Infection (2012) 40:319–321
DOI 10.1007/s15010-011-0181-x

CASE REPORT

Rat bite fever as a presenting illness in a patient with AIDS

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Received: 9 March 2011 / Accepted: 9 August 2011 / Published online: 30 August 2011

Abstract The etiology of culture-negative septic arthritis is poorly characterised in persons infected with human immunodeficiency virus (HIV). New molecular methods may assist in the investigation of culture-negative infections of sterile sites, including septic arthritis. We describe the first case of septic arthritis due to the cause of rat bite fever (RBF), *Streptobacillus moniliformis*, confirmed by 16s rRNA sequence analysis, in a patient with newly diagnosed HIV infection.

Keywords Rat bite fever · HIV · Septic arthritis

Introduction

Infections by *Streptobacillus moniliformis*, the etiology of rat bite fever (RBF), are rare in immunocompetent hosts and are even more scantily reported in immunocompromised patients. We describe the first case of culture-negative *S. moniliformis* septic arthritis, confirmed by 16S rRNA sequence analysis, in a patient with advanced human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) infection.

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Case description

A 30-year-old man who has sex with other men, with a history of injecting drug use and newly diagnosed chronic hepatitis C, presented with a 1-month history of intermittent fever, malaise, myalgias, headaches, diarrhoea and a weight loss of 15% body weight over 6 months. There was neither urethral discharge nor symptoms of decompensated liver disease. Clinically, he was cachectic, febrile 39°C and had oral candidiasis. He had neither skin rash nor other abnormalities on the remainder of the physical examination. Initial investigations revealed a normal full blood examination, electrolytes and serum creatinine. The liver function test showed alkaline phosphatase 270 U/L (reference range 30–120 U/L), gamma-glutamyl transferase 128 u/L (reference range 7–64 u/L) with normal transaminases and total bilirubin. The C-reactive protein level was 219 mg/L (reference range 0–5 mg/L) and the erythrocyte sediment rate was 114 mm/h (reference range 0–10 mm/h). Hepatitis C viral load was 84,599,395 IU/ml (log 7.93), whilst hepatic ultrasound did not show changes of cirrhosis.

There was no bacterial growth on three blood culture sets, urine and faecal cultures taken before antibiotic therapy. An HIV antibody test was negative when tested 2 years previously. Now, HIV-1 antibodies were detected on enzyme immunoassay and confirmed on Western blot; the HIV-1 viral load was >100,000 copies/ml and a CD4 count of 53×10^6/L (9%) was noted. Serological testing revealed no evidence of hepatitis B, syphilis or toxoplasma, or past cytomegalovirus (CMV) infection. Serum cryptococcal antigen was not detected. Mycobacteria blood cultures had no growth. Echocardiography and polymerase chain reaction (PCR) of blood was not undertaken, as the patient did not fulfill the modified Duke's criteria for

infective endocarditis and endocarditis was not suspected clinically.

On the third day of admission, he developed right knee pain. The knee was warm, tender, had limited movement and displayed a moderate-sized effusion. A joint aspirate was performed and synovial fluid analysis revealed 19,000 $\times$ 10^6/L polymorphs, 150 $\times$ 10^6/L lymphocytes and 2,000 $\times$ 10^6/L red cells. Crystals were not seen. There was no growth of fungi and bacteria on routine synovial fluid culture after 7 days of incubation. Mycobacterial synovial cultures were also negative at the end of 6 weeks. *Neisseria gonorrhoeae* and *Chlamydia trachomatis* were not detected by PCR on urine, rectal swabs or synovial fluid. He was commenced empirically on intravenous (IV) ceftriaxone and flucloxacilin, just prior to a knee washout. Fever slowly resolved but he continued to have significant right knee pain.

Fever >38°C recurred 7 days after the washout. Upon re-evaluation, it was noted that he had two pet rats, one of which bit the man on his right index finger 1 month prior to presentation. The bite had healed by the time of presentation.

Bacterial DNA was extracted from the original synovial fluid and 16S rRNA was amplified, sequenced and analysed using the MicroSeq 500 system (Perkin Elmer Applied Biosystems Inc., Foster City, CA, USA). The 16S rRNA gene sequence had >99.9% homology with *S. moniliformis*. He went on to complete 6 weeks of IV benzylpenicillin, followed by 4 weeks of oral doxycycline. He clinically improved with the normalisation of inflammatory markers but continued to have restricted knee movement. Highly active anti-retroviral therapy (HAART) was commenced 2 months after diagnosis.

Discussion

RBF is a rare zoonotic infection caused by *S. moniliformis* in North America, Europe and Australia, or, more rarely, by *Spirillum minus* in Asia [1]. *S. moniliformis* RBF typically results from a rat bite, close contact with rats or rodent-like animals, or ingesting rat excreta-contaminated milk [1]. It is a difficult-to-culture fastidious organism [1]. Its prevalence may be increasing [2].

S. moniliformis RBF typically causes a relapsing-remitting rash, migratory polyarthritis or arthralgia, and fever [1]. Whilst it is postulated that the polyarthritis is immunological in origin, the isolation of *S. moniliformis* from synovial fluid causing a true septic arthritis is well-described [3]. Clinical and epidemiological differences between immunocompetent and immunocompromised hosts, including those with HIV infection, are difficult to isolate due to the probable under-diagnosis and rarity of the disease, especially in the latter group.

The case presented here demonstrates the diagnostic challenges of septic arthritis. Synovial fluid analysis, culture and blood cultures remain critical in the diagnoses of septic arthritis and determination of the microbiological etiology [4, 5]. However, up to 18% of septic arthritis in the non-HIV population [6–8] and between 0 and 50% of septic arthritis in HIV-infected patients are culture-negative [9–14]. Culture-negativity is commonly due to prior antibiotic therapy and fastidious organisms [7]. In this setting, molecular techniques such as 16S rRNA PCR amplification using universal primers are important adjunctive investigative tools previously shown to be non-inferior to culture-based methods [7]. 16S rRNA sequencing has previously been used to diagnose *S. moniliformis* septic arthritis in a non-HIV patient from colonies growing on media inoculated with joint fluid [15]. In our case, we successfully used 16S rRNA sequencing directly on synovial fluid without growth on media.

Septic arthritis is uncommonly described in the HIV population. The microbiological etiology of septic arthritis is strongly dependent on the patient epidemiology and risk factors for HIV acquisition [16]. In injecting drug users with HIV infection, the most common causative organisms are *Staphylococcus aureus* and *Candida albicans* [16], but many other opportunistic pathogens have been described [17].

The only previous report of *S. moniliformis* in HIV infection described a case of infective endocarditis resulting from a pet rat bite in a man with known HIV and injecting drug use. He had 3 months of fevers and chills, and 1 week of polyarthritis. Echocardiography confirmed mitral valve endocarditis and *S. moniliformis* was isolated on blood cultures [18]. This case, like ours, also highlights an important epidemiological point. Pet ownership levels amongst the HIV population is not dissimilar to the non-HIV-population, including up to 2% of pet owners owning pet rodents [19]. Physicians need to be cognisant of this relationship in order to prevent missing the diagnoses of zoonotic infections in their patients.

Conclusion

This is a first case of culture-negative *Streptobacillus moniliformis* septic arthritis described in a human immunodeficiency virus (HIV)-infected patient. Physicians need to be aware of unusual causes of septic arthritis. Pet ownership amongst patients, including those with HIV infection, must lead the treating doctor to think about potential zoonotic infections, much like our case here of *S. moniliformis*. Molecular diagnostics may be useful in the diagnosis of culture-negative septic arthritis among patients.

Conflict of interest None.

References

1. Elliott SP. Rat bite fever and *Streptobacillus moniliformis*. Clin Microbiol Rev. 2007;20:13–22.
2. Graves MH, Janda JM. Rat-bite fever (*Streptobacillus moniliformis*): a potential emerging disease. Int J Infect Dis. 2001; 5:151–5.
3. Dendle C, Woolley IJ, Korman TM. Rat-bite fever septic arthritis: illustrative case and literature review. Eur J Clin Microbiol Infect Dis. 2006;25:791–7.
4. Mathews CJ, Weston VC, Jones A, Field M, Coakley G. Bacterial septic arthritis in adults. Lancet. 2010;375:846–55.
5. Jenney A. Rheumatological disease. In: Hoy J, Lewin S, Post JJ, Street A, editors. HIV management in Australasia: a guide for clinical care. Sydney: Australasian Society of HIV Medicine; 2009.
6. Eder L, Zisman D, Rozenbaum M, Rosner I. Clinical features and aetiology of septic arthritis in northern Israel. Rheumatology (Oxford). 2005;44:1559–63.
7. Fenollar F, Roux V, Stein A, Drancourt M, Raoult D. Analysis of 525 samples to determine the usefulness of PCR amplification and sequencing of the 16S rRNA gene for diagnosis of bone and joint infections. J Clin Microbiol. 2006;44:1018–28.
8. Weston VC, Jones AC, Bradbury N, Fawthrop F, Doherty M. Clinical features and outcome of septic arthritis in a single UK health district 1982–1991. Ann Rheum Dis. 1999;58:214–9.
9. Hughes RA, Rowe IF, Shanson D, Keat AC. Septic bone, joint and muscle lesions associated with human immunodeficiency virus infection. Br J Rheumatol. 1992;31:381–8.
10. Muñoz Fernandez S, Quiralte J, del Arco A, Balsa A, Cardenal A, Peña JM, et al. Osteoarticular infection associated with the human immunodeficiency virus. Clin Exp Rheumatol. 1991; 9:489–93.
11. Ventura G, Gasparini G, Lucia MB, Tumbarello M, Tacconelli E, Caldarola G, et al. Osteoarticular bacterial infections are rare in HIV-infected patients. 14 cases found among 4,023 HIV-infected patients. Acta Orthop Scand. 1997;68:554–8.
12. Monteagudo I, Rivera J, Lopez-Longo J, Cosin J, Garcia-Monforte A, Carreño L. AIDS and rheumatic manifestations in patients addicted to drugs. An analysis of 106 cases. J Rheumatol. 1991;18:1038–41.
13. Vassilopoulos D, Chalasani P, Jurado RL, Workowski K, Agudelo CA. Musculoskeletal infections in patients with human immunodeficiency virus infection. Medicine (Baltimore). 1997;76:284–94.
14. Zalavras CG, Dellamaggiora R, Patzakis MJ, Bava E, Holtom PD. Septic arthritis in patients with human immunodeficiency virus. Clin Orthop Relat Res. 2006;451:46–9.
15. Wallet F, Savage C, Loïez C, Renaux E, Pischedda P, Courcol RJ. Molecular diagnosis of arthritis due to *Streptobacillus moniliformis*. Diagn Microbiol Infect Dis. 2003;47:623–4.
16. Medina F, Pérez-Saleme L, Moreno J. Rheumatic manifestations of human immunodeficiency virus infection. Infect Dis Clin North Am. 2006;20:891–912.
17. Cuellar ML. HIV infection-associated inflammatory musculoskeletal disorders. Rheum Dis Clin North Am. 1998;24:403–21.
18. Rordorf T, Züger C, Zbinden R, von Graevenitz A, Pirovino M. *Streptobacillus moniliformis* endocarditis in an HIV-positive patient. Infection. 2000;28:393–4.
19. Conti L, Lieb S, Liberti T, Wiley-Bayless M, Hepburn K, Diaz T. Pet ownership among persons with AIDS in three Florida counties. Am J Public Health. 1995;85:1559–61.