Case Report: Severe Disseminated Gonococcal Infection with Polyarticular Gout: Two Cases in Older Travelers

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Abstract. Two male travelers with histories of gout and hazardous alcohol consumption, presented with a triad of severe culture-positive disseminated gonococcal infection, crystal-positive polyarticular gout, and gonococcal soft tissue collections, following unprotected sexual contact in The Philippines. Both men initially attributed symptoms to gout, since their usual joints were affected, but clinical deterioration occurred with self-administration of anti-inflammatory agents alone. The clinical courses were severe and protracted, requiring aggressive management of infection with prolonged intravenous antimicrobials and repeated surgery, and prolonged anti-inflammatory agents for gout. Joint symptom onset in each case occurred within a week of sexual exposure in conjunction with hazardous alcohol ingestion. We speculate that acute dissemination of infection to previously damaged joints triggered polyarticular gout, with progressive infection, exacerbated by unopposed anti-inflammatory agents and delayed antibiotics. Disseminated gonococcal infection can occur with polyarticular gout and delays in recognition and treatment, including while traveling, can lead to severe disease from both.

INTRODUCTION

Disseminated gonococcal infection (DGI) results from bacteremic spread of *Neisseria gonorrhoeae*, occurring in approximately 0.5–3% of individuals with gonorrhea.^{1–3} Disseminated gonococcal infections can present with two distinct clinical entities: either the triad of tenosynovitis, dermatitis, and polyarthralgia; or oligo-articular purulent arthritis typically affecting distal joints.^{3,4} Guidelines indicate that both forms of DGI usually respond rapidly to treatment, often requiring only a 1-week antibiotic course, shorter than septic arthritis from other organisms.^{5,6} Host and organism factors determine the likelihood of development of DGI; previously identified host factors include complement deficiencies, pregnancy, and systemic lupus erythematosus,^{7–10} and a variety of pathogen factors have also been described.^{11–14} With the increase in chronic disease and older travelers, the roles of gout, diabetes and hazardous alcohol in DGI are less well-defined.

Simultaneous DGI and gout is rarely reported,^{15,16} as is culture-proven gonococcal pyomyositis as a manifestation of DGI.^{17–22} We report two older males with chronic disease and hazardous alcohol intake who each had delayed presentations with severe DGI characterized by purulent polyarticular septic arthritis and extensive gonococcal pyomyositis/soft tissue abscesses, with severe polyarticular gout, following travel to the Philippines in 2013 and 2017, respectively.

CASE REPORTS

Case 1. A 53-year-old Australian male presented to Royal Darwin Hospital (RDH) in 2013 following travel to Manila, Philippines. He had a history of up to six episodes per year of acute gout for 10 years and hazardous alcohol use (35–40 standard drinks/week). He was not taking regular preventative therapy for gout.

Four days after unprotected sexual intercourse with a commercial sex worker in Manila, he developed fevers, chills,

and left ankle pain and swelling. Following an initial response to self-medication with indomethacin for presumed gout, he developed polyarthritis including the left first metatarsophalangeal joint and ankle. The metatarsophalangeal joint began spontaneously discharging pus. He had no dysuria or penile discharge. He presented to hospital 10 days after symptom onset. On examination, temperature was 38.2°C, with tenosynovitis of the left elbow, hand, foot, and ankle. The left great toe was erythematous, swollen, and openly discharging. There was a mildly tender left para-spinal fluctuant collection. Inflammatory markers were markedly raised (C-reactive protein 308 mg/L; leucocytes $21.5 \times 10^9/L$; blood glucose was normal (5.6 mmol/L). Left foot X-ray showed soft tissue swelling and first metatarsophalangeal joint space narrowing, bony proliferation, erosions, and subchondral cysts consistent with chronic gouty changes. Computed tomography (CT) showed a para-vertebral collection adjacent to the spinous processes from T12–L5 levels (Figure 1).

Human immunodeficiency virus (HIV) and syphilis serologies were negative and two pre-antibiotic blood cultures were sterile. Left metatarsophalangeal joint aspirate drew 0.5 mL of pus with $450,000 \times 10^6/L$ leucocytes. Monosodium urate crystals were visible on microscopy and beta-lactamase-negative *N. gonorrhoeae* was isolated on culture. A para-spinal collection aspirate 6 days after commencing antibiotic therapy was culture-negative; however, *N. gonorrhoeae* was detected on polymerase chain reaction (PCR) testing of aspirated material.

Treatment comprised intravenous ceftriaxone 1 g daily for 42 days with regular nonsteroidal anti-inflammatory drugs for management of acute gout. He required incision and drainage of the para-spinal collection, three debridement and washout procedures of the left metatarsophalangeal joint, and a subsequent split-skin graft. He was discharged after 42 days with oral amoxicillin for 14 days thereafter. He did not attend further follow-up clinic appointments.

Case 2. A 63-year-old Australian male presented to RDH in 2017 with a 10-day history of fevers and painful, swollen joints which developed during travel in Manila. He had a history of multiple attacks of gout, hazardous alcohol use, obesity, and impaired glucose tolerance. One week after arrival in Manila,

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FIGURE 1. Case 1: Computed tomography scan showing the left para-spinal abscess at the level of L2 vertebrae (highlighted by the white arrow).

he developed fever and chills, generalized joint pain, myalgia, inter-scapular pain, and swelling of hands and feet. He reported sexual intercourse with a Filipina partner, but denied other recent sexual contacts. He took a medication assumed to have been colchicine for treatment of presumed gout, and developed diarrhea (four episodes of loose stools/day), and polydipsia and polyuria. He had no dysuria or penile discharge. He returned to Australia and was hospitalized 10 days after symptom onset. On examination, he was diaphoretic but afebrile. He had exquisitely tender knee joints bilaterally with effusions, generalized pitting edema in the lower limbs, and tenosynovitis of both feet and arthritis of both ankles. He had inter-scapular tenderness and reduced range of shoulder movement. There was tenderness of both elbows, with swelling and severe tenderness of the small joints of the hands and wrists. He had a maculopapular rash across his torso and arms with palmar sparing. Inflammatory markers

were markedly raised (C-reactive protein, 330.6 mg/L; leucocytes, $24.7 \times 10^9/L$); blood glucose was 26 mmol/L and HbA1c 10%. HIV and syphilis serologies were negative. Admission blood cultures yielded beta-lactamase-positive *N. gonorrhoeae* (susceptibilities: azithromycin, 0.125 mg/L; ceftriaxone, 0.0008 mg/L; ciprofloxacin, 2 mg/L; penicillin > 32 mg/L). Thoracic CT revealed features suggestive of pyomyositis involving the subscapularis muscles and gas-forming phlegmonous collections with evidence of communication with the gleno-humeral joints bilaterally (Figure 2).

Ceftriaxone 1 g daily was commenced with ibuprofen and opiate analgesia for joint pain. He required operative washouts of six joints (bilateral knees, ankles, and shoulders). Cultures of all aspirates were sterile, however on PCR testing, penicillinase-producing *N. gonorrhoeae* DNA was detected from the right knee and both ankles. Monosodium urate crystals were detected by microscopy in both knee synovial fluid samples.

Neisseria gonorrhoeae was not identified in urine, and stool cultures were negative. Repeat washouts were required of both knees. Because of ongoing polyarthritis, prednisolone was commenced on day 9 of admission with colchicine added on day 15 because of ongoing marked joint pain and inability to mobilize. Repeat CT on day 15 showed reduction in the caliber of the gas loculation within the subscapularis muscles in keeping with resolving pyogenic infection. The collections were too small for drainage. He was discharged on day 32, having completed 32 days of intravenous ceftriaxone. He made a good recovery although requiring significant rehabilitation.

DISCUSSION

These cases are notable for their severity, with requirement for multiple surgical joint washouts and prolonged intravenous antibiotic therapy, contrasting with the usual clinical course of DGI. Superimposed polyarticular gout appeared to be an important contributing factor to the severity and prolonged nature of symptoms. Both men consumed hazardous quantities

FIGURE 2. Case 2: Thoracic computed tomography scan showing features suggestive of pyomyositis involving the subscapularis bilaterally with gas-forming phlegmonous collections (highlighted by the white arrows).

of alcohol and self-administered anti-inflammatory drugs for presumed gout, and one had newly diagnosed type II diabetes, all of which are likely to have impaired neutrophil and other cellular function,^{23,24} potentially increasing risk of gonococcal dissemination. These cases represent two out of 87 cases of DGI documented to have been managed by the Infectious Diseases service at RDH from 2006 to 2017. A previous RDH report identified *N. gonorrhoeae* as the third leading cause of septic arthritis (12%).²⁵

Both cases also had soft tissue collections, one confirmed from *N. gonorrhoeae*. Gonococcal pyomyositis has only rarely been reported previously.^{17–22} One previous case reported poorly controlled diabetes as a potential risk factor. In the cases we present, bacteremic seeding to the para-spinal soft tissue and subscapularis muscles represent a plausible route of spread. However, because the first case demonstrates that spontaneous joint rupture can occur with gonococcal arthritis in the presence of concurrent acute gout, the pyomyositis in the second case could represent contiguous spread from bilateral shoulder joint rupture, especially given the continuity with both joints demonstrated on CT.

These cases raised diagnostic and management challenges. It was difficult to determine the extent to which persisting, disabling inflammatory joint symptoms should have been treated with repeated surgical washouts for management of septic arthritis in addition to antibiotic therapy, or escalating anti-inflammatory treatment of gout, or both. Even with implementation of both strategies, symptom control took longer than expected for either DGI or gout alone. In this era of rising gonococcal resistance to first- and second-line antibiotics, particularly in Southeast Asia, both were relatively susceptible, suggesting that any intrinsic propensity for these strains to disseminate was not linked with multidrug-resistance.

Case 1 had proven gouty arthropathy on X-ray and Case 2 may have had subclinical gouty arthropathy. The onset of each case within a week of the sexual encounter suggests that acute dissemination of infection occurred to previously damaged joints, with infection then triggering an acute attack of polyarticular gout. Both men misinterpreted their infective symptoms initially as being gout, because the symptoms affected their usual joints. Progressive infection was likely exacerbated by unopposed anti-inflammatory agents^{23,24} and delayed antibiotics.

Organism factors are important in determining the likelihood of dissemination. Disseminated gonococcal infection is well-recognized in Australia's Northern Territory, where both men lived and sought health care, with circulation of serovars, usually beta-lactamase-negative, associated with increased propensity for disseminated disease.^{2,14,25} Although typing of their isolates was not possible, the history of recent high-risk unprotected sexual contact suggested that both patients may have acquired their gonococcal infection in the Philippines.

In conclusion, DGI can occur with polyarticular gout and delays in recognition and treatment, including while travelling, can lead to severe disease from both. Underlying gouty arthropathy, hazardous alcohol, diabetes, and immunoaging may potentially increase the risk of gonococcal dissemination and severity. With the rising numbers of older travelers with chronic disease, DGI-gout comorbidity may become more common. Disseminated gonococcal infection should be included in the differential diagnosis of polyarticular gout, and older groups should be included in routine pre-travel safe-sex advice.

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