Fox-Lewis, A; Eades, CP; Manson, JJ; Morris-Jones, S; Miller, RF (2017) Neisseria meningitidis serogroup C sepsis and septic arthritis in an HIV-positive man. International journal of STD & AIDS. p. 956462417691439. ISSN 0956-4624 DOI: 10.1177/0956462417691439

Downloaded from: http://researchonline.lshtm.ac.uk/3417076/

DOI: 10.1177/0956462417691439

Usage Guidelines

Please refer to usage guidelines at http://researchonline.lshtm.ac.uk/policies.html or alternatively contact researchonline@lshtm.ac.uk.

Available under license: Copyright the author(s)
Neisseria meningitidis serogroup C sepsis and septic arthritis in an HIV-positive man

A Fox-Lewis1,2, CP Eades1,2, JJ Manson1,3, S Morris-Jones4 and RF Miller1,2,5,6

Abstract
A patient with well-controlled HIV-1 infection presented with fever and rigors, a widespread maculopapular rash, and severe generalised arthralgia. Sepsis of unknown aetiology was diagnosed, and treatment with broad-spectrum antimicrobials commenced. Following initial clinical improvement, a right knee septic arthritis developed. Microscopy and culture of the joint aspirate were negative for organisms but 16S rDNA PCR identified Neisseria meningitidis DNA, subsequently verified as capsular genogroup C, thus confirming a diagnosis of disseminated meningococcal sepsis with secondary septic arthritis.

Keywords
Neisseria meningitidis, septic arthritis, HIV, 16S rDNA

Date received: 5 July 2016; accepted: 2 January 2017

Introduction
Meningococcal sepsis and septic arthritis are medical emergencies. While Staphylococcus aureus and other Gram-positive bacteria such as streptococci are the most common causes of septic arthritis worldwide, Neisseria meningitidis must not be forgotten as an important pathogen in this setting. Reactive arthropathy complicating meningococcal sepsis is well recognised, typically occurring one to two weeks after bacteraemia; however, early-onset septic arthritis is also seen in 2–10% of invasive meningococcal disease. Typically a mono-arthritis, the knee is most commonly affected with concurrent bacteraemia in this context unusual.

Case report
A 52-year-old white man with well-controlled HIV-1 infection (receiving tenofovir/emtricitabine and etravirine, HIV-1 viral load <50 copies/mL, CD4 cell count 670 cells/μl) presented with three days of fevers, rigors, severe generalised arthralgia and profuse watery diarrhoea. He had returned from the USA 16 days previously. While he was there, he had resided in the mid-west in a rural setting and had not visited any clubs or saunas. He was a man who has sex with men and denied any sexual exposures in the six months prior to presentation. Examination revealed an erythematous, maculopapular rash on the shins and severe symmetrical polyarticular arthralgia with tenderness most marked on palpation of the fingers, wrists, knees and ankles. At this point, there was no evidence of synovitis or joint effusion. There was no pharyngitis or urethral discharge. Respiratory and cardiovascular examinations were normal with no murmurs audible, and neurological examination was normal with no meningism or focal neurology. Observations at presentation revealed a peripheral pulse = 120/min, regular, blood pressure = 121/76 mmHg, respiratory rate = 16/min.

1TB Ward, University College London Hospitals NHS Foundation Trust, London, UK
2Mortimer Market Centre, Central and North West London NHS Foundation Trust, London, UK
3Department of Rheumatology, University College London Hospitals NHS Foundation Trust, London, UK
4Department of Clinical Microbiology, University College London Hospitals NHS Foundation Trust, London, UK
5Research Department of Infection and Population Health, University College London, London, UK
6Clinical Research Department, Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, UK

Corresponding author:
A Fox-Lewis, Hospital for Tropical Diseases, Mortimer Market Centre, off Capper Street, London WC1E 6JB, UK.
Email: afoxlewis@gmail.com
peripheral oxygen saturation = 95% (on room air), and tympanic temperature = 38°C.

Initial investigations included a chest radiograph showing bibasal consolidation; markedly elevated inflammatory markers with C-reactive protein = 560 mg/L (normal < 5 mg/L) and total white cell count = $11 \times 10^9$/L (of which, neutrophils = $9 \times 10^9$/L); serum creatinine = 103 μmol/L and eGFR = 68 mL/min/1.73 m² in keeping with acute kidney injury (baseline: 70 μmol/L and >90 mL/min/1.73 m², respectively); and an elevated alkaline phosphatase = 139 IU/L. Lumbar puncture was not performed as it was considered safe to continue. Pharyngeal and rectal NAATs were not performed as they were not felt to be indicated, given the sexual history.

The initial impression was of sepsis of uncertain origin. Empirical antimicrobial therapy with intravenous meropenem 1 g eight-hourly and gentamicin 5 mg/kg once-daily was initiated due to a history of previous severe anaphylaxis to penicillin, meaning that a carbapenem was preferential to a cephalosporin. While aztreonam would be a suitable agent in cases of beta-lactam allergy such as this, it was unavailable for use in the current setting. The patient had no adverse reactions following initiation of meropenem and so it was considered safe to continue.

Over 24 hours, the rash spread to the legs, arms and hands, becoming confluent with scattered petechiae. There was no hypotension, multiorgan failure or desquamation to suggest toxic shock syndrome. On day two, the patient had no adverse reactions following initiation of meropenem and so it was considered safe to continue.

By day 3 of hospitalisation, consideration was given to adding a macrolide to treat presumed gonococcal sepsis with reactive arthritis. Blood cultures taken on admission, and clinical diagnosis was of presumed gonococcal sepsis with early-onset septic arthritis. The patient's status as an HIV-infected man who has sex with men played a large role in the initial clinical suspicion of gonococcal sepsis, with the finding of symmetrical polyarticular arthralgia on examination leading the clinicians to consider associated reactive arthritis. The patient's denial of recent sexual activity, negative urine NAAT for NG, and lack of urethritis or pharyngitis failed to dissuade the treating clinicians of this presumed diagnosis; however, the emergence on day 3 of isolated right knee pain prompted reinvestigation, eventually leading to a diagnosis of meningococcal septicemia.

The patient completed a ten-day course of intravenous meropenem and made good progress post-discharge, although at three months, he continued to have recurrent non-inflammatory effusions in his right knee related to the meniscal tear, and has subsequently been followed up by both the Rheumatology and Orthopaedics teams.

**Discussion**

On reflection following this case, it was felt that the patient’s status as an HIV-infected man who has sex with men played a large role in the initial clinical suspicion of gonococcal sepsis, with the finding of symmetrical polyarticular arthralgia on examination leading the clinicians to consider associated reactive arthritis. The patient’s denial of recent sexual activity, negative urine NAAT for NG, and lack of urethritis or pharyngitis failed to dissuade the treating clinicians of this presumed diagnosis; however, the emergence on day 3 of isolated right knee pain prompted reinvestigation, eventually leading to a diagnosis of meningococcal sepsis with early-onset septic arthritis.

This case is particularly interesting as the patient’s capsular genogroup probably reflects the epidemiology of his recent travel, as approximately one-third of adult meningococcal disease in the USA is serogroup C, whereas in the UK this serogroup is responsible for only 4% of the current invasive meningococcal disease. This is well illustrated by a recent outbreak of serogroup C meningococcal disease in men who have
sex with men (MSM) in Southern California. The diagnosis of meningococcal disease might have been considered sooner if the patient had visited a city in the USA with an ongoing meningococcal outbreak among MSM (e.g. Chicago, New York, Los Angeles) or if he had frequented crowded venues that could have increased his risk of acquiring meningococcal carriage/disease. Of note, MSM are known to have high rates of Neisseria meningitidis carriage (42.5% in one study) and an increased risk of invasive meningococcal disease has been associated with HIV infection and worse outcomes. Thus, in cases of HIV-infected MSM presenting with septic arthritis, clinicians may wish to consider empirical antimicrobials which cover against both N. gonorrhoeae and N. meningitidis.

Of note, the patient had not been vaccinated against meningococcus, and this illness caused by N. meningitidis serogroup C may have been prevented had he previously received the MenC or MenACWY vaccine. This is an important learning point and a reminder that all HIV-infected MSM should be offered meningococcal vaccination as per UK national guidelines.

This case also underscores the utility of PCR-based techniques in the microbiological diagnosis of septic arthritis, especially when joint aspiration is performed after antimicrobial initiation. Gram stain and culture may become negative shortly after initiation of antimicrobial therapy whereas bacterial rDNA persists and may be detected by molecular methods several weeks later. The addition of 16S rDNA PCR to routine processing of joint specimens increases diagnostic yield over culture alone in paediatric septic arthritis.

In conclusion, in cases of HIV-infected MSM presenting with sepsis or septic arthritis, it is important to keep a broad range of aetiological agents in mind, including less typical causes of septic arthritis such as N. meningitidis, an important notifiable organism. A thorough travel, sexual and vaccination history is invaluable, especially in this group of patients. 16S rDNA PCR can be a useful adjunctive investigation in septic arthritis and can be of particular use both early in the course of the disease if initial microscopy and culture fails to yield a microbiological diagnosis, or at a later juncture if joint aspiration is performed after the initiation of antimicrobial therapy.

Declaration of conflicting interests
The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding
The author(s) received no financial support for the research, authorship, and/or publication of this article.

References
