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Marrow cryptococcosis in an autologous stem cell transplant patient after standard therapy for cryptococcal meningitis

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Abstract

The patient is a woman in her 60s with a history of plasma cell myeloma, status post high-dose melphalan and autologous stem cell transplant, followed by maintenance lenalidomide. She was admitted for severe headaches with concern for meningitis. CSF culture yielded *Cryptococcus neoformans*. Cryptococcal antigen was present at high titer in the CSF (1:640) but was negative in serum. A diagnosis of cryptococcal meningitis was rendered. She was treated with over 2 weeks of intravenous amphotericin plus flucytosine. Upon discharge, her CSF cryptococcal antigen test remained positive (1:2560) but CSF culture was negative. She continued to experience mild headaches after discharge and was maintained on daily oral fluconazole. Several months later, a bone marrow biopsy was performed to evaluate for residual myeloma post-transplant. There was no morphologic, immunohistochemical, or flow cytometric evidence of residual plasma cell neoplasm. However, the core biopsy revealed suspicious clusters of histiocytes (A) with numerous cytoplasmic inclusions, some of which appeared to contain thick cell wall-like structures (B). Special stains, including periodic acid-Schiff (PAS, C) and Grocott's methenamine silver (GMS, D), identified variably sized yeast forms, morphologically compatible with *Cryptococcus*. Infected histiocytes were not visualized on the aspirate smears. A repeat serum cryptococcal antigen test was positive (1:640). She was kept on daily oral fluconazole and is being closely followed by infectious disease. Immunocompromised patients are at increased risk for a variety of marrow infections, including *Cryptococcus*. Patients with plasma cell myeloma are at risk for invasive fungal infections after autologous stem cell transplant and while taking lenalidomide, which alters CD4 + and CD8 + T-cell function through multiple mechanisms. Due to a lack of standardized treatment protocols for therapy-refractory non-pulmonary non-meningeal cryptococcal disease, therapy regimens are often tailored on a case-by-case basis.

Keywords Plasma cell myeloma · Marrow/stem cell transplantation · *Cryptococcus* · Opportunistic infection

The patient is a woman in her 60s with a history of plasma cell myeloma, status post high-dose melphalan and autologous stem cell transplant, followed by maintenance lenalidomide. She was admitted for severe headaches with concern for meningitis. CSF culture yielded *Cryptococcus neoformans*. Cryptococcal antigen was present at high titer in the CSF (1:640) but was negative in serum. A diagnosis of cryptococcal meningitis was rendered. She was treated with over 2 weeks of intravenous amphotericin plus flucytosine. Upon discharge, her CSF cryptococcal antigen test remained positive (1:2560) but CSF culture was negative. She continued to experience mild headaches after discharge and was maintained on daily oral fluconazole.

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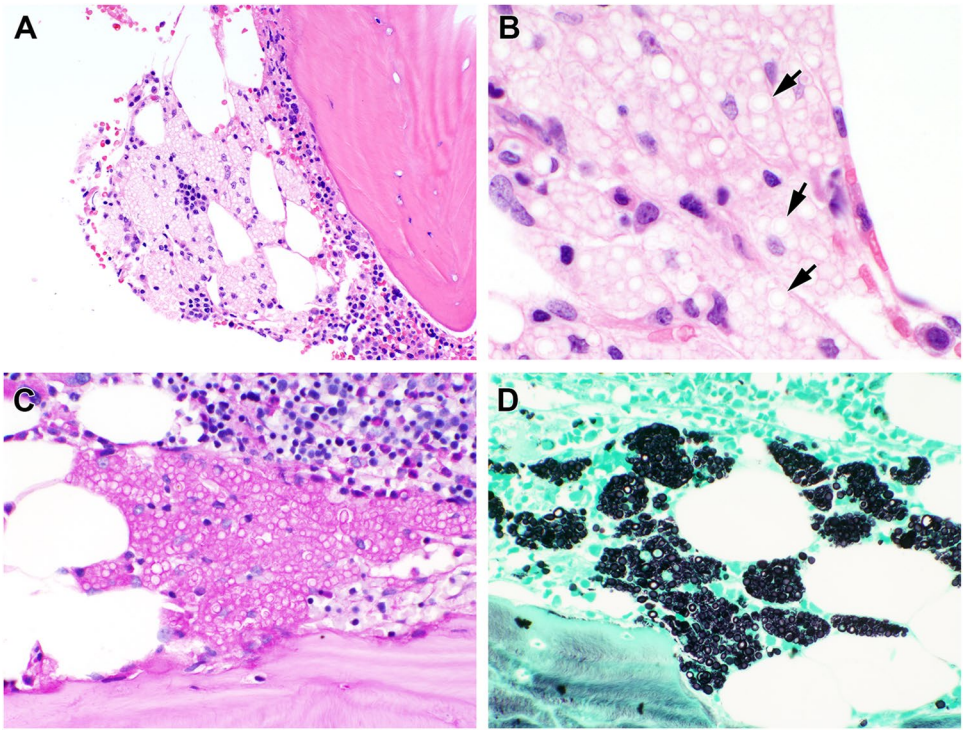

Fig. 1 **A** Hematoxylin and eosin (H&E)-stained section of the marrow core biopsy with clusters of vacuolated histiocytes. 10x magnification. **B** H&E stain, showing some vacuoles with thickened cell wall-like structures. 40x magnification. **C** PAS stain, highlighting fungal cell walls. 20x magnification. **D** GMS stain, highlighting fungal cell walls. 20x magnification

Immunocompromised patients are at increased risk for a variety of marrow infections, including *Cryptococcus*[1]. Patients with plasma cell myeloma are at risk for invasive fungal infections after autologous stem cell transplant[2] and while taking lenalidomide[3], which alters CD4 + and CD8 + T-cell function through multiple mechanisms[4]. Due to a lack of standardized treatment protocols for therapy-refractory non-pulmonary non-meningeal cryptococcal disease, therapy regimens are often tailored on a case-by-case basis[5].

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Declarations

Ethical approval This study was granted exemption by the Duke University Health System Institutional Review Board.

Consent to participate/informed consent This was not deemed necessary by the IRB since no identifiable data is being reported and only histologic images are being presented.

Consent for publication This was not deemed necessary by the IRB since no identifiable data is being reported and only histologic images are being presented.

Conflict of interest The authors declare no competing interests.

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