

Disseminated GC infection without urogenital symptoms

Disseminated gonococcal infection is rare—and significantly more rare in men than in women. The patient described in this case proves that exceptions do exist.

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CASE

The patient is a 34-year-old white male with severe pain in the left ankle. The pain progressed over several days until he was unable to walk, and he was admitted to the hospital. The patient denied any acute injury or trauma to the ankle. He described the pain as “constant and throbbing” and maintained that it was limited to the left ankle but generalized in this area. He also reported several “hot flashes” and sweating that began about the same time as his ankle pain. The patient had had a similar occurrence about 7 to 10 days previously, when he was seen in the same hospital emergency department (ED) for right shoulder pain. He had a history of gout, and the ED physician and the patient both believed that the shoulder pain was a gouty attack. The shoulder pain had resolved over 2 to 3 days with rest, ice, and indomethacin (50 mg every 8 hours). The patient said he had tried rest, ice, and OTC pain medications for his ankle pain but these had provided no relief.

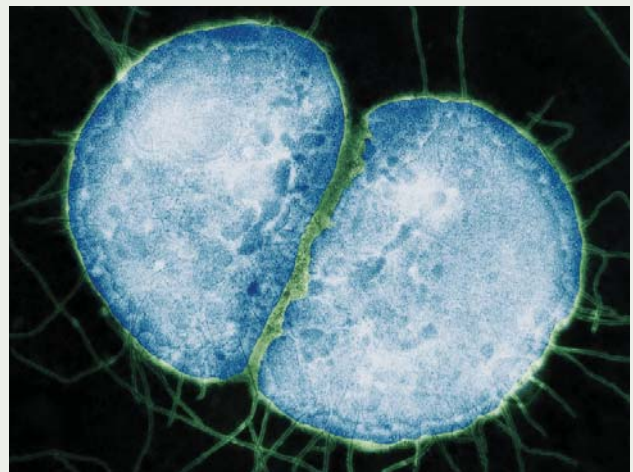
The patient had recently received a diagnosis of type 2 diabetes mellitus and had a history of asthma. His sexual history was significant for unprotected intercourse, but he reported that it was within the limits of a monogamous, 2-year heterosexual relationship. He denied any other sexual partners in the past 2 years, any history of sexually transmitted diseases (STDs) or infection, and any knowledge of his current partner having an STD. The patient was taking metformin for diabetes and OTC ibuprofen for his ankle pain at the time of his admission. He reported a history of GI intolerance to allopurinol. He had no known allergies.

Upon admission, the physical examination documented abnormalities limited to decreased range of motion in the left ankle and tenderness over the area. The patient was afebrile at the time of admission. He was again treated for presumed gout, although serum uric acid levels obtained on admission were normal, at 4.5 mg/dL. Joint aspiration and fluid culture were not obtained at that time.

On the second day of his hospital course, the patient developed an unexplained fever, prompting the taking of

routine blood cultures. Initial Gram’s stain revealed gram-negative cocci. At this point, infectious disease (ID) was consulted. When further questioned by the ID physician, the patient denied urethritis, urethral discharge, or pharyngitis. The patient also denied similar symptoms in acquaintances or recent travel. The examination performed by the ID physician revealed multiple small, hemorrhagic vesicles over the superficial aspect of both ankles; this finding was not documented at the time of admission. Upon further questioning, the patient stated that he believed these were from sandals he had been wearing, although the lesions did not follow a pattern for trauma related to footwear. Along with the continued fever, the patient continued to have tenderness to palpation over the left ankle, particularly over the Achilles tendon. The tenderness was exacerbated with passive ankle movement.

At this point, the ID physician suspected that the patient had a disseminated gonococcal infection (DGCI). This clinical diagnosis was later confirmed by the blood culture results. Once confirmed, the case was reported to the county health department, and the patient was instructed to inform any sexual partners that they may be infected and require treatment. A CBC with differential and a creatinine level



Transmission electron micrograph of *N gonorrhoeae*

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had been previously ordered, and the ID physician noted these values for monitoring before planning antibiotic therapy. The WBC count was 12,300 cells/mm³, and the creatinine level was 0.6 mg/dL.

The patient was treated with ceftriaxone, 1 g IV every 24 hours until 48 hours after symptoms improved, and doxycycline, 100 mg by mouth twice daily for 7 days. Symptoms almost entirely resolved within 48 hours after the initiation of antibiotic therapy. Treatment continued with ceftriaxone for an additional 48 hours, at which time the patient was switched to ciprofloxacin, 400 mg by mouth twice daily for 7 days. Repeat blood cultures were confirmed to be negative prior to discharge. The patient completed oral antibiotic therapy as an outpatient.

DISCUSSION

DGCI is often overlooked as a cause of monoarticular joint pain. This is not surprising, because infection with *Neisseria gonorrhoeae* becomes disseminated in only 0.5% to 3% of patients, most of them female.^{1,2} It is even rarer for DGCI to occur in a male patient without the initial symptoms of urethritis and urethral discharge.¹

Gonococcal infection is often asymptomatic in women, and gonococcal arthritis is more likely to develop in women as a result.³ DGCI may manifest in atypical ways and cause serious rare conditions, as was the case in one patient with an epidural abscess.⁴ Rarely, disseminated infection may cause endocarditis, hepatitis, osteomyelitis, meningitis, or further systemic involvement.^{1,4} Potential cases of DGCI are important to recognize, even in unlikely candidates. Early recognition may prevent serious consequences.

Risk factors Although rates of DGCI have decreased overall in the United States in the past several decades, several factors influence the probability of an infection becoming disseminated. Being female is a risk factor, as previously noted, and dissemination is more likely following menstruation and in the postpartum period.⁴ Risk may increase during these periods because of alterations in vaginal pH and cervical mucus, which enable bacteria to more easily enter the submucosal blood vessels and the bloodstream through the endometrium.²

Some gonococcal strains have been shown to disseminate more easily than others. The decreasing rates of disseminat-

ed infection reflect the decreasing prevalence of such strains.⁵ Phenotypes of gonococci that are expressed during menstruation are believed to be more likely to disseminate, whereas, for example, strains of *N gonorrhoeae* introduced rectally in homosexual men do not express phenotypes likely to disseminate. Strains with a higher potential for causing disseminated infection evade bactericidal defense of human serum, thereby minimizing genital inflammation.⁵ The patient in this case, who denied urogenital symptoms, may have been infected by such a strain. Reduced local inflammatory response to gonococcal strains may also occur with a defect of terminal complement factors. Patients with recurrent DGCI should be suspected of having terminal complement deficiency, which compromises the humoral immune response.⁵ This case demonstrates that exceptions do exist, despite the known risk factors and more common epidemiology regarding DGCI.

The clinical picture Classic DGCI typically manifests in one of two forms: 1) a combination of dermatitis, tenosynovitis, and asymmetric polyarthralgia without purulent arthritis; or 2) as purulent arthritis (usually monoarticular or pauciarticular) without skin lesions.^{4,5} The first presentation is typically caused by gonococemia, whereas the second, rarer presentation is most often due to direct synovial or periarticular infection.^{4,5} The patient in this case exhibited the first presentation, but dermatitis was not discovered until after the initial diagnosis and the initiation of treatment.

Hemorrhagic pustules over tendonous areas, as well as asymmetric arthralgias, should raise suspicion of DGCI. Pustules are the result of hematogenous dissemination of gonococci.¹ Blood, synovial, or skin lesion cultures are positive in fewer than half of cases of DGCI,² and DGCI is often diagnosed clinically. Mucosal surface cultures—including urethral, pharyngeal, rectal, and cervical samples—are more likely to grow *N gonorrhoeae* than are blood, synovial, or skin lesion cultures. Mucosal surface cultures are positive in 80% of patients with disseminated infection.² Because of the clinical picture and positive blood cultures, the diagnosis could be made in our patient without relying on these mucosal surface cultures.

Treatment Ceftriaxone is the appropriate treatment for DGCI.⁶ Recent CDC guidelines state that fluoroquinolones—as administered as part of this patient's treatment—are no

TEACHING POINTS

- Disseminated gonococcal infection (DGCI) occurs rarely enough that it is often overlooked as a cause of monoarticular joint pain. DGCI occurs even more rarely in men without the initial symptoms of urethritis and urethral discharge.
- Classic DGCI typically manifests as a combination of dermatitis, tenosynovitis, and asymmetric polyarthralgia without purulent arthritis; or as purulent arthritis (usually monoarticular or pauciarticular) without skin lesions. The first presentation is typically caused by gonococemia, whereas the second is most often due to direct synovial or periarticular infection.
- Ceftriaxone is the appropriate treatment for DGCI.
- Infective arthritis should be considered in any sexually active patient with joint pain. Patients may not always disclose risk factors or sexual exposures that may have led to infection.

COMPETENCIES

●●●● Medical knowledge

●●● Interpersonal & communication skills

●●●● Patient care

● Professionalism

● Practice-based learning and improvement

● Systems-based practice

longer generally recommended for DGCI because *N gonorrhoeae* is increasingly resistant to them. Fluoroquinolones should not be used for infections in men who have sex with men; in those with a history of recent foreign travel or partners' travel; acquired in California or Hawaii; or acquired in other areas with an increased prevalence of quinolone-resistant DGCI. Alternatively, cefixime, 400 mg by mouth twice daily, may be substituted following appropriate intravenous treatment.⁷

The standard of care requires treating the patient presumptively for chlamydia as well—hence the addition of doxycycline to the regimen. As an alternative, azithromycin, 1 g by mouth given as a single dose, can be used.

CONCLUSION

The initial misdiagnosis of this patient resulted from the assumption that a previously known condition, gout, had flared up. The serum uric acid level did not confirm this diagnosis, however, and other causes of arthralgia were not investigated initially. In this patient's case, closer attention to the symptoms and examination findings could have produced an earlier diagnosis.

Infective arthritis should be considered in any sexually active patient with joint pain, particularly pain with the migratory pattern seen in this patient. Patients may not always disclose risk factors or sexual exposures that may have led to infection; and even when the sexual history is

inconsistent with sexually transmitted infection, the patient may not know about exposures of sexual partners.¹ This case highlights the importance of obtaining a thorough history, performing a physical examination, and taking the time to put the clues they offer together. [JAAPA](#)

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DRUGS MENTIONED

Allopurinol (Aloprim, Zyloprim)	Doxycycline
Azithromycin (Zithromax)	Ibuprofen
Cefixime (Suprax)	Indomethacin (Indocin)
Ceftriaxone (Rocephin)	Metformin (Fortamet, Glucophage)
Ciprofloxacin (Cipro, Proquin)	

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