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Case Report

Orbital proptosis in a young immunocompetent female patient

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Introduction

Invasive fungal infections of the nasal and paranasal sinuses are emerging health care problems and are increasingly being reported in healthy immunocompetent persons. Fungal rhinosinusitis (FRS) broadly encompass a wide spectrum of immune and pathological responses that include invasive, chronic, granulomatous and allergic disease. A wide range of fungal species are involved but Aspergillus species is the most common etiological agent. Granulomatous invasive FRS is one of the variants particularly prevalent in Sudan, India, Pakistan and Saudi Arabia. Herein we report a case of chronic granulomatous invasive fungal sinusitis in an immunocompetent adult female.[1–3]

Case report

A 28 year young female patient immunocompetent and non-diabetic from urban background presented with right sided nasal obstruction, mucous discharge and gradual development of proptosis and telecanthus of 3 months duration. There was no history of nasal bleed or visual defect. Anterior rhinoscopy revealed a multilobulated polypoid mass in the right nasal cavity not bleeding to touch. Detailed examination of head and neck and laboratory parameters did not reveal any abnormality. Hematological and biochemical parameters were within normal limits. A plain radiograph followed by a CT scan of the paranasal sinuses was reported as follows: A polypoidal mass lesion epicentered in the right ethmoidal sinus extending into the right nasal cavity and the right orbit causing destruction of the bony septae of the ethmoidal sinus and medial wall of the orbit resulting in deviation of the bony nasal septum to the left, but no intracranial extension of the lesion was noted (Fig. 1). A partial functional endoscopic sinus surgery (FESS) was performed and a polypoidal mass with large quantity of blackish yellow debris was removed and sent for histopathological examination (HPE) that revealed a chronic granulomatos lesion with multinucleated giant cells.

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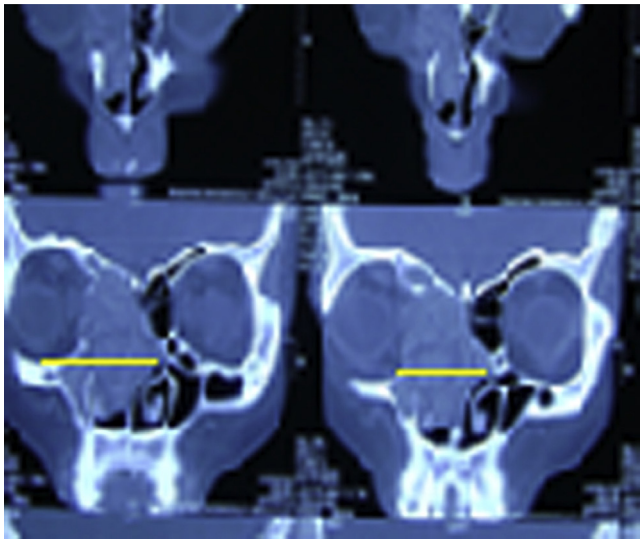

Fig. 1 – CT scan right paranasal sinus: A polypoidal mass lesion epicentered in the right ethmoidal sinus extending into the right nasal cavity and the right orbit causing destruction of the bony septae of the ethmoidal sinus and medial wall of the orbit resulting in deviation of the bony nasal septum to the left. But, no intracranial extension of the lesion was noted.

Acid fast bacilli (AFB), malignant cells and fungal elements were not seen. Based on the HPE findings, a diagnosis of tuberculosis was made and the patient was started on antitubercular treatment (ATT). She, however, reported back to hospital after 6 weeks of ATT without any regression in proptosis or telecanthus. Recurrence of the nasal mass was confirmed on anterior rhinoscopy and a repeat CT scan. FESS was carried out again with complete removal of the mass along with all its extensions. Appropriate media were inoculated for bacterial isolation. A 20% KOH mount and culture on plain Sabouraud's dextrose agar (SDA) and SDA with gentamicin and cycloheximide at 25 °C and 37 °C respectively was done for isolation of fungal pathogens.

No significant bacterial growth was seen after 48 h of incubation in 10% CO_2 and no fungal elements were seen on direct KOH mount. Tissue sections showed noncaseating granulomatous lesions with foreign body type of multinucleated giant cells and infiltrating lymphomononuclear cells, predominantly plasma cells (Fig. 2). Gomori's methenamine silver (GMS) stained tissue sections revealed hyaline septate hyphae with dichotomous branching (Fig. 2). Fungal elements within the giant cells were not visualized on GMS stain. Neither could we demonstrate any ''negative image'' of the fungal hyphae inside the giant cells on H&E staining. There was no evidence of vasculitis, vascular proliferation or perivascular fibrosis in the lesion. The fungal culture on plain SD agar yielded velvety yellow to green colonies with a golden-brown tan on the reverse within a week. Microscopic examination of the colony on plain SD agar (Fig. 3) by tease mount in lacto-phenol cotton blue stain showed conidiophores with biseriate phialides covering the entire vesicle (Fig. 3) and the isolate was identified as *Aspergillus flavus*. Based

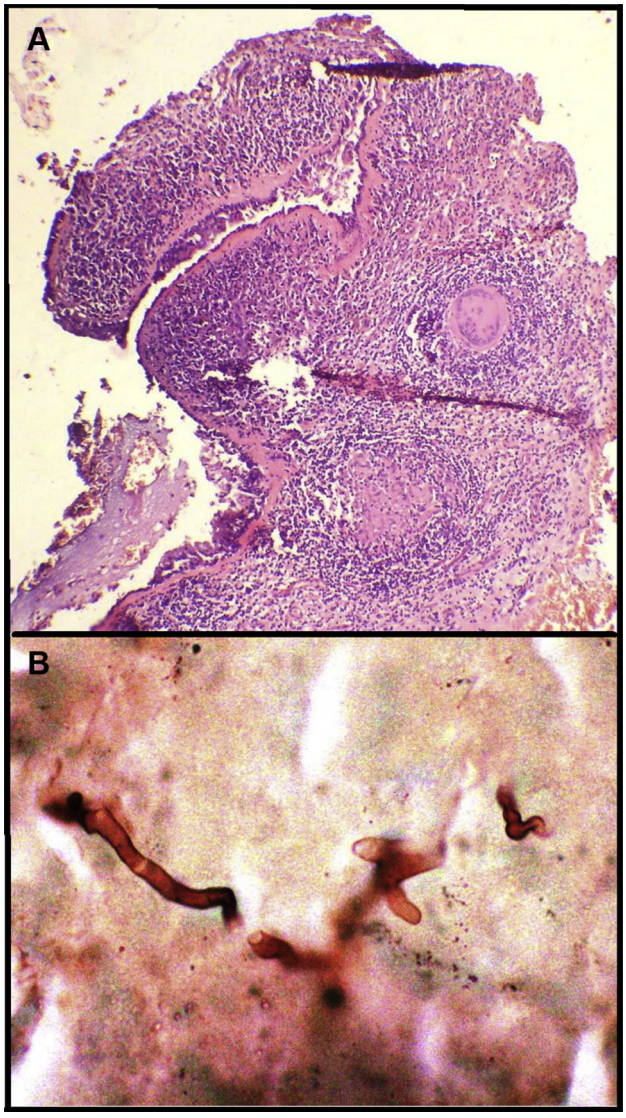

Fig. 2 – A: Photomicrograph of the paranasal mass (H&E stain; 400×) showing noncaseating granulomatous lesions with foreign body type of multinucleated giant cells and infiltrating lymphomononuclear cells. B: Gomori's methenamine silver (GMS; 400×) stain showing hyaline septate hyphae with dichotomous branching.

on the overall clinical, radiological and laboratory findings, the case was diagnosed as ''Granulomatous invasive fungal sinusitis caused by *A. flavus*''.

Oral Itraconazole 100 mg bid with a short course of steroid therapy was given during the post-operative period. The response to therapy was excellent and within 15 days there was complete regression of the proptosis without recurrences on follow up at 3 months.

Discussion

Granulomatous invasive FRS is typically characterized by a clinical course of 12 weeks or more and associated with an

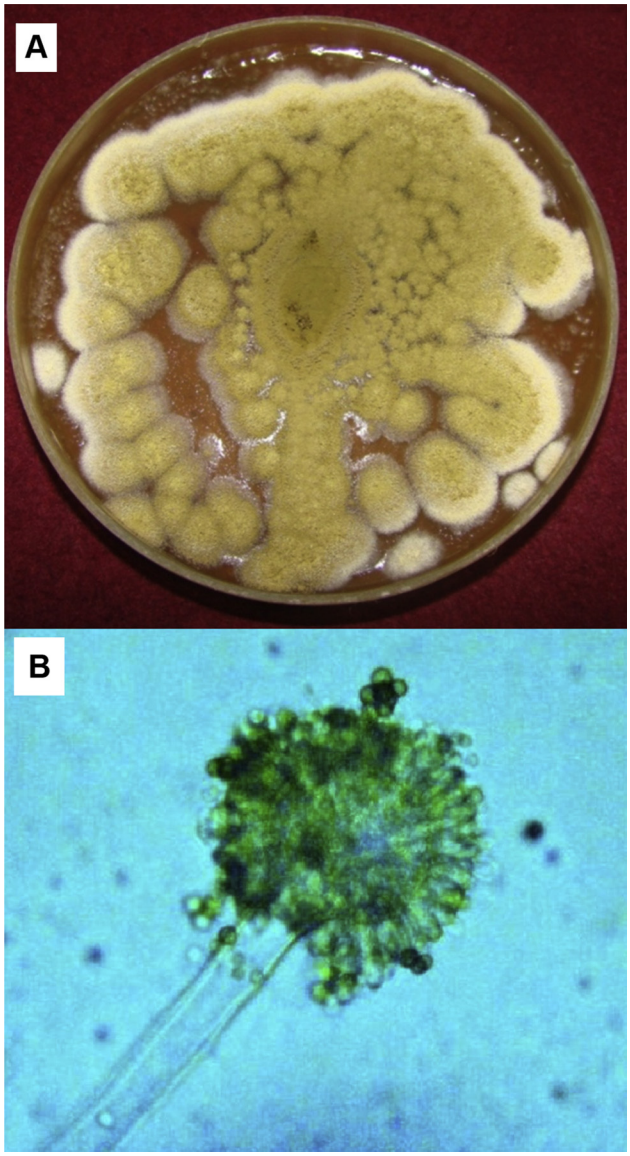

Fig. 3 – A: Plain SD agar showing velvety yellow colonies of *Aspergillus flavus* with a white apron around the individual colonies. B: Tease mount examination of the colony on plain SD agar in lacto-phenol cotton blue stain (LCB; 100×) showing conidiophores with biseriate phialides covering the entire vesicle.

enlarging mass in the paranasal sinuses, nose, cheek and the orbits. It is usually seen in Sudan, India, Pakistan and Saudi Arabia and primarily affecting immunocompetent individuals. Prominent proptosis is often a hallmark of this condition. Noncaseating granulomatous lesions with foreign body or Langhans type giant cells are seen on histopathological sections along with vasculitis, endothelial cell proliferation and perivascular fibrosis. Hyphal fragments may be scanty or absent in these lesions. The primary fungal agent isolated is *A. flavus*. The disease progression can be assessed by the presence of antibody levels against the isolated fungal pathogen.[4–6]

deShazo et al in the late 1990s proposed a classification for invasive FRS wherein they classified invasive FRS based on

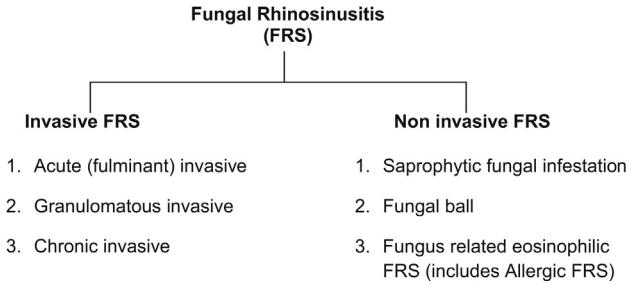

Fig. 4 – Classification of Fungal Rhinosinusitis (FRS). deShazo RD et al. Arch Otolaryngol Head Neck Surg 123: 1181–1188.

clinical condition, immune status, histopathology, and fungus infection: acute (fulminant) invasive, granulomatous invasive, and chronic invasive types[7] (Fig. 4).

The clinicopathological distinction between granulomatous invasive FRS and chronic invasive FRS is vague as both conditions have a chronic course with orbital involvement, similar prognosis and therapeutic options. Chronic invasive FRS is often seen in immunocompromised patients especially those with diabetes mellitus and on corticosteroid treatment. Dense accumulation of hyphae with tissue invasion on HPE and in association with the orbital apex syndrome may be seen. *Aspergillus fumigatus* is the commonly isolated fungus from such lesions.[4]

A working group formed by The International Society for Human and Animal Mycology after detailed deliberations in February 2008 in Chandigarh, India concluded that despite the existing controversies, an effort should be made to differentiate the two conditions till more data are available as pathological findings are distinct[4] (Table 1). Indian reports on FRS suggest that it is an emerging health care problem due to its morbidity and diagnostic dilemmas.[8–10]

Table 1 – Comparison between granulomatous and chronic invasive FRS.

	Granulomatous invasive FRS	Chronic invasive FRS
Geographical distribution	India, Sudan, Pakistan and Saudi Arabia	Worldwide
Duration >3 months	Yes	Yes
Patient's immune status	Immunocompetent	Immunocompromised
Involvement of orbit	Yes	Yes
Salient histopathological findings	Granulomatous lesion with foreign body or Langhans type of giant cells with vascular proliferation	Vascular invasion with sparse chronic inflammatory response
Hyphae in lesion	Scanty	Dense accumulation
Local tissue destruction	Minimal or absent	Prominent
Predominant isolate	*A. flavus*	*A. fumigatus*

Our case fulfills the diagnostic criteria that define granulomatous invasive FRS. Our patient presented with nasal obstruction with proptosis of more than 4 months duration. CT scan confirmed the extension of the nasal mass into paranasal sinuses and invasion of the right orbit. HPE showed typical granulomatous response with multinucleate giant cells and fungal hyphae. We isolated *A. flavus*. All these finding establish the diagnosis of granulomatous form of invasive FRS. Additionally, the patient was immunocompetent and hailed from a warm and dry climate that may also have favored granulomatous FRS.

The patient was cured with complete surgical removal of the mass and its paranasal and orbital extensions in conjunction with appropriate antifungal therapy (Itraconazole) prescribed for 3 months during the post-operative period. The prognosis in this type of FRS is generally good if the disease is timely diagnosed. However, it is often neglected and misdiagnosed especially in developing countries like India. Our case suitably highlights the need for high degree of clinical suspicion along with appropriate radiological and microbiological investigation including fungal workup. Correct and timely diagnosis can effectively prevent nonspecific treatments, chronicity or morbidity in patients.

Conflicts of interest

All authors have none to declare.

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