A 36-year-old female from Kuwait with AIDS presenting with fever and abdominal pain

Keywords

acid-fast; AIDS; mycobacterium; mycobactin J.

Case summary

A 36-year-old woman from Kuwait with AIDS [CD4 cell count $43 \text{ cells } \mu\text{l}^{-1}$, human immunodeficiency virus (HIV) viral load $70 \text{ copies ml}^{-1}$] was transferred to our institution for evaluation and management of fever, abdominal pain, altered mental status, pancytopenia and generalized debility. She was treated for *Pneumocystis jiroveci* pneumonia, *Cytomegalovirus* encephalitis and *Candida albicans* fungaemia. Her medications included emtricitabine/tenofovir 200–300 mg once daily, raltegravir 400 mg twice daily, trimethoprim-sulfamethoxazole 160–800 mg orally every 48 h, azithromycin 1250 mg orally once weekly and valganciclovir 900 mg twice daily. Initial laboratory data comprised a white blood cell count of $1.9 \times 10^9 \text{ l}^{-1}$, neutrophil count of $1.5 \times 10^9 \text{ l}^{-1}$, platelet count of $61 \times 10^9 \text{ l}^{-1}$, haemoglobin 9.9 g dl^{-1} , aspartate transaminase 47 U l^{-1} , alanine transaminase 59 U l^{-1} , alkaline phosphatase 258 U l^{-1} and serum creatinine 0.2 mg dl^{-1} . Computerized tomography of the abdomen showed moderate mesenteric and retroperitoneal lymphadenopathy without hepatosplenomegaly. A fine-needle aspiration biopsy of the mesenteric lymph node showed an extensive histiocytic infiltrate containing innumerable acid-fast bacilli following Fite and Ziehl Neelsen acid-fast stains (Fig. 1a). The biopsy aspirate was plated onto Middlebrook 7H11/7H11 selective agar, and grew small, pinpoint, translucent colonies after

Question

This acid-fast organism grew after prolonged incubation and following Mycobactin J supplementation of the medium. What is the most likely aetiological agent in this HIV-positive host?

Answer options

1. *Mycobacterium avium* complex
2. *Mycobacterium genavense*
3. *Mycobacterium tuberculosis* complex
4. *Mycobacterium hemophilum*
5. *Mycobacterium leprae*

6 weeks of incubation at 37°C (Fig. 1b). A nucleic acid hybridization probe (Hologic GenProbe AccuProbe) specific for *Mycobacterium avium* complex (MAC) was negative. A definitive identification was made using 16S rRNA gene sequencing. The organism was also subcultured onto Mycobacterial Growth Indicator Tubes (MGIT; Becton Dickinson) with and without Mycobactin J supplementation. After 5 weeks of incubation at 37°C , the MGIT broth containing Mycobactin J produced a positive signal, whilst no growth was detected in the unsupplemented broth after 6 weeks.

Discussion

Correct answer: 2. *Mycobacterium genavense*.

The 16S rRNA gene sequence of the isolate was a 100 % match to a *M. genavense* type strain. *M. genavense* is a fastidious, slow-growing, non-tuberculous mycobacterium best known for causing opportunistic infections in patients with AIDS and in

solid-organ transplant patients (Hoefsloot *et al.*, 2013; Pechere *et al.*, 1995). The clinical features of disseminated *M. genavense* resemble those of disseminated MAC infection (Thomsen *et al.*, 1999). *M. genavense* rarely grows on conventional mycobacterial media (Coyle *et al.*, 1992), but growth may be enhanced by the addition of Mycobactin J (an iron-containing compound), or blood and charcoal, to acidified Middlebrook agar under microaerophilic conditions. In addition, avoidance of pre-treatment and extended incubation for up to 8 weeks may increase the detection of *M. genavense* (Thomsen *et al.*, 1999). Colonies are typically smooth, pale yellow or white. In our patient, the original growth of *M. genavense* on solid medium in the absence of added Mycobactin J may have been due to the introduction of blood containing iron from the biopsy specimen. *M. genavense* isolates are generally susceptible to rifamycins, macrolides and fluoroquinolones and resistant to isoniazid. There is evidence of *in vivo* resistance to ethambutol and clofazimine (Thomsen *et al.*, 1999).

Fig. 1. (a) Fite stain of a mesenteric lymph node sampled by fine-needle aspiration biopsy showing histiocytic infiltrates containing many acid-fast bacilli. Magnification, $\times 400$. (b) Middlebrook agar plate with small, pinpoint, translucent colonies after 6 weeks of incubation at 37 °C.

After MAC, *M. genavense* is the second most common non-tuberculous mycobacterium causing infection in AIDS patients, comprising 12.8 % of all non-tuberculous mycobacterium infections in such patients (de Lastours *et al.*, 2008). *M. genavense* can also produce infection in select immunosuppressed non-HIV-infected patients (Hoefsloot *et al.*, 2013; Santos *et al.*, 2014). It typically produces disseminated disease that can be similar to that of MAC and can frequently be recovered from blood, bone marrow, lymph nodes, stool, hepatic tissues and other organ tissues. *M. genavense*, however, is probably under-recognized due to difficulty in culture recovery of the organism. In our institution, this is the only case of *M. genavense* that we have encountered in the last 8 years. In samples from an appropriate immunological host with positive acid-fast bacillus smears but negative mycobacterial cultures, *M. genavense* should be included in the differential diagnosis, and the culture medium should be augmented with Mycobactin J and molecular diagnostics used to enhance diagnostic accuracy. In this case, the patient was

treated initially with clarithromycin, ethambutol and rifabutin for presumed disseminated MAC infection. This treatment regimen was maintained after identification of *M. genavense*, and the patient is expected to continue therapy for at least 6 months after immune reconstitution (CD4 cell count >100 cells mm^{-3}).

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