

CASE REPORT

Fungal ball-type maxillary sinusitis associated with *Penicillium* species: A case report and management perspective

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Abstract

Penicillium is a diverse genus of fungus that widely exists in the environment and is often non-pathogenic. Only a handful of literature have reported its association as a cause of infection in humans. Here, we report a case of a *Penicillium* maxillary sinus fungal ball in an elderly man complaining of chronic headache, progressive unilateral nasal blockage and post-nasal drip. The role of *Penicillium* in a fungal ball and management are further discussed.

Keywords: *Penicillium*, fungal ball, maxillary sinusitis, middle meatal antrostomy

INTRODUCTION

Fungal ball, previously known by its misnomer ‘mycetoma’, is a collection of non-invasive, dense fungal concretions that can occur in the lungs and paranasal sinuses.¹ It is the most common variant of non-invasive fungal rhinosinusitis and usually develops in the unilateral sinuses, most frequently in the maxillary sinus.^{1,2} Historically, *Aspergillus* species have been the most commonly isolated pathogen, accounting for more than 60% of cases of fungal ball cases.³ *Penicillium* species have been associated with 10% or fewer of fungal balls reported in the literature.^{1,2} It is a saprophytic fungus commonly found in the environment, isolated from soil, decaying organic matter and plants.⁴ Despite its widespread distribution, *Penicillium* species are seldom associated with human infection. Here we report the first case of fungal ball due to *Penicillium* species in Malaysia. The objective of this case report is to discuss the presentation of *Penicillium* fungal ball compared with other common pathogens (i.e. *Aspergillus*) and its management.

Case Report

A 67-year-old Chinese man presented with 3-months history of progressively worsening right nasal obstruction, epiphora and chronic

post-nasal drip. This was preceded by a history of long-standing headache for the past 1 year. The headache was throbbing in nature, non-radiating and localised to the right frontal and periorbital region. He was subsequently referred to the Otorhinolaryngology and Head and Neck outpatient as his symptoms worsened. He had no fever, purulent rhinorrhoea or anosmia. His medical co-morbidities included diabetes mellitus, hypertension and ischaemic heart disease, for which he was under regular follow-up and treatment.

On examination, he was well. Nasoendoscopic evaluation showed bulging or medialisation of the right lateral maxillary sinus wall with purulent discharge seen at the right osteomeatal complex. No nasal polyps or mass seen. He did not elicit any facial tenderness and other examination of head and neck region were unremarkable.

Contrasted-enhanced computed tomography (CT) of the paranasal sinuses revealed the diagnosis of right maxillary fungal ball. A non-enhancing, heterogeneous mass was present within the right maxillary sinus, with multiple foci of calcification within the lesion. Erosion and thinning of the medial maxillary wall and right nasolacrimal duct, together with widening of the right osteomeatal complex were present. There was also opacification at the anterior ethmoid sinus (Figure 1).

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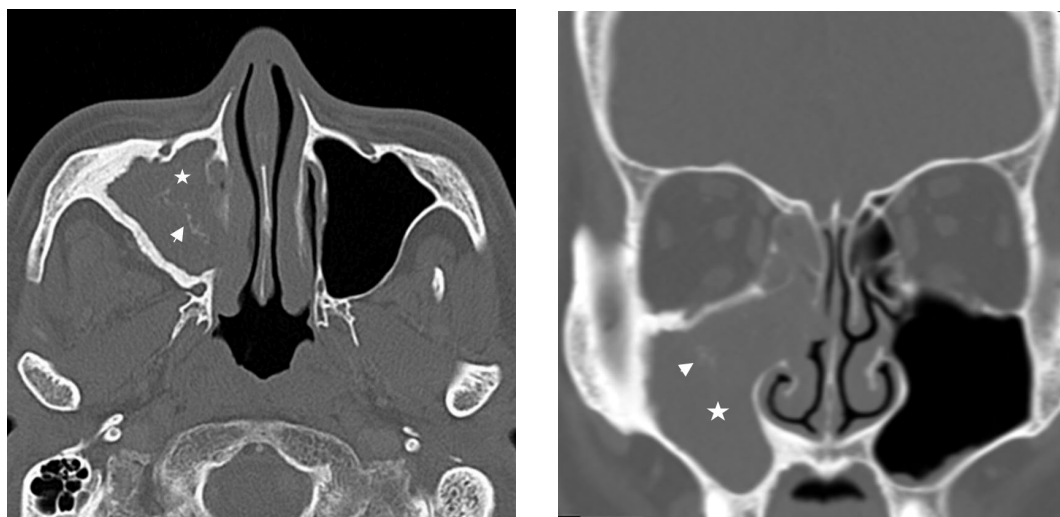


FIG. 1. Axial and coronal computed tomography (CT) scans showing heterogeneous mass (white star) with calcifications (white arrow) within the right maxillary sinus, a characteristic of fungal ball. Erosions of the bony medial maxillary wall and nasolacrimal duct and sclerosis of the right anterior and lateral wall of the maxillary sinus can also be visualised, indicating chronic infection.

The patient underwent an elective anterior functional endoscopic sinus surgery (FESS) under general anaesthesia. Intraoperatively, a dense, darkened clay-like mass surrounded by mucopurulent discharge was seen occupying the right maxillary sinus cavity. Polyps were in the maxillary sinus cavity, and the surrounding mucosa was inflamed and oedematous without clinical evidence of frank necrosis. The debris was removed and sent for evaluation.

Histopathological examination showed abundant irregular fungal hyphae arranged in solid sheets against a background of mixed inflammatory cells with no evidence of mucosal invasion. The hyphae were variably septate with calcifications present in some areas (Figure 2). Fungal culture revealed growth of *Penicillium* species (Figure 3). The patient did not receive any antifungal treatment. His symptoms showed significant improvement one week after the operation.

He made a good recovery post-procedure. He performed nasal douching daily. At one-year follow-up, his right middle meatal antrostomy (MMA) was patent with no recurrence of disease on surveillance endoscopy.

DISCUSSION

Fungal ball is the most frequent non-invasive fungal rhinosinusitis.² It has been termed interchangeably in the literature as mycetoma,

aspergilloma and chronic non-invasive granuloma to describe extra-mucosal conglomeration of intertwined fungal hyphae or pseudohyphae, without histopathological evidence of invasion.^{3,5} It has been mainly reported in the maxillary sinus followed by sphenoid, frontal and ethmoid sinuses.^{3,6} Most fungus balls remain a mild disease in immunocompetent patients with good prognosis.

The clinical presentation of fungal ball varies depending on the location of the sinus involved. Maxillary fungal ball typically presents with nasal congestion, mucopurulent discharge, post-nasal drip, facial pains and epistaxis. Additional symptoms such as headache and epiphora may manifest depending on the location and extension of the disease.⁸ Our patient had a typical presentation of fungal ball; immunocompetent elderly patient with unilateral infection involvement of the maxillary sinus. Apart from the headache and nasal congestion, he also had right eye epiphora for 3 months duration, suggesting more extensive disease involvement.

Radiological modalities such as CT and MRI are crucial in the management of fungal ball. CT scan particularly may help to delineate the bony structures and to rule out other possible pathologies. Usual findings of fungal ball in CT shows 'hyperdense spots' within a hypoattenuated paranasal sinus lining, associated with sclerosis of the bony sinus wall.⁹ Calcific foci within the opacity are typically seen due to the presence of

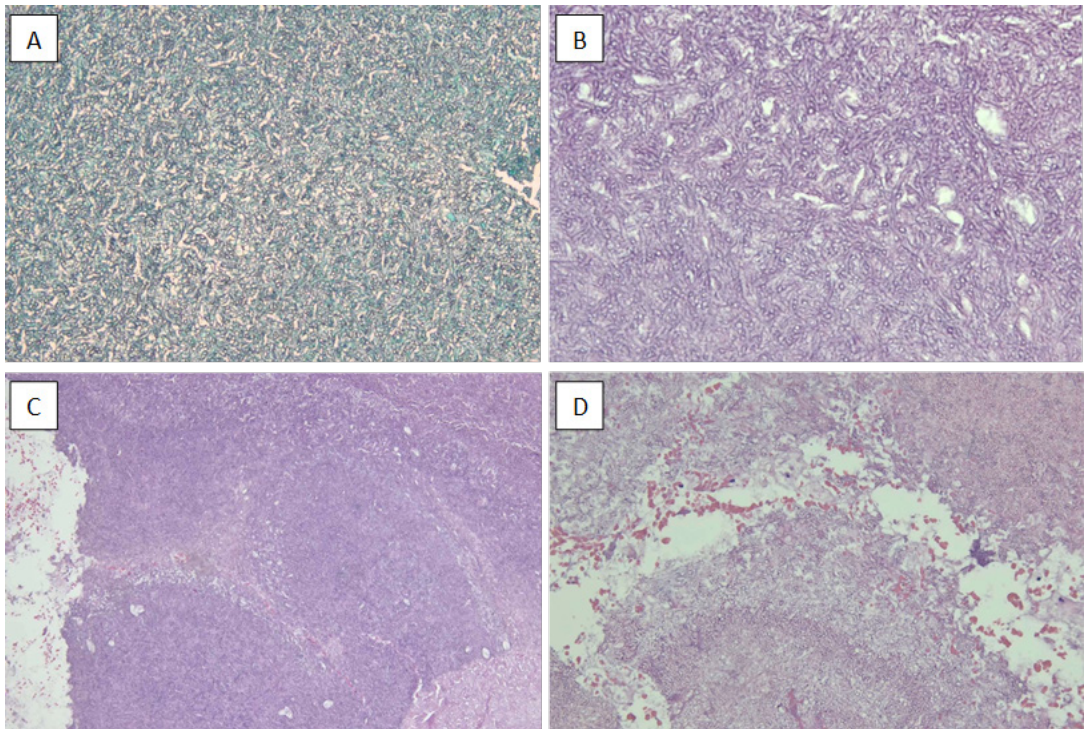


FIG. 2. A & B) variably septate fungal hyphae with presence of calcification in areas (GMS, $\times 20$, H&E, $\times 40$). C) Abundant fungal hyphae arranged irregularly in solid sheets with no tissue invasion (H&E, $\times 10$). D) Background of mixed inflammatory cells and red blood cells (H&E, $\times 20$)

heavy metal deposits such as zinc and calcium.

Several studies have shown that *Aspergillus* is the most commonly isolated species in fungal balls, comprising more than 60% of the fungal ball.³ However, recently emerging rare species have been reported in the literature,

due to the advancement and accessibility of histopathological analysis. This includes non-fumigatus-non-flavus *Aspergillus*, *Fusarium*, *Alternaria*, *Bipolaris*, *Paecilomyces*, *Scedosporium*, *Cladosporium*, and *Penicillium*.^{3,7} In a retrospective study done by Montone *et al.*,⁷

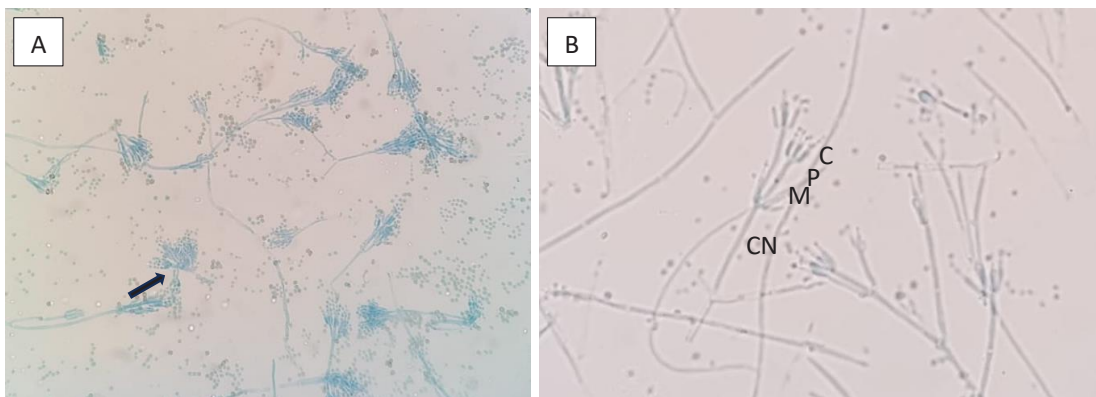


FIG. 3. A) Microscopic examination after lactophenol blue staining showing conidiophores (black arrow) branching from the mycelium hyphae, giving the brush-like appearance of *Penicillium*. B) Other key structures of *Penicillium* can be seen here, including the conidia, phialides and metulae. (C=conidia, P=phialides, M=metulae, CN=conidiophore)

Table 1: Common fungal organisms associated with fungal rhinosinusitis⁷

Non-Invasive	Overall %	Invasive	Overall %
<i>Aspergillus</i> sp	34 - 65	<i>Aspergillus</i> sp	49
<i>Dematiaceous</i> sp	9 - 30	<i>Rhizopus</i> sp	33
<i>Fusarium</i> sp	6	<i>Fusarium</i> sp	6
<i>Paecilomyces</i> sp	5	<i>Paecilomyces</i> sp	6
<i>Scedosporium</i> sp	5	<i>Alternaria</i> sp	6
<i>Penicillium</i> sp	5		
<i>C. Albicans</i>	2 - 5		
<i>Mucor</i> sp.	2		
Multiple isolates	35		

Penicillium in particular has been implicated in 5% of cases of fungal balls (Table 1). *Penicillium* is a common fungus found in a diverse range of habitats from soil to vegetations to air, various food products and indoor environments. It plays an important role in agriculture and foods industry whereby it is used as decomposers of organic materials, production of specialised cheeses and fermented sausages.⁴ Despite that, it is seldom associated with human infection in medical literature. Endocarditis, brain abscess, peritonitis, kidney infections and esophagitis are among the few cases of invasive infections reported.

Involvement of the respiratory tract, particularly the nose and paranasal sinuses are rarely described. In 2018 Radulesco *et al.*¹⁰ reported the first case of *Penicillium roqueforti* causing a left maxillary fungal ball in an immunocompetent patient, with a presentation similar to that of as our patient. They were able to identify the exact species through DNA amplification and sequencing, which was unfortunately not performed in our case. The use of nucleic acid sequencing or matrix-assisted laser desorption/ionisation time-of-flight (MALDI-TOF) may provide more precise species identification; however, these are not routinely available in all settings. Up to 50% of fungal ball cultures may be negative, and without further identification, cases of rare fungal organisms may therefore be missed.⁷

Endoscopic sinus surgery remains the standard treatment of fungal balls.² Antifungal provides no benefit due to the non-invasive nature of the disease. Systemic antifungal may benefit in certain cases, such as sphenoid fungal ball where the risk of invasion into the cavernous

sinus is present.¹¹ Otherwise, with good surgical clearance, a good prognosis with complete resolution of symptoms is generally seen.³ In this case, the patient underwent successful surgical clearance without antifungal therapy and demonstrated complete clinical resolution with no recurrence at one-year follow-up.

Although identification of the specific fungal species does not alter the surgical management of fungal ball, it has clinical relevance. Accurate identification aids in differentiating non-invasive fungal ball from early invasive fungal disease, particularly in patients with comorbidities such as diabetes mellitus. Certain fungal species such as *Aspergillus* sp. may occur in both invasive and non-invasive fungal infection, whereas *Penicillium* sp. has never been identified as a cause of invasive fungal sinusitis. In cases of invasive fungal sinusitis, surgery alone is inadequate, and patients require targeted systemic antifungal therapy.

Our case highlights a *Penicillium* fungal ball, which is a rarity compared with other species such as *Aspergillus* sp and *Dematiaceous* fungus. To our knowledge, no case of *Penicillium* has yet been reported in Malaysia. We hope this report will raise awareness among clinicians, mycologists and epidemiologists on the possibility of emerging uncommon fungal pathogens in the future.

CONCLUSION

Penicillium fungal ball is a rare entity and presents similarly to *Aspergillus* and a commensal in healthy immunocompetent individuals.

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Conflict of interest: The authors declared no conflict of interest.

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