

SHORT COMMUNICATION

Gonococcal Osteomyelitis Resulting in Permanent Sequelae

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Gonorrhoea is one of the most common sexually transmitted infections. It mostly manifests in the genitourinary tract, rectum and pharynx. Gonococcal arthritis and, especially, osteomyelitis occur infrequently and probably arise from blood dissemination of *Neisseria gonorrhoeae* (1). Disseminated gonococcal infection (DGI) has been reported to develop in 0.5–3% of infected patients. DGI typically presents with fever, pustular skin lesions and joint involvement (2, 3). However, the symptoms can be discrete, the rate of positive gonococcal cultures and nucleic acid amplification tests (NAATs) from blood or synovial fluid is low, and genital symptoms are often absent (4, 5). These factors contribute to difficulties in reaching the correct diagnosis and may delay adequate treatment. As shown below, this delay can result in permanent sequelae.

CASE REPORTS

We report here 2 cases of gonococcal osteomyelitis. As this aetiology was not suspected initially, selective media suitable for gonococci were not used, except where explicitly stated below. Antibiotic susceptibility testing was carried out using Etest (AB bioMérieux, Solna, Sweden) and interpreted according to breakpoints published by the European Committee on Antimicrobial Susceptibility Testing (EUCAST).

The first case was a 61-year-old man who, 2 weeks after unprotected fellatio and vaginal intercourse with multiple female partners in Thailand in November 2011, experienced pain in his left ankle. The pain moved to his left knee and in December, upon arrival in Sweden, he was admitted to the Department of Infectious Diseases and received intravenous (iv) benzylpenicillin, 1.6 million IU 3 times daily, due to suspected erysipelas. An X-ray showed no osteitis, blood tests revealed elevated C-reactive protein (CRP 180 mg/l, normal <5 mg/l), white blood cell count ($16.1 \times 10^9/l$, normal $3.5\text{--}8.8 \times 10^9/l$) and leukocytes in the joint fluid ($63 \times 10^9/l$, normal $<0.2 \times 10^9/l$). Bacterial cultures of joint fluid and blood were negative, as was gonococcal culture and NAAT for *Chlamydia trachomatis* from the urethra. Since bacterial cultures were negative, benzylpenicillin was stopped after 3 days and reactive arthritis was suspected. In January 2012, the patient was referred to the Department of Rheumatology, and oral prednisolone, 40 mg once daily, was started. Intra-articular triamcinolone (40 mg) was administered and this treatment was repeated twice during the following 2 months. The patient did not improve and in February oral sulfasalazine, 1,000 mg twice daily, was added. An X-ray in April showed active arthritis and sulfasalazine was changed to methotrexate, 15 mg/week. In May, an arthroscopy showed destruction of joint and bone, but bacterial culture and 16S rRNA gene sequencing from joint fluid were negative (6). In July, new bacterial and fungal cultures were collected, still with negative results. By August, the patient

could not work, required morphine, and was using a wheelchair. At this point, prednisolone (previously tapered to 5 mg/daily) and methotrexate were discontinued. A new X-ray (Fig. 1A) and arthroscopy were performed. Finally, 8 months after the initial short course of antibiotic and after 8 months of immunosuppressive therapy, 16S rRNA gene sequencing and subsequent specific gonococcal culture from joint fluid were found to be positive for *N. gonorrhoeae*. The strain was sensitive to cefixime, ceftriaxone and spectinomycin, but resistant to ciprofloxacin. It was assigned to the *N. gonorrhoeae* multi-antigen sequence typing NG-MAST ST8617 (7). The patient was referred to a dermatovenerologist. Cultures, using media suitable for gonococci, and NAATs for *N. gonorrhoeae* and *C. trachomatis* from urethra, urine and pharynx were negative, as was serology for HIV, hepatitis B and syphilis. Treatment was initiated with intravenous ceftriaxone, 2 g once daily for 9 days, and subsequently oral cefixime 400 mg twice daily. Treatment was planned for 3–6 months, but since the patient was not improving satisfactorily this was prolonged to 12 months. At the time of publication the patient works fulltime, but uses a walking frame, and will need a knee prosthesis operation.

The second case was a 65-year-old man who reported that, during a vacation in Thailand in April 2012, he fell on the beach, injuring his left hand. No open wound was seen, but 10 h later he experienced pain in the third metacarpophalangeal (mcp) joint of his left hand. On arriving in Sweden one week later he contacted primary healthcare. An X-ray was normal, but due to tenderness and redness, erysipelas was suspected. Flucloxacillin, 1 g 3 times daily, was started. Two weeks later, he had not improved and an orthopaedic surgeon was consulted. Septic arthritis was suspected and the patient received cloxacillin, 2 g \times 3 times daily iv. After 2

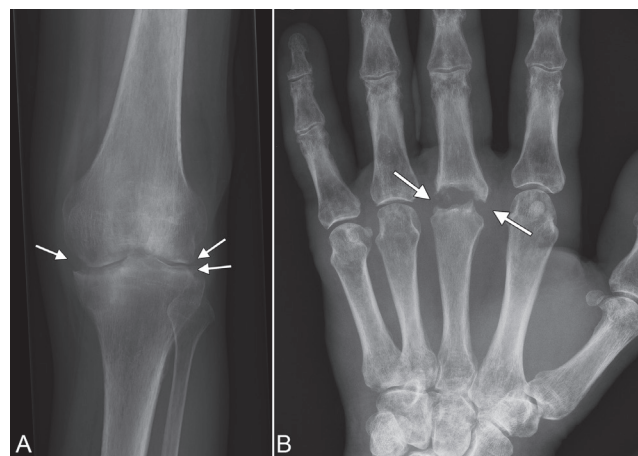


Fig. 1. (A) X-ray of the left knee joint showing reduction in height of the cartilage laterally and medially (arrows), fissures on the tibial articular surface and general osteopaenia. (B) X-ray of the left hand showing that adjacent edges of the articular surfaces in the 3rd metacarpophalangeal joint (arrows) are irregular and sclerotic, corresponding to status post-septic arthritis.

days the affected joint was opened and flushed. Bacterial cultures were negative, as was 16S rRNA PCR. The patient was discharged with flucloxacillin, orally 1.5 g × 3 times daily. Twelve days later, he returned because of deterioration. Blood tests showed CRP 14 mg/l (<5 mg/l) and a white blood cell count of $9.0 \times 10^9/l$ ($3.5\text{--}8.8 \times 10^9/l$). X-ray now showed osteitis and the wound was reopened. New biopsies were collected for 16S rRNA gene sequencing, and samples from the bone were found to be positive for *N. gonorrhoeae*. The patient was referred to a dermatovenerologist, where he denied having had sexual contacts in Thailand. His Swedish female partner was negative for *N. gonorrhoeae* in gonococcal cultures collected from the cervix, urethra and pharynx. Samples from the urethra and pharynx were collected from the patient for analysis on media suitable for gonococci. The pharyngeal culture was positive for *N. gonorrhoeae*. Antimicrobial susceptibility testing showed sensitivity to cefixime, ceftriaxone and spectinomycin, but resistance to ciprofloxacin. The gonococcal strain was assigned to the NG-MAST ST11846. The patient received cefixime, 400 mg orally twice daily, for 4 months and an X-ray performed at the end of the treatment showed no signs of active infection (Fig. 1B). The patient experienced impairment of the affected joint after completion of treatment.

DISCUSSION

The global incidence of gonorrhoeae is estimated to be 106 million cases per year (8). In Sweden, 1,336 (13.7/100,000) cases were reported in 2014, and in 2013, 37% of heterosexual Swedish males who contracted gonorrhoea abroad were infected in Thailand (9).

Neither of the cases reported here experienced urogenital symptoms, which is often the case in DGI, gonococcal arthritis and osteomyelitis (2–5). The site of bacterial entry can be difficult to determine, since DGI often develops from an asymptomatic mucosal infection. However, pharyngeal infection has been reported to be a common cause (10). In our report, the first patient had had unprotected fellatio in Thailand, but a pharyngeal test was not taken until 9 months after the sexual contact. The second patient denied having had sexual contact in Thailand and we cannot be sure of the transmission route, even though his symptoms started after a 3-week stay in Thailand, his pharyngeal test was positive for *N. gonorrhoeae* and his Swedish sexual contact was repeatedly negative when tested. However, gonococci are fastidious bacteria and therefore culture may be false negative. It is therefore important to collect samples from different sites and, if negative, to collect samples repeatedly. Furthermore, NAAT specimens should be analysed.

N. gonorrhoeae is a known cause of septic arthritis, primarily in young adults, but gonococcal osteomyelitis is rare (1). The risk of gonococcal osteomyelitis is said to increase if there is a delay between the onset of joint infection and initiation of appropriate therapy, as was the case in our patients (11). There is limited information available regarding treatment of gonococcal osteomyelitis (12, 13) and the treatment choice for our patients was based on antimicrobial resistance,

clinical evaluation and published case reports (1, 4, 5). Information on the long-term prognosis of gonococcal osteomyelitis is scarce, but permanent joint damage has been described (11).

In order to avoid sequelae from gonococcal infection we must be aware of the increasing bacterial resistance to most available therapeutic drugs (14) and not forget the different, and sometimes uncommon, clinical presentations of *N. gonorrhoeae*.

The authors declare no conflicts of interest.

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