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Cerebral fungal infection with mycotic aneurysm of basilar artery and subarachnoid haemorrhage

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ABSTRACT

A 28-year-old Pakistani man was admitted with unresolved severe headaches for the past four weeks. Magnetic resonance (MR) imaging and MR angiography showed an enhancing mass in the sphenoid sinus, bilateral cerebellar infarcts and aneurysmal dilatation of the basilar artery. The differential diagnosis included fungal infection versus neoplastic lesion. The scrapings taken through the endoscope from the sphenoid sinus were initially negative for fungal infection. However, the second biopsy, done after putting him on antifungal, itraconazole 200 mg twice daily, revealed the presence of a fungal infection (aspergillosis). MR imaging revealed extension of the fungal infection from the sphenoid sinus into the clivus, and then intracranially. Imaging also revealed aneurysmal dilatation of the basilar artery and infarctions in the cerebellum and subarachnoid haemorrhage. Despite aggressive antifungal treatment, the patient died after 29 days. This case report describes the probable mechanism of fungal mycotic aneurysmal vascular dilatation and growth. It also points to the need for a rapid diagnosis of potential cases and an aggressive treatment approach of confirmed cases of fungal infections of the central nervous system.

Keywords: aspergillosis, aspergillus sinusitis, cerebral fungal infection, mycotic aneurysm, sinonasal infections, subarachnoid haemorrhage

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INTRODUCTION

Fungi are considered to be low virulence organisms that generally cause opportunistic infections when the host's defences are lowered. Among all the central nervous system (CNS) fungal infections, aspergillosis, especially the sinocranial form, is the most commonly reported fungal infection in India and other tropical and desert countries, such as Sudan, Saudi Arabia and Pakistan.⁽¹⁾ Although more common in immunosuppressed patients,

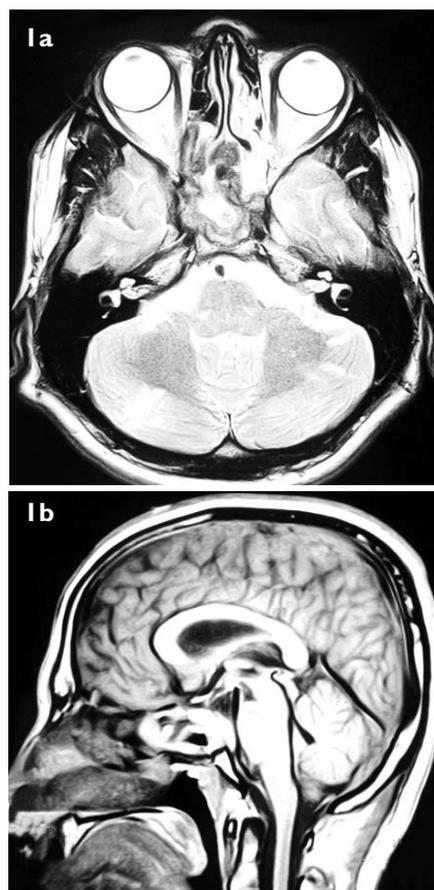


Fig. 1 (a) Axial T2-W MR image of the brain and sinuses shows a T2-hypointense mass in the sphenoid sinus with bilateral cerebellar infarctions. (b) Sagittal contrast-enhanced T1-W post MR image shows an enhancing mass in the sphenoid sinus extending into the prepontine space abutting the basilar artery.

aspergillosis of the CNS among immunocompetent patients is a rare but life-threatening disease.⁽²⁾

One of the most lethal but rare sequels of CNS fungal infection is intracranial aneurysms. It has been reported on less than 15 times since it was first described in 1968.⁽³⁾ However, this devastating disease has the potential to result in more cases as the survival of patients suffering from immunosuppression is increasing. Due to high fatality, the early diagnosis and prompt treatment of cases with CNS fungal infections is crucial. The current case report presents a case of a basilar artery aneurysmal dilatation resulting from

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Fig. 2 Magnetic resonance angiography shows an irregularly dilated aneurysmal basilar artery.

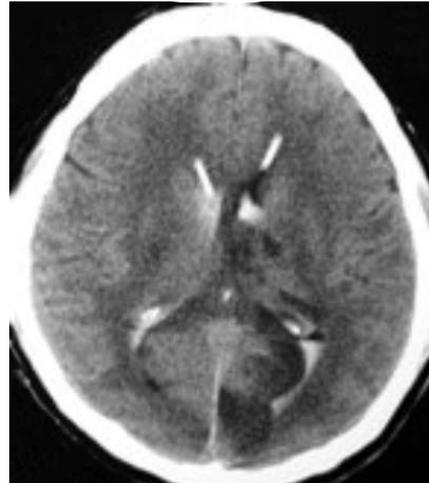


Fig. 3 Axial CT image of the brain shows subarachnoid haemorrhage and intraventricular blood.

aspergillus sinusitis. The infection caused subarachnoid haemorrhage (SAH) and cerebral infarction. The case also explains the usefulness of the imaging-pathological methods in prompt diagnosis and in determining site and progression.

CASE REPORT

A 28-year-old Pakistani man with a history of headache of increasing severity for the past one month, presented at the emergency department of Aga Khan University Hospital. He was an engineer and worked in the United Arab Emirates. Magnetic resonance (MR) imaging showed an abnormal signal intensity mass in the sphenoid sinus and bilateral posterior ethmoid sinuses, causing their expansion. Superiorly, the mass was causing the erosion of the floor of sella turcica abutting against the pituitary gland. Posteriorly, the mass was causing the erosion of the clivus, extending into the prepontine cistern (Fig. 1a). The mass was hypointense on T2-weighted images, isointense on T1-weighted images and showed intense solid heterogeneous enhancement. On axial T1- and T2-weighted images, the basilar artery appeared to be dilated and thick-walled and on post-contrast images, it showed enhancement of its wall. Multiple T2-hyperintense areas representing infarctions were also noted in both cerebellar hemispheres, the pons and right thalamus. These were also seen on diffusion weighted images. MR angiography also revealed an irregularly-dilated aneurysmal basilar artery (Fig. 1b). On the basis of imaging, the diagnosis of a fungal infection of sphenoid sinus with intracranial extension and mycotic aneurysmal dilatation of the basilar artery with vasculitic infarctions of the cerebellum, pons and right thalamus was made. However, the neoplastic lesion was also considered as an alternative cause.

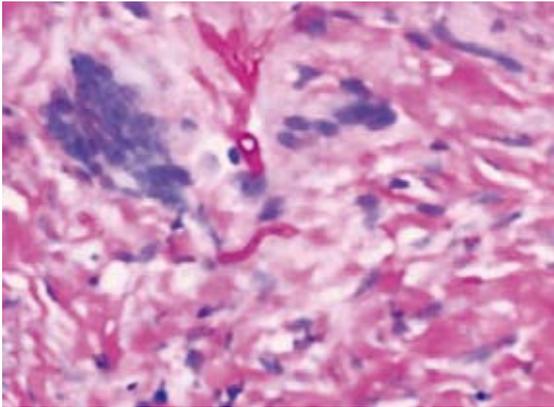
The patient did not report any past history of drug intake or an immunocompromised state. Neurological

examination indicated a palate deviated to the right. The rest of the physical examination was normal. Laboratory evaluation showed haemoglobin of 13.7 gm/dL, a white blood cell count of $6.5 \times 10^9/L$ and an erythrocyte sedimentation rate of 9 mm/hr. The patient was not diabetic and his human immunodeficiency virus status was also negative. Endoscopic approach to the sphenoid sinus revealed inspissated secretions and debris, which were sent for pathological examination and culture. Although the culture was negative in the initial test, due to clinical suspicion, the patient was treated with intravenous amphotericin B, itraconazole and steroids. The second biopsy revealed an aspergillus infection.

The steroids were stopped after the biopsy report. Approximately five days later, the patient had a severe headache and generalised tonic-clonic seizures. He continued to have a severe headache and his Glasgow Coma Score (GCS) dropped. The patient was then intubated due to a low GCS. MR imaging was repeated and revealed SAH, which was later confirmed on computed tomography (CT) (Fig. 2). Antifungal therapy (amphotericin B and itraconazole) was continued. No surgical therapy was considered possible. CT showed an episode of SAH and acute right thalamic infarct. Life support was withdrawn and the patient died two days later. Histopathological examination of the biopsy from the sphenoid sinus showed severe acute and chronic inflammation. The septate and branching fungal hyphae with adjacent foreign body giant cell reaction were seen on periodic acid-Schiff stain (Fig. 3).

DISCUSSION

A literature review suggests an increasing incidence of systemic and CNS fungal infections due to the widespread use of immunosuppressive therapy, broad-spectrum antibiotics and corticosteroids, HIV infection



(Courtesy of Prof Sheema Hasan, Aga Khan University)

Fig. 4 Photomicrograph shows septate and branching fungal hyphae with adjacent foreign body giant cell reaction on periodic acid-Schiff stain ($\times 300$).

and longer survival of organ transplant recipients. It has also been reported that certain fungi such as *Aspergillus* spp., Zygomycetes and Chromomycetes can cause infection in apparently healthy individuals.⁽³⁾ *Aspergillus fumigatus* infection of the sinuses and orbit can be either noninvasive or invasive. While noninvasive infections could invade the mucosa, there is usually no invasion of the tissue and bone. The invasive infections are either localised or fulminant. The localised disease often starts in the sinuses and spreads to adjacent structures through focal bony erosion or even through vessel walls, causing stroke and death.⁽⁴⁾ Moreover, cerebral arteritis due to fungus has also been reported in many case reports of postoperative patients. One of the reports describes a case of aspergillus arteritis that caused SAH without aneurysm formation, followed by successive brainstem and cerebellar infarction.⁽⁵⁾

In our case, the biopsy revealed that the patient had invasive aspergillus sinusitis. The extension of fungal hyphae into the CNS later caused aneurysmal dilatation of the basilar artery and a sequence of events that caused his death. The reason for the involvement of the basilar artery is perhaps because of the close proximity of the vessel to the sphenoid sinus. Multiple perforators in the basilar artery could be another factor that made it susceptible to the fungal infection. It has also been suggested that fungal infection mostly involves arteries with multiple perforators.⁽⁶⁾ For a fungal organism with arterial involvement, endothelial cells have been shown to engulf the organism and the internal elastic lamina has been seen to be infiltrated and destroyed.⁽⁷⁾

Due to the involvement of the basilar artery, the patient developed acute infarctions in the cerebellum, which was followed by subarachnoid haemorrhage due to rupture of the basilar artery after mycotic aneurysmal

dilatation/arteritis. Despite intravenous treatment with amphotericin B, progressive distal involvement of the walls of the basilar artery caused extension of the aneurysm, with subsequent fatal SAH and cerebral infarction. MR imaging in our case revealed an enhancing mass in the sphenoid sinus with low signal intensity on T2-weighted images, characteristic of fungal infections. The hypointensity is attributed to the dense population of aspergillus hyphal elements and the presence of haemorrhage in the capsular wall.⁽⁸⁾ Further, Fellows et al⁽⁹⁾ and Zinreich et al.⁽¹⁰⁾ in their *in vitro* analysis, suggested paramagnetic elements, especially iron and magnesium, as the cause of hypointensity. This finding suggests the usefulness of MR imaging as a diagnostic tool for fungal infections.⁽¹¹⁾ Biopsy is necessary and must be done on the focal hypodense areas identified on MR imaging. The diagnosis can still be difficult to make, as patients also needed multiple biopsies, as reported by Mauriello et al and Austin et al.^(12,13)

In our case, despite the standard treatment and immunocompetence, the patient died. Similar patterns have been reported by other studies as well.⁽²⁾ The literature suggests that the prognosis of invasive sino-orbital aspergillosis in immunocompetent patients is significantly worse than the prognosis of other forms of sinus aspergillosis.⁽¹⁴⁾ This is because of the penetration of bone and blood vessel walls, which makes growth difficult to remove by surgery and/or by drug treatment. This case indicates the usefulness of pathological-radiological diagnosis of one of the rarest but most devastating types of fungal involvement affecting the CNS, i.e. invasive aspergillosis with fungal aneurysm.

The current case report suggests that mycotic aneurysm was a result of the direct extension of fungal sinusitis to the intracranial circulation in an immunocompetent patient. Aneurysm and SAH are rare but devastating complications of invasive aspergillosis, especially in immunocompetent patients. Intracranial fungal infection is a challenging diagnosis which requires early detection. Biopsy of the brain is required for a definitive diagnosis, although it is not an easy option. It is important to consider clinical, pathological and radiological findings to diagnose cases and understand the progression of the disease. Due to a specific T2 signal of the fungus, the diagnosis of fungal disease can be made early in the course of the disease by MR imaging. MR imaging can also identify vascular involvement and SAH with great ease, which makes it the modality of choice in the investigation of intracranial fungal infections with mycotic aneurysms. The difficulty in preventing a fatal outcome of CNS

fungal infections once vascular involvement has occurred places increased emphasis on suspicion of the diagnosis, prompt use of technology and initiation of aggressive therapy.

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