abuse, alcoholism, diabetes mellitus, intra-articular corticosteroid injection and skin infections [2].

The usual case definition for septic arthritis relies on having at least one of the following four criteria: (1) isolation of a

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Table 1
Reported cases of infectious arthritis with *Moraxella spp*.

Year	Moraxella species + sites	Age/gender	Predisposing medical conditions	Clinical presentation/joint tap	Treatment
1969 [6]	*M. osloensis* From joints + vaginal secretions	2 years Female	none	Monoarticular right knee swelling, fever and vaginal discharge in an African American girl. Joint tap results: 26,000 PMNs/cu.mm	Intravenous penicillin for 3 weeks then 2 weeks of oral penicillin
1975 [7]	*Moraxella spp*. from the joint	19 months Male	Juvenile rheumatoid arthritis on salicylates	Monoarticular left knee swelling and fever after starting treatment with salicylates. Joint tap results: 9000 WBC/cu.mm with 32% PMN	Intravenous penicillin for 19 days and surgical drainage
1980 [8]	*Moraxella spp*. from the joint	42 years Female	none	Fever, erythematous macular rash and bilateral wrists swelling. Joint tap results: 25,5600 WBC/cu.mm with 97% PMN	Intravenous penicillin for 2 weeks then 2 weeks of ampicillin
1983 [9]	*M. nonliquefaciens* from blood	75 years old Female	Multiple myeloma on carmustine, melphalan, cyclophosphamide, vincristine and prednisone	Proximal interphalangeal joint of the right 3rd finger left hand small joint swelling and fever. Joint tap results: not done	Intravenous gentamicin and benzylpenicillin for 6 days
1983 [10]	*M. catarrhalis* from joint	23 years Male	none	Right Hip involvement. Joint tap results: not reported	Penicillin for 3 weeks
1986 [11]	*M. osloensis* from joint	45 years Male	none	Protracted course of fever, right knee pain waxing and waning on antibiotics. Diagnosis made on arthroscopy drawn synovial samples. Joint tap results: clotted sample	Intravenous then oral cephalosporin for a total course of 2 weeks
1989 [12]	*M. catarrhalis* from joint	3 months Female	none	Right Hip involvement Joint tap results: not reported	Cefuroxime and gentamicin for 2 weeks and trimethoprim-sulfamethoxazole for 2 weeks with surgery
1991 [13]	*M. lacunata* from joints	73 years Male	Bilateral shoulders osteoarthritis	Rotator cuff rupture and low-grade fever. Patient has a history of purulent bilateral shoulder fluid for which he has undergone wash 1 year prior to presentation. Joint tap results: 5000 WBC/cu.mm with 30% PMN	Cephalothin for 3 months
1992 [14]	*M. catarrhalis* from blood	41 years Male	Intravenous heroin use	Recurrent swelling of left knee. Joint tap results: 9350 WBC/cu.mm l with 97% PMN	12 days of cefazolin with gentamicin. On the second recurrence he received intravenous penicillin for 6 days then discharged against medical advice on oral ampicillin
1995 [15]	*M. nonliquefaciens* from joint	54 years Female	Knee osteoarthritis hemodialysis and diabetes	Swollen left knee. Joint tap results: 51,600 WBC/cu.mm l with 96% PMN	Intravenous ceftriaxone foe 6 weeks and joint lavage
1995 [16]	*Moraxella spp*.	50 years Female	History of ovarian and axillary abscesses	Swollen right elbow. Joint tap results: not reported	Ciprofloxacin for 2 weeks and surgery
2004 [17]	*M. catarrhalis* from joint	45 Years Male	Aortic valve replacement and undifferentiated spondyloarthritis started on infliximab 1 month prior to presentation	Swollen right knee. Joint tap results: not reported	Ciprofloxacin with teicoplanin for 2 weeks and joint drainage
2005 [18]	*M. catarrhalis* from joint	73 years Female	Rheumatoid arthritis on leflunomide, methylprednisolone and anakinra along with bilateral knee prosthesis	Swollen right knee, fever after receiving treatment with cefuroxime for a lower respiratory tract infection. Joint tap results: 10,000 WBC/cu.mm with 85% PMN	10 days of Intravenous ciprofloxacin with clindamycin and closed drainage followed by a 30 days course of oral ciprofloxacin
2008 [19]	*M. lacunata* from joints and blood	78 years Male	Esophageal cancer status post distal esophageal resection 20 years prior to his presentation, HIV, chronic hepatitis C, cardiac pacemaker and aortic graft surgery for repair of abdominal aortic aneurysm	Swelling of bilateral knees, ankles, elbows, wrists, and proximal, middle, and distal phalangeal joints along with confusion. Joint tap results: 51,120 WBC/cu.mm with 93% PMN	Imipenem for 6 weeks and drainage
2009 [20]	*M. lacunata* from joints and blood	24 years Female	Lupus nephritis on prednisone and mycophenolate mofetil	Swollen knees, and a tender swollen right wrist. Joint tap results: not reported	Piperacillin-tazobactam for 10 days
2009 [22]	*M. canis* from Joint (detected by 16S RNA)	55 years male	Hypertension and multiple myeloma (diagnosed after this episode)	Swollen knees, right wrist, the right acromioclavicular and the first metacarpophalangeal joints along with fever. Joint tap results: 98,000 WBC/cu.mm with 90% PMN	5 weeks of intravenous cefotaxime with ofloxacin and arthroscopic lavage followed by 5 weeks of oral amoxicillin and ofloxacin
2014 [22]	*M. lacunata* from joints and blood (detected by 16S RNA)	74 years Female	Hemodialysis and aortic valve replacement	Bilateral hip pain, bilateral knee swelling, hypothermia, septic shock and endocarditis. Joint tap results: not reported	Multiple regimens that included (imipenem, ampicillin, cefazolin, ceftriaxone with gentamicin, ceftriaxone alone) along with incision and drainage of the knees

Table 1 (*Continued*)

Year	Moraxella species + sites	Age/gender	Predisposing medical conditions	Clinical presentation/joint tap	Treatment
2015 [23]	*M. Catarrhalis* from joint	75 years Female	Osteoarthritis status post total arthroplasty of the right knee 4 months before the episode	Fever and a swollen right knee. Joint tap results: not reported	3 weeks of ceftriaxone with levofloxacin followed by 9 weeks of oral levofloxacin alone along with debridement and joint washing with a change of the mobile polyethylene component of the prosthesis
2016 [24]	*M. osloensis* from joint	40 years Male	Alcoholic patient with alleged history of fall following attack by a pet	10 days history of fever and swollen left knee. Joint tap results: not reported	7 days of cefaperazone + Sulbactam with amikacin followed by meropenem for 7 days along with Arthrotomy and debridement

the pathogenic organism from sterile joint fluid (2) isolation of a pathogenic organism from a specimen other than joint (e.g. blood) in the setting of a hot red joint suspicious for septic arthritis (3) presentation with typical symptoms along with a turbid joint fluid in the setting of previous antibiotics exposure (4) postmortem or histologic evidence of septic arthritis [3]. The most common cause among all age groups is *Staphylococcus aureus* followed by other Gram-positive bacteria. Gram-negative septic arthritis is encountered in 5–20% of patients, with Enterobacteriaceae being the most common. Occurrence of other Gram-negative organisms depends on specific risk factors [1,4]. Among Gram-negative organisms, *Moraxella spp*. are an infrequent cause of septic arthritis [18].

We report the third case of *M. nonliquefaciens* septic arthritis and the first case of moraxella septic arthritis in a HSCT patient. We also present a review of literature on septic arthritis with *Moraxella species*.

Case presentation

Mr. HH is a 43 years old gentleman with history of low-grade peripheral T-cell lymphoma diagnosed in 2013 for which he received R-CHOP chemo regimen (Rituximab, Cyclophosphamide, Doxorubicin, Vincristine and Prednisolone) along with intrathecal methotrexate and radiation therapy. In 2016 the patient relapsed with bone marrow involvement for which he had to undergo HSCT from a matched related donor. The patient's transplant course was complicated with multiple infections including cytomegalovirus (CMV), Epstein Barr Virus (EBV) and BK polyoma virus reactivations.

The patient presented to the rheumatology clinic 8 months after his transplant for evaluation of a one-week history of pain at the level of the medial plantar aspect of the right foot and posterior aspect of the left knee. The patient had no other associated upper or lower respiratory tract symptoms. At the time of presentation, the patient was only receiving valacyclovir for viral prophylaxis and a recent bone marrow biopsy showed a disease-free marrow with maturing trilineage hematopoiesis. Upon presentation, the patient was afebrile and had stable vital signs. Physical exam showed tenderness and swelling around the left knee and right foot. Complete Blood count with differential (CBCD) showed: white blood cell count (WBC) of 6700/cu.mm with 67% polymorphonuclear (PMN), uric acid of 6.2 mg/dL, erythrocyte sedimentation rate (ESR) of 2 mm/hr, CRP 41 mg/L. Left knee X-ray showed a large suprapatellar knee joint effusion. Subsequently, a knee arthrocentesis was performed showing a WBC of 2080/cu.mm with 61% PMN, negative Gram stain, absence of crystals and lack of bacterial growth in the synovial fluid culture. As a result, the patient received a short course of prednisone 20 mg orally once daily for 7 days with major improvement in his symptoms.

Three weeks later, he developed right elbow pain, swelling and decreased range of motion; which were associated with 2 episodes of fever 38.6 °C. Significant swelling, erythema, and decreased range of motion (flexion, extension, pronation and supination) were noted on the physical examination.

A joint tap was performed, a small amount of fluid was aspirated and sent for culture. The culture grew *Moraxella nonliquefaciens* after 5 days of incubation. The patient was initially started on doxycycline with minor improvement. After culture results became available, he was switched to moxifloxacin 400 mg orally daily for 4 weeks with complete resolution of the elbow arthritis. Of note, the patient denied any preceding respiratory symptoms prior to this illness.

Discussion

Bacteria belonging to genus Moraxella are Gram negative catalase and oxidase positive rods or cocci. They are usually non-motile requiring aerobic conditions to survive. *Moraxella* genus currently comprises 22 different species, only 6 species are medically important: *Moraxella catarrhalis, Moraxella osloensis, Moraxella lincolnii, Moraxella nonliquefaciens, Moraxella lacunata and Moraxella atlantae. Moraxella* species are mostly fastidious except for *M. Osloensis. Moraxella spp*. have been implicated in infections of the upper respiratory tract, conjunctiva, middle ear, blood, maxillary sinus, bronchial aspirate, joints and bursa, nasal cavity, spleen, cerebrospinal fluid and genitourethral tract [5].

Review of the literature using Pubmed and Google Scholar for cases of septic arthritis with *Moraxella spp.* yielded 19 cases with the following species: *M. catarrhalis* 6 cases, *M. lacunata* 4 cases, *M. osloensis* 3 cases, *M. nonliquefaciens* 2 cases, *M. canis* 1 case and other *Moraxella spp*. 3 cases. Cases are summarized in Table 1 [6–24].

Septic arthritis with *Moraxella spp.* affected patients from all age groups ranging from 3 months to 79 years. The characteristics of affected patients were variable: 5 patients were healthy and without any predisposing conditions [6,8,10–12], 2 patients had end stage kidney disease and were on hemodialysis [15,22], 2 patients had a prosthetic joint [19,23], 6 patients had a predisposing rheumatologic disorders (osteoarthritis, rheumatoid arthritis, gout, spondyloarthritis and systemic lupus erythematosus) [7,13,15,17–18,23], 2 patients had multiple myeloma [9,22], 1 patient with coinfection of HIV and hepatitis C [19], 4 patients were on immunosuppressive therapy [9,17–18,20] and 1 patient reported heroin intravenous drug use [14]. Our patient was most likely predisposed to develop moraxella septic arthritis due to his intense immunosuppressed state following his allogeneic stem cell transplant. HSCT patients are known to be at risk for various opportunistic infections.

Moraxella spp. induced septic arthritis mostly manifested as a monoarticular arthritis (12 out of the 19 cases), oligoarticular (involvement of 2–5 joints) and polyarticular (involvement of >5 joints) cases were reported as well (5 and 2 cases out of 19 respectively). Only 5 cases were associated with coexisting bacteremia [6–23]. In only one case report there were signs of lower respiratory tract infection symptoms that preceded the arthritis [18].

Joint taps results were reported in 9 out of the 19 cases with WBC count ranging from 5000 to 25,5600/cu.mm with PMN percentage ranging from 30% to 97%. All reported patients were treated with antibiotics with complete resolution of the arthritis. The treatment duration varied from 6 days in some reports up to 10 weeks in others. Surgical intervention was done in 11 out of the 19 cases [6–24].

Moraxella spp. are generally susceptible to beta lactams, tetracyclines, quinolones and aminoglycosides. However, most *M. catarrhalis* isolates produce an inducible beta-lactamase [5]. We have chosen to treat with moxifloxacin to benefit from the high bioavailability of this drug and because of the patient's refusal to receive intravenous therapy. There is no clear consensus on the best way to manage septic arthritis with such rare pathogens. However, it appears that unlike septic arthritis with other bacterial pathogens such as *S. aureus*, antibiotics alone without surgery can be effective in the management of moraxella septic arthritis.

Conclusion

Moraxella spp. should be considered among the causative pathogens of septic arthritis especially in patients with comorbid conditions. The outcome is usually more benign than septic arthritis due to other pathogens. Most patients respond to medical treatment with antibiotics without the need for surgical interventions.

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Competing interests

None declared.

Ethical approval

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