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Hypophyseal fossa aspergillosis mimicking a pituitary macroadenoma with bleed: A case report

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Summary

Background:	<i>Aspergillus</i> infection of the sinuses is a common condition in those predisposed due to immunosuppression. However, its intracranial extension is rare, with sellar extension being even rarer and therefore is difficult to diagnose on imaging.
Case Report:	A case of sellar and sinus aspergillosis mimicking a pituitary macroadenoma with bleed is presented. The initial CT examination of head of a diabetic patient revealed a hyperdense lesion in the hypophyseal fossa and in the sphenoid sinus with extension into the right cavernous sinus, showing foci of calcification. The differential diagnosis included fungal disease or meningioma and MRI was advised. Unfortunately, the imaging was done after a five months delay when CT and MRI revealed interval growth of the lesion. Although, the MRI presentation was highly suggestive of pituitary macroadenoma with bleeding, the diagnosis of invasive aspergillosis was made when clinical data became available. The diagnosis of aspergillosis was proven by histology.
Conclusions:	The diagnosis of hypophyseal extension of aspergillosis is difficult, because of its rarity. It is important to consider possibility of fungal infection in those predisposed to it. The judgment based only on MRI findings and incomplete clinical data could easily lead into false diagnosis of an invasive pituitary macroadenoma with bleed.
Key words:	CT • MRI • sella turcica • hypophyseal fossa • sphenoid sinus • aspergillosis • invasive lesion • bleeding • pituitary gland • macroadenoma
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Background

Aspergillus species are common fungi. They are known to exist in soil, vegetation, food and also as saprophytes in upper respiratory tract mucosa [1,2]. Human diseases are most often caused by *Aspergillus niger*, *Aspergillus flavus* and *Aspergillus fumigatus* [3]. The diagnosis of aspergillosis has been mostly made either per-operative or on histopathology [2,4].

Findings of sinus and intracranial fungal disease are non-specific on plain radiographs. However, it has characteristic diagnostic features on imaging; more specific on MRI than on CT [5]. Hence, the reporting radiologist should have a high index of suspicion, especially in the patients predisposed to the infection, to enable early and appropriate

treatment. The radiological features are stressed upon in the discussion.

In the case described below the diagnosis was made preoperatively based on the imaging findings, clinical data and it was confirmed by histopathology.

Case report

A 41-year old, female, diabetic out-patient presented with headache for which an unenhanced CT head was performed. It revealed slightly hyperdense lesion in the sella turcica, sphenoid sinus and right para-sellar region, with a few calcific foci within and also erosion of intervening wall of the sphenoid sinus (Figure 1). The radiological differential diagnosis included pituitary macroadenoma, fungal dis-



Figure 1. Initial non-enhanced CT of head: hyperdense lesion in the sella and in the sphenoid sinus (arrow heads); the component of the lesion in the right parasellar region is mostly hypodense centrally and hyperdense peripherally (open arrow).

ease, and meningioma. Consequently, hospitalization and MRI examination were advised.

Unfortunately, the patient did not turn up either for MRI or admission and instead of that showed up five months later with increasing headache and diplopia. Clinical examination revealed right 6th nerve palsy. All laboratory parameters, including hormone levels, were normal. The patient's chest radiograph was unremarkable.

Repeat CT revealed increase in size of the lesion with other findings seen previously (Figure 2A,B). Subsequent MRI demonstrated presence of the lesion appearing heterogeneously iso- to hypointense to cerebral parenchyma in T2W images in the sphenoid sinus extending into the hypophyseal fossa, the right para-sellar region and into right cavernous sinus with encasement of the right internal carotid artery (Figure 3B). The hypophysis was not demarcated from the lesion and the optic chiasm was mildly displaced superiorly; the signal intensity was seen to be iso- to hyperintense in T1W images (Figure 3A,C). There was no extension into the orbital apex. A diagnosis of sphenoid sinus aspergillosis invading into the sella turcica and the right cavernous sinus was made.

Consequently, transphenoidal surgery was carried out during which most of the lesion was removed and adequate drainage was applied. The histopathological examination of the lesion showed fungal hyphae with acute branching and significant haemorrhagic component in the surrounding tissue. *Aspergillus fumigatus* was isolated. Post-operatively the patient was put on Amphotericin B. She recovered well and was discharged eight days later.

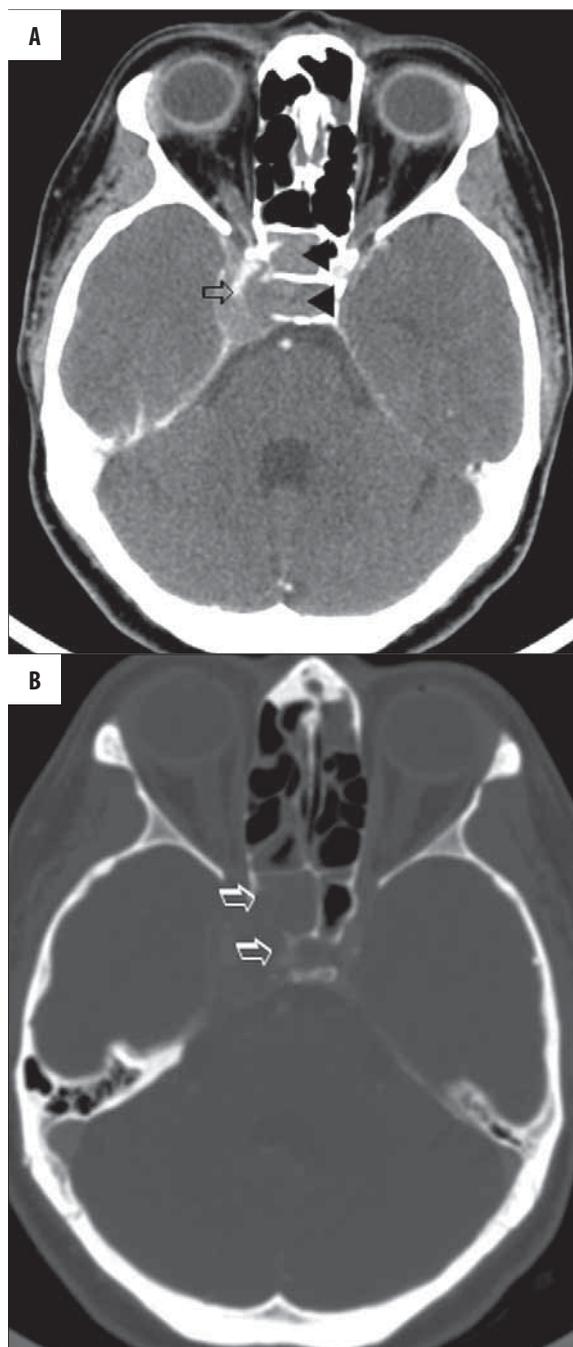


Figure 2. Contrast enhanced CT of head done five months later: (A) soft tissue window: hyperdense lesion in the sella and sphenoid sinus (arrow heads) with extension into right parasellar region and into the cavernous sinus, where it is encasing the internal carotid artery (open arrow). The lesion is larger when compared with the previous examination. (B) bone window: erosion of the right lateral wall of the sphenoid sinus, right anterior clinoid process and the right side of dorsum sella (open arrows).

Discussion

Fungal spores are inhaled through the airway of the host, accounting for a higher incidence in the respiratory system and the paranasal sinuses [1,6]. Although, aspergillosis of

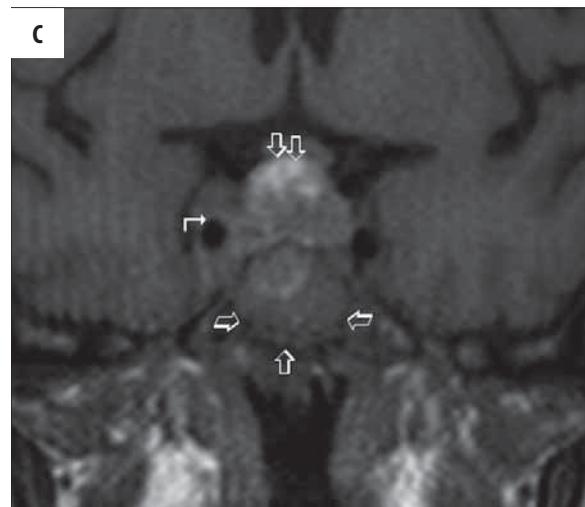
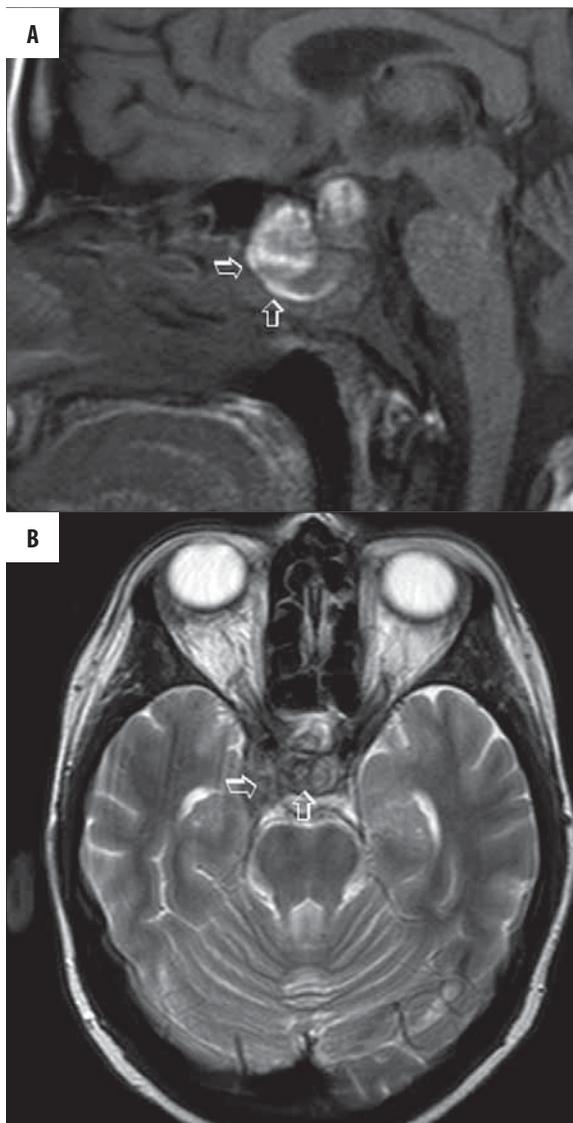


Figure 3. MRI of head five months later after initial CT: (A) sagittal T1W: mostly hyperintense signal of the lesion in sphenoid sinus extending into the sella (open arrows). Based on MRI findings alone, a wrong diagnosis of pituitary macroadenoma with a larger component in sphenoid sinus with bleed could be made easily. (B) Axial T2W: isointense to hypointense signal of the lesion in the sella extending into the right cavernous sinus (open arrows). (C) Coronal T1W: the lesion appearing isointense to hyperintense is seen in the sphenoid sinus extending into the sella (open arrows) and into the para-sellar region encasing the cavernous portion of right internal carotid artery (angled arrow).

the paranasal sinuses is a well recognized form of fungal infection, intracranial extension from the sinus is a rare event. Further on, involvement of pituitary gland by aspergillosis is extremely rare [1,2,6-8].

Pinzer et al in 2006 stated "Only four such cases have been reported in the English literature" in his analysis on Aspergillosis of the sphenoid sinus extending into the sellar region and stimulating a pituitary tumour [2]. Sellar invasion is frequently misdiagnosed as pituitary adenoma [9]. Intracranial invasion carries a poor prognosis [10].

Fungal sinusitis due to *Aspergillus* can have both invasive and non invasive forms. The non-invasive form may present as sinusitis unresponsive to conventional therapy [6-8]. The invasive form, as seen in our patient, involves extension of the infection through sinus wall into contiguous tissues. Spread of the infection to the central nervous system is an ominous sign with mortality rate reported as high as 85-100% [10]. A third, the fulminant form of fungal sinusitis has also been described [11].

The earliest of radiological modalities such as plain radiograph and tomograms have reported of up to half of paranasal sinus fungal diseases showing dense foci in substance, this had been attributed to deposits of calcium salts in necrotic areas of fungal sinusitis [12].

Out of the 25 patients who were diagnosed to have fungal sinusitis on CT in a study done by Zinreich et al, 19 had focal areas of increased density in soft tissue masses on CT [5]. Of these 19, 3 patients yet actually having bacterial sinusitis were falsely diagnosed as fungal sinusitis due to presence of either thick bacterial pus or haemorrhage, which had caused focal areas of increased density on CT. The study had a proven correct diagnosis of fungal sinusitis in 76% patients; a false positive rate of 12% and false negative rate of 12% was found. Four out of the 15 patients in his study showed intracranial extension, the precise area where the invasion occurred to was not specified in the article [5].

The signal intensity of fungal disease is usually iso- to hypointense in T1W images and hypointense in T2W images [5]. Presence of occasional haemorrhage in the bacterial sinusitis can also produce decrease in signal intensity in T2W images, which can cause one to falsely diagnose fungal sinusitis [9]. Although histopathology revealed fungal disease, it had a significant haemorrhagic component to the lesion which caused an increased signal in T1W images [6,12].

Our patient showed generally increased attenuation of the lesion on the initial CT with foci of calcification. The MRI

examination done five months later showed the lesion to have iso- to hyperintense signal in T1W and hypointense signal in T2W images. One of the possibilities initially with non enhanced CT was fungal disease due to high index of suspicion, as patient was diabetic. In the differential diagnosis, although less likely, pituitary adenoma and meningioma were added. The MRI findings were fairly specific for fungal disease enabling a pre-operative diagnosis. This is contradictory to our literature review which shows the diagnosis to be made mostly per-operatively or by microscope or culture [2,4]. Hyperintensity on T1W images is uncommon but may be seen due to haemorrhagic component [2]. Hypointense signal on T2W images is most often caused by bleed, proteinaceous concretions or calcification; this has fewer differentials compared to what would be when hyperintense signal is seen on T1W images. MRI was found to be more sensitive than CT in detecting the presence of fungal concretions [5].

Presence of calcium in the fungal concretions with iron, magnesium and manganese on analysis with atomic absorption spectrometry and metal analysis was noted, these cause increase in attenuation on non enhanced CT. Paramagnetic effect is responsible for decrease in signal intensity on increasing the T2 weightage [5,13]. If the volume of fungal disease is small compared to the associated mucosal thickening, the above features may not be observed [5].

Of the other causes of decreased signal intensity in T2W images in the paranasal sinuses, fungal sinusitis causes the maximum decrease in signal on increasing the T2 weight age; while acute haemorrhage causes a lesser decrease. Subacute haemorrhage causes increased signal in T1W images [5].

The final histopathological diagnosis of our case was invasive aspergillous sinusitis. Mucormycosis can cause a similar imaging picture as aspergillosis; the two of these can't be differentiated based on imaging criteria [5,13]. Aspergillus is the most common cause of invasive sinusitis [14].

Invasive fungal sinusitis requires accurate radiological description of extent and diagnosis for surgical intervention [5]. Typically, the disease is first seen as chronic sinusitis that does not respond to antibiotic treatment or irrigation [5].

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Also what is of interest and a known fact is that Aspergillosis tends to invade wall of blood vessels, large as well as small, hence causes infarction, haemorrhage and/or aneurysm [6,15,16].

Fungal sphenoid sinusitis invading into the pituitary has been described previously. Howard et al in 1985 reported a case of aspergillosis of sphenoid sinus that invaded into the sella and was falsely diagnosed by CT as non functioning pituitary tumour [9].

On the clinical side, our patient had 6th cranial nerve palsy. Dubey et al in 2004 reported 3rd, 4th, 6th cranial nerves as being the most common cranial nerves involved with intracranial aspergillosis [16]. Diabetes mellitus in our patient predisposed her to fungal infection. Other predisposing factors for fungal infection have been found to be tuberculosis, renal transplant, HIV infection, lymphoma and radiotherapy [16].

Ostrov et al found bleed within pituitary adenoma to range from a focus within the gland to diffuse bleed involving whole of it [17]. CT was found less sensitive in picking up bleed within adenoma when compared to MRI; it also cannot differentiate cystic transformation from chronic bleed. The commonest finding on MR was found to hyperintense signal in T1W images [17].

Based on MRI findings of the lesion in the hypophyseal fossa, sphenoid sinus, right cavernous sinus showing iso- to hypointense signal in T2W images and iso- to hyperintense signal in T1W images a false diagnosis of invasive pituitary macroadenoma with bleed into its substance could easily be made. Nevertheless, what contributed to not falsely diagnosing this entity in our case were clinical details of the patient not fitting into pituitary apoplexy, and more importantly a five months earlier non enhanced CT, which had shown hyperdense lesion in the same regions with foci of calcification.

Conclusions

In conclusion, features of fungal sinusitis on imaging that are essential or helpful in diagnosis are: increase in attenuation on CT and hypointensity in T2W images as well as clinical details, which are of paramount importance in cases having a high index of suspicion for diagnosis based on imaging.

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