CASE REPORT

INFECTION AND IMMUNE-MEDIATED MENINGOCOCCAL-ASSOCIATED ARTHRITIS: COMBINATION FEATURES IN THE SAME PATIENT

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SUMMARY

We present a case of a 16-year-old male patient with sudden-onset, rash, arthritis and meningitis by Neisseria meningitidis one week after an acute upper respiratory infection. On the 10th day of treatment followed by neurological and arthritis clinical improvement, he presented once again a tender and swollen left knee with a moderate effusion, and active and passive range of motion was severely limited secondary to pain, and when he was submitted to surgical drainage and synovial fluid analysis he showed inflammatory characteristics. A non-steroidal anti-inflammatory drug was taken for five days with complete improvement of symptoms. The case is notable for its combination of features of septic and immune-mediated arthritis, which has rarely been reported in the same patient.

KEYWORDS: Meningococcal disease; Arthritis; Neisseria meningitidis.

INTRODUCTION

The clinical spectrum of meningococcal infection can be extremely variable; it can range from an asymptomatic carriage until life-threatening meningitis with septic shock. Neisseria meningitidis is associated with several forms of arthritis. It is a recognized complication of meningococcal infection and its frequency in adults ranges from 4 to 50%10. Septic arthritis may occur in isolation or at the time of primary meningitis or bacteremia10. The second type is an immune-mediated arthritis which may occur as a late complication of meningococcal infection6.

The presentation can mimic the acute arthritis/dermatitis syndrome seen commonly in gonococcemia. Another differential diagnosis would be systemic vasculitis, either primary or secondary. As we could see in MRI, the patient presented a left knee synovitis, which is common in gonococcemia, but not in meningococcemia11.

Herein, we present a case with characteristics of both septic and immune-mediated arthritis.

CASE REPORT

A 16-year-old man presented in the emergency room after a 5-day history of onset of headache, fever, and stiffness of the neck, accompanied by nausea and vomiting. The following day, he presented an acute pain and swelling in his left knee and wrist, followed by a decreased ability to flex and extend the knee and an extreme pain when walking. The pain became worse, described as 6/10 at rest, and 10/10 when walking, limiting the movement, but non-radiating. Headache and fever persisted. The rash quickly evolved into a petechial phase with further coalescence into a purpuric form. Two weeks before presentation, the patient had experienced self-limited upper respiratory infection symptoms such as cough, sore throat and fever that were solved without treatment. He denied any genital-urinary or eye symptoms. He had no medical records, and was not taking any medication. He had not been sexually active in the past three months. He did not have any other positive epidemiological history, except a left knee trauma one year before.

He was promptly transferred to the Intensive Care Unit of Department of Infectious Diseases of University of São Paulo with a presumptive diagnosis of meningococccemia and meningitis. Lumbar puncture was performed and dexamethasone and ceftriaxone were administered. On physical examination, he had an axillary temperature of 38.0 °C, heart rate of 134 bpm, respiratory rate of 24/min, and blood pressure of 120/80 mmHg. He presented an erythematous macular rash affecting the trunk and limbs (Fig. 1). The left knee was tender and swollen with a moderate effusion, and active and passive range of motion was severely limited by pain. His mental status changed and a nuchal rigidity and Kernig’s sign

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On admission, he presented $10.59 \times 10^9/\text{L}$ white cell count, with 90% neutrophils. C-reactive protein (CRP) measured 300.6 mg/L and in rheumatological tests it was found that C3 and C4 had mildly increased. Syphilis, HIV-antibodies, Cytomegalovirus, Epstein-Barr virus, and Hepatitis B and C serology were negative. Biochemistry including serum uric acid were normal and the urinalysis was clear. Urine and blood cultures were negative. Cerebrospinal Fluid (CSF) examination by lumbar puncture showed $2,160/\text{mm}^3$ white cells (89% neutrophils, 4% lymphocytes and 7% monocytes), protein 359 mg/dL and glucose 4 mg/dL. Microscopic examination of the Gram-stained smear revealed numerous polymorphonuclear neutrophils with intracellular Gram-negative diplococci as well as *Neisseria meningitidis* DNA Serogroup C on polymerase chain reaction (PCR), with no growth. Blood and CSF culture were sterile. Left knee arthrocentesis yielded 30 cc of purulent fluid (Fig. 2), and showed a high white cell count ($163,000 \times 10^3/\text{mm}^3$ with predominant polymorphonuclear cells). Neither organisms nor crystals were seen, and Gram stain and culture fluid were negative. Due to the great amount of purulent fluid, a left knee surgical drainage became mandatory. He had a favourable outcome, presenting subsequent neurological and articulation clinical improvement, associated with a reduction in CRP to 57.5 mg/L and normalization of white blood cells count. He was transferred to the ward, on day 6 of treatment; he presented again stiffness of the neck and a strong headache, without fever. A central nervous system magnetic resonance imaging (MRI) revealed numerous polymorphonuclear neutrophils with intracellular Gram-negative diplococci as well as *Neisseria meningitidis* DNA Serogroup C on polymerase chain reaction (PCR), with no growth. Blood and CSF culture were sterile. Left knee arthrocentesis yielded 30 cc of purulent fluid, with septic arthritis characteristics.

**DISCUSSION**

Meningococcal infection is a disease whose incidence varied between 1.31-2.52 per 100,000 in the last decade in Brazil\(^9\). The disease usually presents as a meningococcemia with or without meningitis and is caused when bacteria is able to penetrate the mucosa and the bloodstream. It is more frequent in children and young adults. Upper respiratory illness increases the risk for carriage transmission and invasive disease due to cough and disruption of the respiratory epithelium\(^8\) and precedes the arthritis in up to 50% of cases\(^10\); a maculopapular rash is another sign, noted in 30% of cases\(^10\). Our patient presented an upper respiratory infection approximately one week before his symptoms.

Septic arthritis may occur as a result of acute meningococcemia, with or without meningitis. Approximately 2% to 10% of cases are associated with some form of rheumatological presentation\(^4,10\). The pathogenesis of these manifestations occurs through a variety of mechanisms: direct haematogenous seeding of the synovium by circulating bacteria, causing a pyoarthrosis; the formation of immune complexes, causing reactive arthritis; and haemarthrosis secondary to coagulopathy\(^4,10,11\). Certain underlying diseases place patients at particular risk for septic arthritis. Pre-existing joint disease is the foremost risk factor and is found in 47% of people who are diagnosed with septic arthritis\(^8\). Our patient had left knee trauma one year before, without further symptomatic joint disease.

Arthritis with meningococcal disease may also occur and frequently manifest as an immune-mediated form with sterile effusions affecting large joints, often with polyarthritis and fever\(^2,3,10\). Arthritis onset shows up between one to 12 days after the initial illness\(^12\). There are some risk factors related to the arthritis immune-mediated reactions that fit with our patient: severe disease, serogroup C infections, and age (higher frequency in teenagers and young adults)\(^12\).

![Image 1](image1.png) **Fig. 1** - Meningococcal erythematous macular rash appeared six days before meningococcal-associated arthritis symptoms.

![Image 2](image2.png) **Fig. 2** - Left knee arthrocentesis yielded 30 cc of purulent fluid, with septic arthritis characteristics.
Physical examination for meningococcal arthritis often demonstrates a swollen, warm, tender, and erythematous joint. Patients may have joint pain at rest and exhibit decreased active and passive range of motion. Attempts to bear weight or move the joint tend to exacerbate the pain. Laboratory studies often reveal leucocytosis with elevated CRP. Synovial fluid analysis may show inflammatory or septic characteristics. It is important to note that while the typical picture of septic synovial fluid usually contains more than 100,000 cells/mm³, this number may be lower in infections with *Neisseria meningitidis*. The magnitude of virulence of this organism may be less than other common bacteria that cause septic arthritis.

Up to 60% to 70% monoarticular involvement is described and the knee joint is the most commonly affected. Our patient presented knee and wrist symmetrical involvement. The pattern of polyarticular involvement was asymmetrical, with predilection for larger joints, most commonly knees. However, hands, wrists and elbow joints have been reported to be involved as well.

The presentation can mimic the acute arthritis/dermatitis syndrome seen commonly in gonococccemia. Another differential diagnosis would be systemic vasculitis, either primary or secondary. As we could see in MRI, the patient presented a left knee synovitis, which is common in gonococccemia, but not in meningococccemia.

Our case is notable for its combination of features of septic followed by immune-mediated arthritis, which has rarely been reported in the same patient. Although the patient’s upper respiratory tract illness, rash, positive CSF PCR, and purulent joint fluid were in keeping with septic arthritis, his relapse of arthritis while taking antibiotics, two subsequent sterile joint fluids of left knee analysis and the prompt response to non-steroidal treatment, were consistent with immune-mediated arthritis.

The treatment of choice for *Neisseria meningitidis* septic arthritis is penicillin as *Neisseria meningitidis* penicillin-resistant strains have not been detected in Brazil; however 16.4% of strains present intermediary resistance. The prognosis is excellent and most patients become symptom free by one month after presentation.

In conclusion, despite being less common, the possibility of *Neisseria meningitidis* septic arthritis followed by immune-mediated arthritis should be kept in mind before thinking on a failure of treatment, especially in places with low antibiotic resistance.

**REFERENCES**

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