Multiple 'doughnut' granulomas in a liver transplant patient with CMV reactivation

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DESCRIPTION

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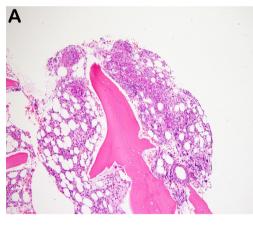
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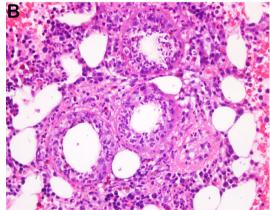
Accepted 15 November 2018

A 50-year-old man with a history of alcoholic cirrhosis and liver failure, postorthotopic liver transplantation 6 months prior, presented with failure to thrive and diffuse body pain for 1 month. Physical examination was unremarkable aside from low-grade fever. There was no adenopathy or rash.

A complete blood count showed leucopenia (white cell count: 1.4×10^9 /L), mild anaemia (haemoglobin: 124 g/L) and thrombocytopenia (platelets: 100×10^9 /L). Liver enzymes were normal. The bone marrow biopsy revealed normocellular marrow with adequate trilineage haematopoiesis and multiple 'doughnut' granulomas consisting of a central lipid vacuole surrounded by epithelioid histiocytes and a dense eosinophilic fibrin ring¹ (figure 1A,B).

Gomori methenamine silver and acid-fast bacilli stains were negative. Serologic testing for fungi,





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To cite: Dejhansathit S, Miller AM, Suvannasankha A. *BMJ Case Rep* 2018;**11**:e227252. doi:10.1136/bcr-2018-227252

Figure 1 Bone marrow biopsy. H&E staining showed a normocellular bone marrow with maturing trilineage haematopoiesis remarkable for multiple 'doughnut' granulomas consisting of a central lipid vacuole surrounded by fibrin and epithelioid histiocyte. (A) 100x, (B) 400x. HIV, *Treponema* and *Brucella* was negative. *Coxiella burnetii* serology testing was negative. Quantitative PCR for cytomegalovirus (CMV)² was below 500 copies/mL 1 month prior but had increased to 190000 copies/mL. Patient was diagnosed with CMV infection and treated with intravenous ganciclovir for 14 days, followed by oral valganciclovir³. Blood counts normalised 2 months after treatment, at which time CMV PCR was negative.

Learning points

- Fibrin ring or doughnut granulomas are a classical finding of *Coxiella* infection, but can also be attributed to other disseminated infections including Epstein-Barr virus, cytomegalovirus (CMV), hepatitis A virus, *Leishmania donovani* and *Staphylococcus* epidermidis, as well as non-infectious causes including allopurinol hypersensitivity and Hodgkin's disease.
- CMV infection is the most common viral infection in liver transplant recipients, caused by both a reactivation of CMV during the immunocompromised state and, less commonly, an acquired infection from seropositive organ donors or blood transfusion.
- Fever and pancytopenia are common presentation of CMV reactivation. Patient with severe or tissue-invasive syndromes should receive initial intravenous ganciclovir or foscarnet, which can be switched to oral regimen on clinical improvement. Mild disease in immunosuppressed patients may be treated with oral valganciclovir.

Contributors AS identified the important nature of this finding. SD reviewed literature, and drafted and edited the article. AS revised and approved the article. AMM is the pathologist concerned in this case. All authors have read and agreed with the content.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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