Neisseria gonorrhoeae Sepsis: an Atypical Manifestation of Disseminated *N. gonorrhoeae* Infection

Brooke Richard, BS¹; Todd Oswald, MD²; Jay Marion, MD²

¹Louisiana State University Health School of Medicine, Shreveport, LA
²Department of Internal Medicine, University Health Hospital, Shreveport, LA

---

**ABSTRACT**

Gonococcal infection most commonly manifests as a localized mucosal infection; disseminated infection occurs in 0.5-3%. Disseminated gonococcal (GC) infection generally manifests as an arthritis-dermatitis syndrome characterized by arthralgias followed by septic oligo- or polyarthritis and is often associated with complement deficiencies. Although transient bacteremia is associated with disseminated infection, disseminated *N. gonorrhoeae* infection resulting in sepsis is exceedingly rare with only a few reported cases. Presented here is a case of gonococcal sepsis in a patient with a past medical history of sickle cell anemia with prior splenectomy that presented with symptoms of a typical sickle cell pain crisis as well as fever and non-productive cough. At presentation, the patient was febrile with an otherwise unremarkable physical exam. Two out of four blood cultures obtained grew gram-negative cocci, later proven to be *N. gonorrhoeae*. The patient was found to have elevated liver function enzymes, which was attributed to perihepatitis. The patient was treated with benzathine penicillin G 2.4 million units IM once, azithromycin 1g for three days, and ceftriaxone 1g for three days. She was discharged with a five-day course of cefixime 400 mg twice daily.

This case highlights the manifestations of gonococcal sepsis as well as predisposing factors for development of disseminated *N. gonorrhoeae* infection. It illustrates the importance of obtaining blood cultures in patients with fevers of unknown origin and/or patients with fever and another predisposing factor for development of disseminated infection. Also reinforced is the importance of obtaining a thorough sexual history in all patients, especially young sexually active patients.

---

**INTRODUCTION**

Disseminated *N. gonorrhoeae* infection results from hematogenous spread of this sexually transmitted infection (STI) and results in a variety of signs and symptoms including tenosynovitis, multiple skin lesions, and dermatitis.¹,² Disseminated infection occurs in 0.5-3% of those infected with *N. gonorrhoeae*, and although most affected are less than 40 years of age, this infection can occur at any age.¹,³ Historically, disseminated gonococcal infection was believed to occur more commonly in women than men; however, recent studies have
shown that the incidence may be higher in men than in women in some western countries.\textsuperscript{1-3}

Although a rare occurrence, disseminated GC infection is a common cause of acute arthritis and arthralgias in young, sexually active, and otherwise healthy individuals.\textsuperscript{1-3} This infection manifests as either a triad of tenosynovitis, dermatitis, and polyarthritis without purulent arthritis or purulent arthritis without associated skin lesions. The separation between the two classic forms is not always absolute and the mechanisms responsible for these different presentations are poorly understood. This may be partly due to differences in the infecting strain.\textsuperscript{1-3}

Patients with clinical syndromes caused by disseminated gonococcal infection often lack simultaneous symptoms of mucosal gonococcal infection, but a localized infection involving the urethra, rectum, cervix, or pharynx typically precedes the onset of disseminated gonococcal infection symptoms.\textsuperscript{1-3} Those with asymptomatic initial infection are more likely to experience disease progression to disseminated gonococcal infection, but no clear time period for progression of disease has been established due to this fact. Manifestations like endocarditis, osteomyelitis, and meningitis can also occur.\textsuperscript{1-3}

Despite its hematogenous transmission, \textit{Neisseria gonorrhoeae} is rarely identified in the blood of those with disseminated infection. This is due to the transient and typically asymptomatic nature of the bacteremia, only resulting in symptoms at its end organ destination (e.g., joints).\textsuperscript{1,3}

In most patients, the spleen can help eradicate encapsulated organisms during this transient bacteremia; however, there is diminished capacity to efficiently clear the blood stream of bacteria in asplenic patients. Because of this, it is likely that the bacteremia will be present for longer in asplenic patients, increasing the likelihood for sepsis and isolation of the infecting organism.\textsuperscript{2,4,5}

In populations with a high incidence of asplenia, like sickle cell disease patients, who often experience both functional and anatomic asplenia (surgical removal), knowledge of risk factors, manifestations, and treatment for infections with encapsulated organisms is crucial in providing optimal care to those patients. Less than 5 cases of \textit{N. gonorrhoeae} sepsis have been described, all with varying presentations. The aim of this report is to illustrate a rare manifestation of gonococcal infection, as this is the first reported case of \textit{N. gonorrhoeae} sepsis presenting in this manner.\textsuperscript{6,7}

\begin{center}
\textbf{CASE PRESENTATION}
\end{center}

An 18-year-old African American female with a past medical history of sickle cell disease (type S beta-zero thalassemia) status post-splenectomy presented to the emergency department (ED) with a 4-day history of pain in the legs, chest, and back refractory to ibuprofen. The patient also reported a fever of 101.9° F and a non-productive cough. She denied any arthralgias, genitourinary symptoms, sick contacts, or recent hospitalizations, and had not been admitted for a crisis in the last 6 months. Vital signs included a blood pressure (BP) of 100/56 mmHg, pulse of 100 beats/minute, temperature of 101.7° F, and a respiratory rate of 17 breaths/minute. There was no palpable lymphadenopathy, and no oropharyngeal exudate or erythema. Lungs were clear to auscultation in all lung fields bilaterally. Abdominal exam was unremarkable. There was no pain with passive or active joint movement and no limited range of motion.

In the ED, the patient was noted to have abnormal lab values including a hemoglobin of 8.5 g/dL (baseline 9.0 g/dL), reticulocyte count of 11.2%, white blood cell count (WBC) of 23,000 K/uL, total bilirubin of 7.6 mg/dL, direct biliru-
bin of 3.0 mg/dL, alkaline phosphatase of 170 U/L, aspartate transaminase (AST) of 86 U/L, and alanine transaminase (ALT) of 69 U/L. Urinalysis was positive for nitrites, WBC 20-30/HPF, few bacteria, and few epithelial cells. A chest radiograph revealed no infiltrate or effusion. In the ED, the patient was started on IV normal saline, morphine 10 mg IV, ceftriaxone 1g IV, supplemental oxygen, and azithromycin 1 g for coverage of atypical pneumonia. The patient displayed symptoms of sepsis including hyperthermia, tachycardia, borderline hypotension (BP may be increased due to pain), and leukocytosis but lacked chills and rigors. Blood and urine cultures were obtained prior to initiating treatment for presumed atypical pneumonia (which is common in sickle cell patients), as well as possible sepsis, and she was admitted to hematology-oncology inpatient service.

The next morning, she reported her pain had improved on intravenous morphine; she denied chest pain, dyspnea, abdominal pain, and dysuria. An abdominal ultrasound was completed secondary to elevated bilirubin and revealed a small echogenic focus in the gallbladder consistent with a small stone, with no ductal dilation. This stone was likely a pigmented stone as such stones are common in sickle cell disease related to chronic hemolysis and do not require treatment unless they are symptomatic. A large portion of the patient’s hyperbilirubinemia was increased unconjugated bilirubin from hemolysis. Direct bilirubin improved to 2.5 mg/dL, total bilirubin to 6.1 mg/dL, alkaline phosphatase to 145 U/L, AST to 66 U/L, and ALT to 53 U/L. Blood cultures were obtained on admission and one out of four cultures showed gram-negative cocci at 1 day and 1 hour. Urine culture showed lactose fermenting gram-negative rods, so ceftriaxone for UTI treatment was started.

On hospital day 3, her pain crisis had resolved and no longer required IV pain management. Two out of four cultures from admission were now positive for *Neisseria spp.* The laboratory was called to confirm presence of *Neisseria* and to rule out lab error. The laboratory confirmed the isolate was *Neisseria spp.* and identification of the species was performed revealing *Neisseria gonorrhoeae*. Further questioning revealed a new sexual partner within the past three weeks with several ED visits for STI-like symptoms within the past year, which were treated empirically, and mild pharyngitis. She had a positive test for *N. gonorrhoeae* 3 months prior to admission, for which she was given ceftriaxone and azithromycin. It is unclear if the patient suffered from unresolved infection from 3 months prior or if this was a new infection from the new sexual contact three weeks prior.

Additional studies obtained showed negative HIV, negative hepatitis serology, reactive syphilis IgG, and nonreactive rapid plasma reagent. Urine polymerase chain reaction (PCR) showed lactamase negative *N. gonorrhoeae*. The pelvic exam completed by gynecology reported no cervical motion tenderness and wet prep was negative. The patient’s elevated transaminases were believed to be secondary to gonococcal perinephritis. Infectious disease (ID) was consulted and recommended treatment for disseminated gonococcal bacteremia with azithromycin 1g and ceftriaxone 1g for three days. She was additionally treated with benzathine penicillin G 2.4 million units IM once. ID advised that she could be discharged with cefixime 400 mg by mouth twice daily for five days, as she received 3 days of ceftriaxone inpatient, per CDC guidelines. The patient was counseled extensively on safe sexual practices, all immunizations were confirmed up to date, and she was advised to have all her prior and current sexual partners undergo STI testing at a local health clinic.
DISCUSSION

A variety of different factors predispose patients to develop disseminated gonococcal infection including host, infecting strain, and immune factors. Predisposing host factors for progression to disseminated infection include recent menstruation, pregnancy or immediate post-partum period, congenital or acquired complement deficiencies (C5, C6, C7, or C8), systemic lupus erythematosus, and sickle cell disease resulting in splenectomy (functional or anatomic) or other causes of asplenia.3,4

Microbial factors that can allow the infecting organism to cause a disseminated infection include a variety of virulence and growth factors. Strains with a specific outer membrane porin isoform PorB1b that is different than the other existing form (PorB1a) seem to have increased bacterial serum resistance and permissive host cell invasion in low phosphate conditions. Other factors that may promote disseminated infection include organisms requiring arginine, hypoxanthine, and uracil for growth (Auxotype AHU) and those organisms that are highly sensitive to penicillin.3

The frequent absence of positive blood, skin, and synovial fluid cultures supports immune mechanism involvement in the development of disseminated gonococcal infections. For example, N. gonorrhoeae organisms are obtained in less than 50% of purulent synovial effusions, positive blood cultures are found in less than 1/3 of patients, and skin lesions seen in disseminated infection are almost always sterile. Although N. gonorrhoeae are notoriously fastidious organisms, the ability for easy recovery from the genitourinary tract suggests that the fastidious nature of the organism is not responsible for the lack of positive cultures. Further evidence supporting an immune component in disseminated gonococcal infection is the presence of gonorrhea cell wall, antibody to gonorrhea, and complement components in skin lesions. Circulating immune complexes have been observed in some studies.3,4

Patients with sickle cell disease undergo autosplenectomy due to vaso-occlusion leading to splenic infarct and atrophy.4,5 Patients with homozygous sickle cell disease usually experience gradual decline in spleen function with eventual complete autosplenectomy by 8 years of age. A review of over 40 years of literature concluded that the presence of hematologic disorders was associated with a higher rate of infection and mortality.5 Post-splenectomy (surgical or nonsurgical), patients have an 8-fold increased risk of bacteremia.3 Although S. pneumonia is the most common cause of post-splenectomy sepsis, accounting for 80-90% of cases, sepsis also occurs from other encapsulated organisms e.g. Neisseria spp., E. coli, and H. influenzae type B.1,4,5 Because antibodies play a crucial role in eliminating such pathogens, the loss of splenic function explains the predisposition of asplenic individuals to such infections.4,5

Perihepatitis (Fitz Hugh Curtis Syndrome) is the inflammation of Glisson’s capsule surrounding the liver and is most commonly associated with Chlamydia trachomatis infection. Although generally associated with pelvic inflammatory disease, it can also result from disseminated infection. The incidence of perihepatitis in the setting of disseminated gonococcal infection is unknown. When associated with a urogenital gonococcal infection, incidence of perihepatitis almost exclusively affects women. Signs and symptoms of perihepatitis include sharp, pleuritic chest pain, pain localized over the right upper quadrant with or without associated nausea, vomiting, and fever. A friction rub may be audible on physical examination along the right anterior costal margin. Liver function tests are frequently normal or only mildly elevated.2 Although this patient did not display symptoms of
pelvic inflammatory disease, this syndrome could be secondary to gonococcal bacteremia and her lack of typical symptoms may have been masked by the pain she was experiencing from her sickle cell crisis.

Limitations in this report include inability to discern the current infection from a prior infection. Furthermore, although there is no way to determine if this infection was the cause of the patient’s sickle cell crisis, knowledge of this would have helped best understand the current case. This case reinforces the importance of obtaining a thorough sexual history in all patients, especially young, sexually active patients. Disseminated gonococcal infection should always be in the differential diagnosis for susceptible patients presenting with fever. This patient’s predisposing factors include being a young, sexually active female not using any form of barrier protection as well as immunocompromise secondary to sickle cell disease and asplenia.

This case also emphasizes the importance of STI screening in at-risk populations as well as treatment for both *N. gonorrhoeae* and *Chlamydia trachomatis* if either is detected. Any patient who is treated for or tests positive for one STI should be screened for the presence of others and treated as indicated. Safe sexual practices should be taught to all at-risk individuals. All patients undergoing treatment for an STI should be counseled on treatment compliance, compliance with follow-up, and advised to notify all sexual contacts. Additionally, this case demonstrates the importance of follow-up with laboratory results. Although an isolate such as *N. gonorrhoeae* from a patient’s blood is unlikely, assumption that this is a result of lab error would have been detrimental to this patient. Calling the laboratory to confirm the results and performing identification testing on the organisms are ways to ensure a patient receives the best care.

Crucial in the management and prevention of such infections in susceptible individuals is identifying those at risk and educating patients about how to best minimize the likelihood of infection. In this case, thorough and frequent counseling about safe sexual practices, preferably as an outpatient, will help to prevent *N. gonorrhoeae* sepsis and disseminated gonococcal infection in the future. Furthermore, it is important to ensure that all vaccinations, particularly those against encapsulated bacteria (*N. meningitides, H. influenzae, and S. pneumonia*), are up to date.

A variety of intrapersonal, interpersonal, and system-level preventative measures can be utilized to optimize patient care. All sexually active patients should be counseled on safe sexual practices. Once a patient has been informed of his or her risks, it is the patient’s responsibility to follow through with the preventative measures taught by the physician. The patient is responsible for practicing safe sexual practices, presenting to the physician when experiencing symptoms of infection, and being compliant with immunizations and medications to help prevent infection. Finally, ensuring that health care professionals are aware of risk factors associated with asplenia as well as appropriate preventative measures, are able to obtain a thorough sexual history, can identify manifestations of infections, and know how to treat these infections will help to provide a system-level approach to prevention.

---

**LEARNING POINTS**

- Obtain a thorough sexual history on all patients, especially young, sexually active patients.
• In patients who are predisposed to infection from encapsulated organisms, it is important to educate patients about minimizing their risk of infection.

• In patients with fever of an undetermined etiology, blood cultures should be obtained to rule out sepsis.

REFERENCES


