Neisseria gonorrhoeae: An Unexpected Cause of Polyarthritis and Meningitis

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Abstract

Neisseria gonorrhoeae, a gram-negative coccus, is a major cause of morbidity among sexually active individuals. Hematogenous spread of N gonorrhoeae from the initial site of infection is thought to occur in only 0.5% to 3% of infected patients. Disseminated gonococcal infections can rarely lead to serious sequelae, such as endocarditis or meningitis. In this article, we present a case that demonstrates a rare finding of disseminated gonococcal infection leading to N gonorrhoeae meningitis, complicated by hydrocephalus. The patient in this case initially presented with intermittent polyarthralgias for two years and later developed a rash. Cultures from blood and joint aspirate were negative. Urine nucleic acid amplification test for N gonorrhoeae was also negative. He was initially started on steroids for what was believed at first to be an autoimmune polyarthritis. The patient later developed acute encephalopathy. Head imaging revealed hydrocephalus. Cerebrospinal fluid analysis was consistent with bacterial meningitis. Blood, joint, and mucosal membrane studies failed to isolate the causative organism, but his cerebrospinal fluid grew N gonorrhoeae. He was treated with high-dose intravenous ceftriaxone for two weeks with rapid improvement in his mental status and resolution of his joint pains and rash.

Keywords
gonorrhoeae, Neisseria, polyarthritis, disseminated gonococcal infection, meningitis, arthritis dermatitis

Introduction

Neisseria gonorrhoeae, a gram-negative coccus, is a major cause of morbidity among sexually active individuals, with an estimated 600,000 cases diagnosed annually in the United States.1 Gonorrhea typically causes cervicitis in females and urethritis in males, although infections can also be asymptomatic. If left untreated, gonococcal infections can lead to pelvic inflammatory disease, ectopic pregnancy, and, rarely, infertility in men.2Extragenital infections are also common, such as infections of the pharynx and rectum.3 An initial infection of a mucosal site can rarely enter the bloodstream and lead to disseminated gonococcal infection, which can result in serious morbidity and mortality. Sequelae associated with disseminated infections may include infectious arthritis, rash, endocarditis, and meningitis.4

Case Presentation

A 56-year-old man with past medical history of chronic hepatitis B and untreated hepatitis C presented with migratory polyarthritis involving bilateral hands, wrists, ankles, and feet. The patient carried a recent presumptive diagnosis of gout, from an outside hospital, though no arthrocentesis had been performed. He reported that the symptoms had been occurring intermittently for two years, and he had been seen at multiple hospitals without resolution. The pain was unresolved with colchicine and other anti-inflammatory medications. He denied being sexually active for past several years. He reported history of oral intercourse; however, he stated that this was several years prior. He had limited access to health care due to lack of health insurance coverage and had recently become homeless. A right wrist arthrocentesis showed inflammatory synovial fluid with 32,800 white blood cells, absence of crystals, and a negative culture. Urine nucleic acid amplification test for N gonorrhoeae was also negative. He was initially started on steroids for what was believed at first to be an autoimmune polyarthritis. The patient later developed acute encephalopathy. Head imaging revealed hydrocephalus. Cerebrospinal fluid analysis was consistent with bacterial meningitis. Blood, joint, and mucosal membrane studies failed to isolate the causative organism, but his cerebrospinal fluid grew N gonorrhoeae. He was treated with high-dose intravenous ceftriaxone for two weeks with rapid improvement in his mental status and resolution of his joint pains and rash.
testing was negative. He had evidence of hypoosmolar hyponatremia, with an initial serum sodium of 131 mmol/L. Urine sodium was 26 mmol/L and urine osmolality was 397 mOsm/kg. The patient reported frequent use of nonsteroidal anti-inflammatory drugs for his joint pains and these findings were attributed to a salt wasting tubulointerstitial nephropathy. An autoimmune polyarthritis was suspected on this initial presentation, and he was discharged with a prednisone taper. The patient, however, returned to the hospital shortly after discharge, with the same complaints, plus a new rash on the left dorsal hand (Figure 1).

Soon after second admission, the patient developed acute encephalopathy, without any focal neurologic deficits. He remained afebrile and blood cultures were negative. Laboratory blood tests at this time showed worsening hyponatremia with sodium of 117 mmol/L, leukocyte count of $17.70 \times 10^3/\mu L$ with neutrophilia, hemoglobin 13 g/dL, and platelet count 567,000/mm$^3$. All other electrolyte levels and liver function tests were normal. Computer tomography scan of head was remarkable for acute communicating hydrocephalus (Figure 2).

The patient subsequently underwent a lumbar puncture, as part of the workup for his acute encephalopathy. The cerebrospinal fluid sample obtained had a leukocyte count of 31,600 cells/mm$^3$ (95% neutrophils, 3% lymphocytes), with glucose and protein levels of 38 mg/dL and 432 mg/dL, respectively. The cerebrospinal fluid culture was positive for $N$ gonorrhoeae. He was treated with intravenous ceftriaxone 2 g every 12 hours for 14 days, with rapid improvement in his mental status. His hyponatremia also resolved.

**Discussion**

Hematogeneous spread of $N$ gonorrhoeae from the initial site of infection is thought to occur in only 0.5% to 3% of infected patients.\(^5\) Disseminated gonococcal infection is rare; its incidence is currently increasing relative to the steady rise of gonorrhea cases worldwide.

Arthritis-dermatitis syndrome is a form of disseminated gonococcal infection that is composed of a triad of tenosynovitis, dermatitis, and polyarthralgia, all of which developed in our patient over a period of months. Tenosynovitis is a finding unique to gonococcal arthritis that is not seen in other forms of septic arthritis. It is characterized by tenderness along the flexor sheath and pain on passive extension. Skin lesions are most commonly present on the trunk and extremities. The polyarthralgia is typically asymmetric and can affect both large and small joints.\(^5\)

Our patient had polyarthralgias for nearly two years. However, he appears to have developed a rash on his dorsal hand only shortly after taking prednisone, for a presumptive initial diagnosis of autoimmune polyarthritis. The prednisone, by suppressing his immunity, likely led to worsening of his underlying infection. This also highlights that even though the patient did have the typical symptoms of arthritis-dermatitis syndrome, which is seen in disseminated gonococcal infection, these symptoms were not present concurrently.

Blood cultures are only positive in less than a third of disseminated gonorrhea cases. Positive blood cultures are more frequently seen in patients who present with arthritis-dermatitis syndrome.\(^5\) Gonococcal bacteremia has been reported to be intermittent in nature, which can explain negative blood cultures in our patient with disseminated gonococcal infection.\(^6\) The intermittent bacteremia can be partially explained by the modulated pathogenic potential that the bacterium has evolved. Although $N$ gonorrhoeae lacks a polysaccharide capsule to protect itself against complement-mediated lysis, it has evolved many other mechanisms to evade the human complement system and survive. The immunosuppressive
mechanisms that this bacterium has evolved include binding and inactivating components of the complement cascade, sialylating its lipo-oligosaccharide to hide from the complement system, and adapting to changing oxygen and nutrient requirements. The diagnostic yield of arthrocentesis can vary as well with even localized, purulent, arthritis, having as little as 25% chances of isolating N gonorrhoeae. Joint aspirate culture is even less sensitive in arthritis-dermatitis syndrome. It has been suggested that NAAT of synovial fluid may be more useful in this scenario.

For patients with sterile blood, urine, and synovial fluid specimens, the next step is usually to obtain specimens from mucosal sites. Mucosal swab cultures have 80% positivity. Urine NAAT for N gonorrhoeae is highly sensitive (>90%) and specific (>99%) and is recommended for initial screening in symptomatic and asymptomatic patients. This modality detects and amplifies nucleic acids specific to the organism being tested. It is unclear why urine NAAT testing was negative in our patient; however, we suspect it may have been because the nidus of infection in his case was likely pharyngeal rather than urethral. There are also reports that NAAT false-negative results can occur because some N gonorrhoeae species lack specific sequences that are targeted by a particular NAAT. Conversely, false-positive tests also occur due to frequent horizontal genetic exchange that causes commensal Neisseria species to acquire N gonorrhoeae genes. Therefore, even NAAT has certain limitations for diagnosis. There is a reported case of an immunocompetent male who was diagnosed with a disseminated N gonorrhoeae infection that was confirmed with synovial NAAT followed by positive synovial culture. His urine NAAT was negative.

There have been many cases reported of N gonorrhoeae infecting the pharynx, after orogenital contact. However, symptoms, such as sore throat, are not always present in infected patients. Interestingly, there have been reports of failure to treat pharyngeal gonorrhea secondary to extensively drug resistant gonococcus, with resistance to both ceftriaxone and azithromycin. This may be in part due to that drug penetration of the pharynx is poor.

The exact mechanism of N gonorrhoeae meningitis in our patient remains unclear but one possibility is hematogeneous spread of N gonorrhoeae from the oropharynx to the meninges. From our review of literature, there are no other cases specifically describing hydrocephalus in a disseminated gonorrhea infection leading to meningitis. However, hydrocephalus has been rarely described in bacterial meningitis, including N meningitides.

Both host factors and microbial factors play a role in disseminated gonococcal infection. Some studies have listed a few factors that may facilitate spread of asymptomatic gonococcal infection, such as pregnancy, menstruation, viral hepatitis, difference in virulence between strains of gonococci, and host immunologic differences. Patients with liver disease, such as our patient, are more prone to immune and nutritional deficiencies, including vitamin, protein, immunoglobulin, and complement deficiencies.

### Conclusion
We describe here a case of untreated N gonorrhoeae that resulted in an invasive infection. The patient subsequently developed meningitis, which was complicated by acute hydrocephalus. Typical symptoms of disseminated N gonorrhoeae infection, including rash, joint pain, and tenosynovitis, may not all be present on initial presentation. It was over the course of months that our patient developed the classic arthritis-dermatitis form of N gonorrhoeae infection. When disseminated gonococcal infection is being considered as part of the differential diagnosis, this cannot be excluded solely on negative urine NAAT. This diagnosis requires a careful history, including sexual history, to allow for testing of appropriate site (eg, rectal, oropharyngeal). Additionally, NAAT of the joint aspirate should be considered when suspicion is high.

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Our institution does not require ethical approval for reporting individual cases.

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