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Invasive granulomatous cryptococcal sinusitis in an adult with multiple myeloma

Richard A. Ferraro [a,*], Jana Ivanidze [a], Elizabeth Margolskee [b], Hamilton Tsang [b], Theresa Sconomiglio [b], Yuliya S. Jhanwar [a]

[a] Department of Radiology, Weill Cornell Medical College, New York-Presbyterian Hospital, New York, NY 10021
[b] Department of Pathology, Weill Cornell Medical College, New York-Presbyterian Hospital, New York, NY 10021

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ABSTRACT

We report a case of cryptococcal sinusitis, a rare presentation of *Cryptococcus neoformans* infection in a patient with multiple myeloma. The objective of this case report is to highlight the utility of structural and functional imaging modalities in the differential diagnosis of sinonasal soft tissue masses in the immunocompromised patient population. PET-CT was the first imaging modality in this patient, who presented for routine follow-up staging of multiple myeloma, and was asymptomatic at the time of his presentation. PET-CT findings prompted further evaluation with MRI, to aid in the differential diagnosis with respect to a neoplastic versus infectious etiology. Ultimately, surgical excision with histopathology was required to provide definitive diagnosis. Final histopathology displayed yeast-organism staining consistent with *Cryptococcus neoformans/gatti.* The patient subsequently underwent treatment for this infection, along continued treatment for multiple myeloma. To our knowledge this is the first known case of cryptococcal sinusitis in a patient with neoplastic disease. Imaging represents an important tool to differentiate fungal infection from neoplasm in the immunocompromised patient population. As the population of immunocompromised patients continues to grow, the relevance of this diagnosis as well as the use of alternative imaging modalities is becoming more important in clinical practice.

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1. Introduction

Cryptococcal infection, primarily acquired via inhalation, commonly occurs in immunocompromised patients [1]. Although pulmonary cryptococcosis represents the most common manifestation of cryptococcal infection, involvement of the central nervous system has previously been reported, particularly in severely immunocompromised patients. In patients undergoing chemotherapy, cryptococcal infection has been reported infrequently, with other fungal infections such as *Aspergillus* and *Candida albicans* being much more common [2].

Cryptococcal sinusitis is exceedingly rare overall, with only very few cases reported in the literature to date [3,4]. Presented here is a case of invasive cryptococcal sinusitis with granulomatous features in a patient with multiple myeloma. To our knowledge, FDG PET-CT imaging features of cryptococcal sinusitis have not previously been reported.

2. Case report

A 64-year-old man with IgG-Kappa multiple myeloma (diagnosed 12 years prior; previously well controlled on bortezomib, lenalidomide and dexamethasone), presented for routine work-up and extent of disease evaluation. Past medical history was significant for pulmonary embolus treated with warfarin. The patient had also previously undergone an L5 kyphoplasty. At the time of his presentation, the patient was in good health and denied any new symptoms. Specifically, no symptoms of sinusitis were reported. Review of systems showed no signs of generalized infection, weight loss, headache or facial pain, rhinorrhea, dysphagia, post-nasal drip, or sinus congestion/obstruction to breathing. Physical exam with nasal endoscope showed no obvious masses or lesions in the sphenoid or ethmoid sinuses, normal mucosa, and no purulent discharge.

Serum immunoglobulin measurement at this visit showed increased paraproteinemia, with a serum IgG of 2050 mg/dL, free Kappa light chain of 6.06 mg/dL, and Kappa/Lambda free light chain ratio of 4.01. The patient was subsequently referred for whole body PET-CT, which showed multiple hypermetabolic bony lesions in the axial and appendicular skeleton, including an FDG-avid masslike lesion in the left sphenoid sinus (Fig. 1). Given the patient's underlying diagnosis of multiple myeloma, these findings prompted a broad differential diagnosis including multiple myeloma lesion, primary neoplasm, metastatic disease of unknown primary, and infectious process. FDG-avidity on PET is not a specific finding and may be seen in both primary and secondary malignancy as well as infection. Follow-up MRI of the lesion was thus obtained, demonstrating a contrast-enhancing soft tissue mass in the left sphenoid sinus and left posterior ethmoid air cells, measuring 1.7 ×

* Corresponding author.
E-mail address: raf2006@med.cornell.edu (R.A. Ferraro).

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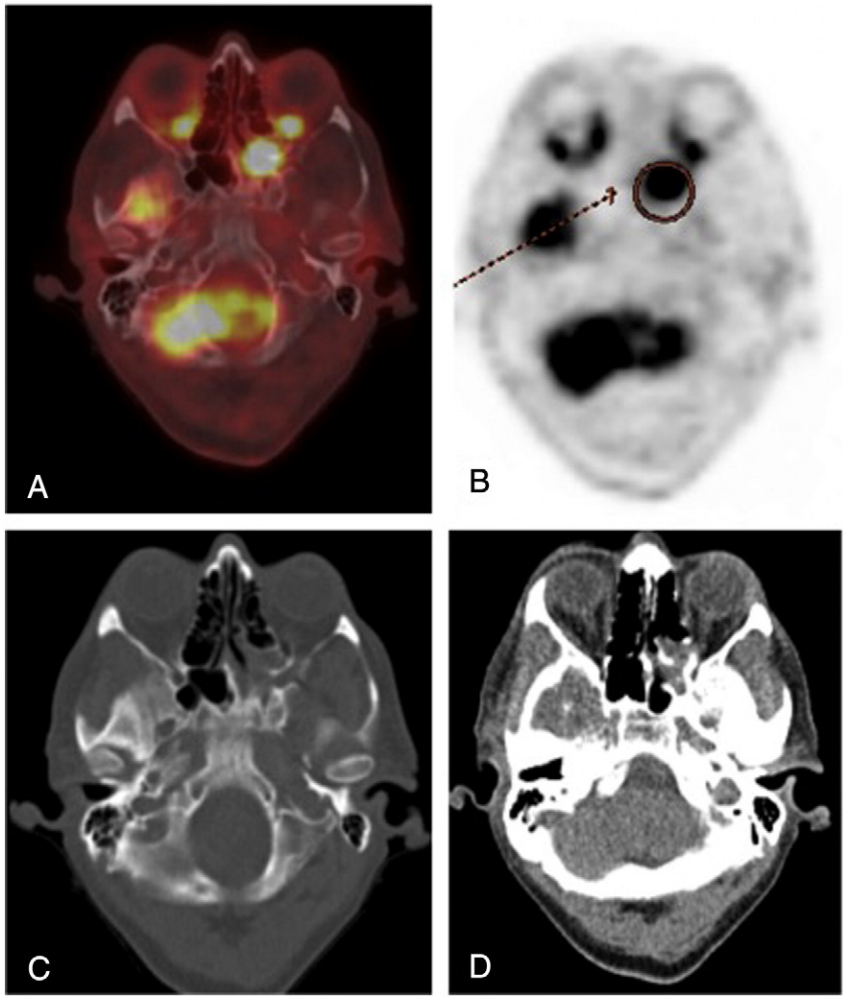

Fig. 1. PET-CT findings in cryptococcal sinusitis. Axial images through the level of the orbits are shown. (A) Axial Fused PET and CT image; (B) Axial PET Image; (C) Axial CT Image; bone window; (D) Axial CT Image, soft tissue window. A hypermetabolic soft tissue mass is identified in the left sphenoid sinus (arrow in image (B)). There is no evidence of associated osseous destruction.

1.0 × 1.3 cm (Fig. 2). No osseous invasion was noted. A maxillofacial CT examination performed shortly thereafter revealed continuous infiltration of the posterior superior nasal cavity, left sphenopalatine foramen, inferior orbital fissure, and pterygopalatine fossa.

Based on the imaging studies, a surgical biopsy was scheduled. A total ethmoidectomy and left sphenoidectomy was performed. Culture of the sample grew *Staphylococcus lugdenesis*, for which trimethoprim/sulfamethoxazole was added, and the patient was additionally scheduled for radiation therapy pending pathology diagnosis.

Biopsies of the left sphenoid and posterior ethmoid sinuses showed chronically inflamed respiratory mucosa with extensive granulomatous inflammation with necrosis. Numerous cystic spaces contained small encapsulated yeast forms. These organisms were positive for Gomori methenamine silver, mucicarmine, and Fontana-Masson stains, consistent with *Cryptococcus neoformans/gattii* (Fig. 3). Acid fast stains for mycobacterial organisms were negative.

The patient was subsequently admitted for lumbar puncture and antifungal therapy. While CSF was found to be negative for cryptococcal antigen, cryptococcal antigen was detected in the serum at 1:64. Given these findings, the patient was started in IV Liposomal Amphotericin B, flucytosine, and piperacillin/tazobactam, along with continued chemotherapy for bony lesions. Treatment was complicated by acute kidney injury, suspected to be secondary to antifungal therapy. The patient was discharged after 15-day induction course, and subsequently treated as an outpatient with fluconazole along with continuation of his chemotherapy regimen. Follow-up culture following discharge was negative, and the patient remained without symptoms or signs of sinus infection. The patient is scheduled to continue antifungal therapy on an outpatient basis for a course of 6–12 months.

3. Discussion

Fungal sinusitis represents an important differential diagnostic consideration in an immunocompromised patient presenting with a masslike lesion in the paranasal sinuses. Common causative organisms for fungal sinusitis include Mucormycosis and Aspergillosis. Cryptococcal sinusitis is exceedingly rare, with only four cases reported in the literature [3]. While a number of the previously reported cases were associated with an immunocompromised state, this case represents, to the best of our knowledge, the first instance of this diagnosis in a patient with multiple myeloma [4]. Moreover, this case represents a unique illustration of PET-CT findings in cryptococcal sinusitis.

CT is often used as the first-line imaging modality for suspected cases of fungal sinusitis, particularly for surgical and procedural planning [5]. MRI has the advantage of no associated radiation exposure, and provides important complementary information, exhibiting greater sensitivity of compared to CT [6].

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