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Case Report

Skull base osteomyelitis secondary to *Scedosporium apiospermum* infection

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ABSTRACT

Scedosporium apiospermum is a common environmental mold which is increasingly reported in the literature as a cause of infection, particularly in the immunocompromised patient population. We present a case of malignant otitis externa due to *S apiospermum*, complicated by spread of infection causing skull base osteomyelitis, internal carotid artery vasculitis and subsequent stroke. Despite the multiple complications encountered, prompt diagnosis and initiation of appropriate antifungal treatment resulted in patient survival. Multiple imaging modalities were used to aid the establishment of the diagnosis in this complex case and highlight the radiological findings associated with skull base osteomyelitis and its possible complications.

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Introduction

Scedosporium apiospermum (Fig. 1) is a filamentous fungus that is found in the environment and associated with infections in both immunocompetent and immunocompromised patients [1,2]. In immunocompromised patients, it can lead to life-threatening disseminated infection [2,3]. One possible source of infection is the external ear, which is the case with malignant otitis externa (MOE). MOE is a non-neoplastic, infective process affecting the external auditory canal with subsequent invasion of the base of the skull [4]. Although rare, there have been a small number of cases reported in the literature of MOE caused by *S apiospermum* [4,5].

Skull base osteomyelitis (SBO) is a rare and life threatening condition with a high mortality rate reaching 10%-20% [6,7].

The majority of reported cases are secondary to *Pseudomonas aeruginosa* infection with much fewer cases caused by fungal species [5–8]. Clinical presentations include headache (90%), cranial nerve palsies, and otalgia with or without purulent discharge [6,9,14,16]. The development of SBO, especially secondary to fungal species, has been associated with intracranial arterial infection with documented complications of mycotic aneurysms and cerebral infarctions [2,10–12].

Case report

An 88-year-old nondiabetic male presented to hospital with a worsening headache associated with increased otorrhea. He had been discharged from the emergency department after a recent presentation during which he reported a headache associated with otalgia. A computed tomography (CT) examination was unremarkable at that time and he was

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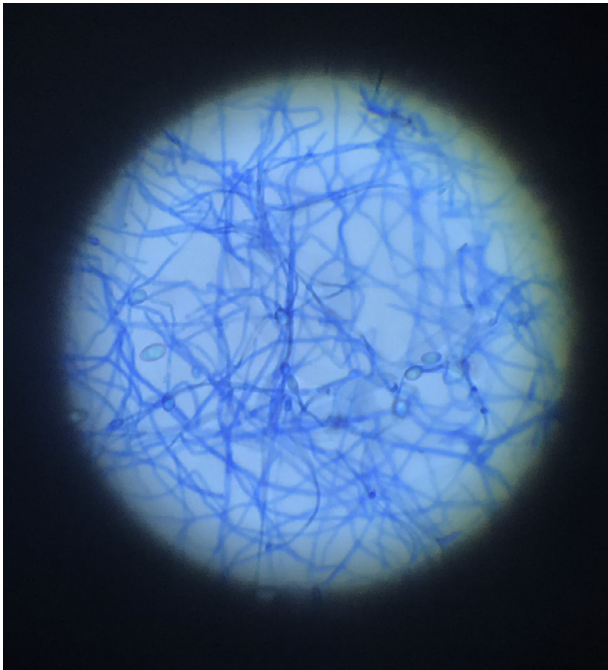


Fig. 1 – Lactophenol cotton blue stain of *Scedosporium apiospermum* isolated from ear swab. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

diagnosed with otitis externa for which he was prescribed ciprofloxacin eardrops. An ear swab was also collected. On his current representation to the emergency department, clinical examination revealed an oedematous external ear canal with large amounts of discharge. No cranial nerve palsy was identified. Laboratory data revealed a white cell count (WCC) of $12.3 \times 10^9/L$ (normal $4-10.5 \times 10^9/L$) and a C-reactive protein (CRP) of 37.5 mg/L (normal 0-10 mg/L). The previously collected ear swab had grown *P aeruginosa*. A CT carotid angiogram was performed and showed focal aneurysmal dilatation with an associated rind of enhancing soft tissue in the distal cervical segment (Fig. 2) as well as marked narrowing of the petrous segment of the right internal carotid artery (ICA) (Fig. 3A). Further distally, the cavernous segment of the ICA was of normal caliber and unremarkable at that stage (Fig. 3B).

He was placed on an intravenous (IV) course of antibiotics (ciprofloxacin and ceftriaxone) due to high fevers during the early stages of his admission. A lumbar puncture to rule out meningitis was negative. Repeat WCC on day 4 was essentially unchanged, however, CRP had increased to 93 mg/L. Erythrocyte sedimentation rate (ESR) measured 124 mm/hr (normal 0-22 mm/hr). On day 6, he developed a decreased level of consciousness, dysarthria and marked left sided upper and lower limb weakness. A repeat carotid angiogram showed complete occlusion of the right petrous segment (Fig. 3C) and interval development of narrowing of the proximal aspect of the cavernous ICA (Fig. 3D). The focal aneurysmal dilatation of the distal cervical ICA was again noted (Fig. 2). A cerebral perfu-

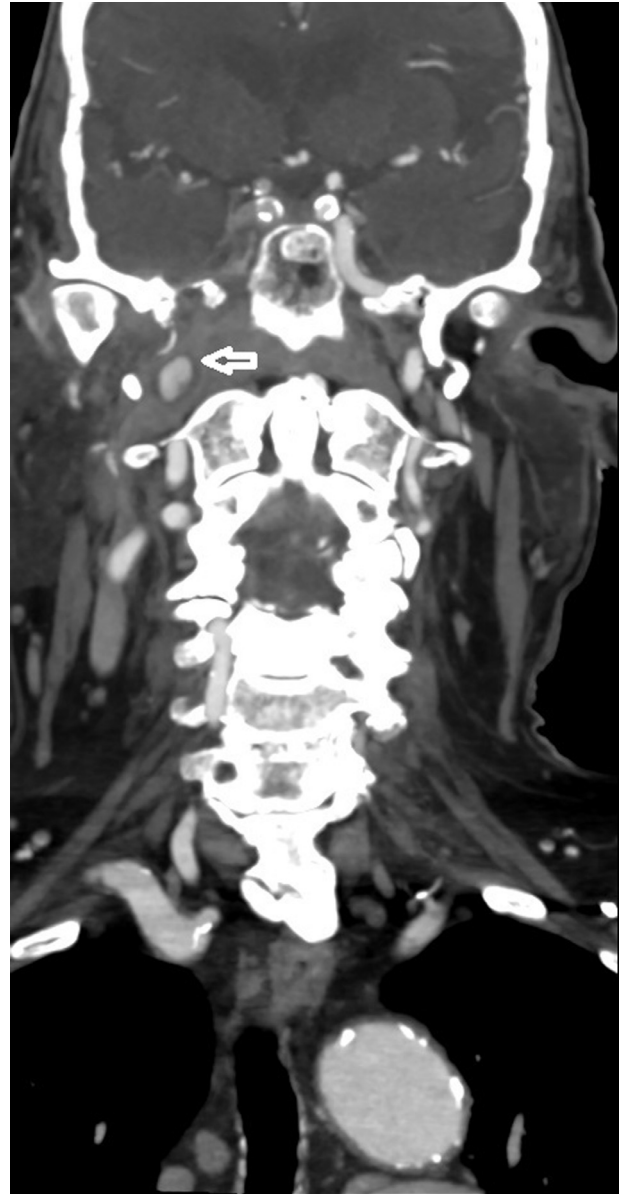


Fig. 2 – Coronal slice of a computed tomography carotid angiogram demonstrates aneurysmal dilatation of the internal carotid artery. Note the abnormal rind of soft tissue surrounding the internal carotid artery (arrow) at this level.

sion study showed an ischemic penumbra in the middle cerebral artery territory without infarction.

On day 7 of admission, culture of ear discharge results was positive for *S apiospermum*. He was commenced on IV voriconazole and antibiotics were switched to tazocin. After ongoing antimicrobial therapy and 48 hours post commencement of antifungals, there were signs of biochemical improvement with a normalising WCC down to 8.0×10^9 and CRP down trending to 27.4 mm/L. A bone scan was performed on day 9, which demonstrated increased uptake in the right skull base compatible with ongoing infection (Fig. 4A). Despite development of marked left sided functional deficits secondary to his cerebrovascular accident, the patient remained otherwise

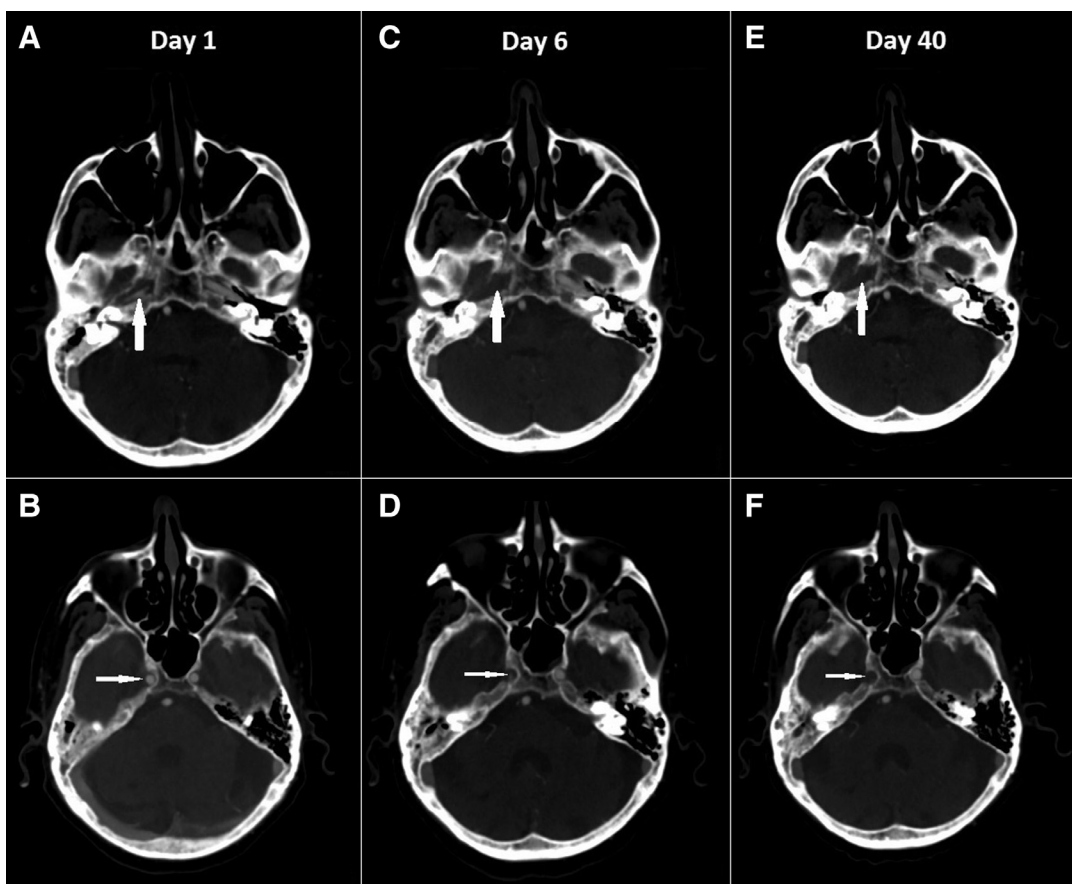


Fig. 3 – Axial slices of computed tomography carotid angiogram on admission at the level of the petrous segment (A) and cavernous segment (B) of the right internal carotid artery (ICA). There is severe luminal narrowing of the petrous segment (arrow), which however remains patent. Note the normal caliber of the cavernous segment of the ICA (arrow). Axial slices on follow-up studies at corresponding petrous segment (C) and cavernous segment (D) levels demonstrate progression of vasculitis manifested in complete thrombosis of the petrous segment (arrow) and development of marked narrowing of the cavernous segment (arrow), which was not previously involved. Further studies revealed unchanged thrombosis of the petrous segment (E) but the cavernous ICA stenosis had worsened and progressed to complete occlusion (arrow) (F).

clinically stable. On day 10, repeat cultures were again positive for *S apiospermum*. No other bacterial or fungal pathogens were isolated on culture.

On day 12, magnetic resonance imaging (MRI) of the brain and a regional gallium scan were performed. MRI diffusion weighted imaging demonstrated multiple scattered small foci of restricted diffusion in the right cerebral hemisphere representative of infarcts (Fig. 5), most likely secondary to worsening ICA stenosis. Gallium scan showed intense uptake in the right skull base involving the carotid canal, body, and greater wing of sphenoid and clivus (Fig. 4B). The uptake on the gallium study was significantly more intense than that which was seen on the bone scan, in keeping with an infective process. Following a fortnight of treatment, the patient improved on his antifungal and antibacterial regime. A repeat ear swab was negative on day 25. Laboratory results

showed improvement in inflammatory markers with CRP down to 19.5 mg/L and ESR of 108 mm/hr on day 30.

On day 40, a progress CT carotid angiogram was performed. Complete occlusion of the right petrous segment of the ICA (Fig. 3E) persisted, and the cavernous ICA stenosis had progressed to complete occlusion (Fig. 3F). The right MCA was however patent, presumably from collateral circulation through the anterior cerebral arteries. Despite radiological evidence of disease progression, the patient remained clinically stable. Antibiotic and antifungal therapy was recommended to continue for at least 8 weeks based on advice from infectious disease specialists. The patient was discharged into a rehabilitation facility on day 48 where he continued to receive IV treatment for the recommended duration and underwent physiotherapy to improve his functional deficits post stroke. Further follow up with progress imaging using a gallium scan was to be arranged at a later date.

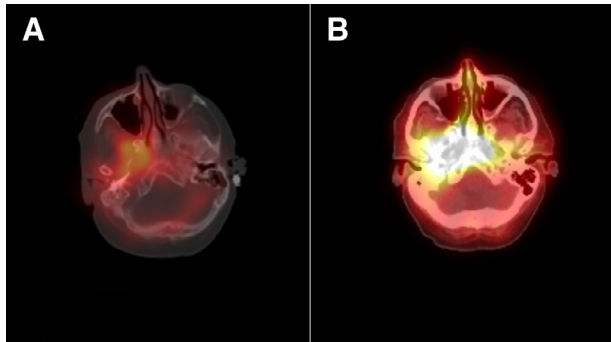


Fig. 4 – Single photon emission computed tomography/computed tomography bone scan fusion image (A) demonstrates marked tracer uptake in the right skull base involving the right carotid canal and greater wing of the sphenoid. Single photon emission computed tomography/computed tomography Gallium fusion image (B) of the same region demonstrates intense tracer uptake, significantly more intense than the degree of uptake seen on the bone study. These findings are consistent with an extensive infective/inflammatory process.

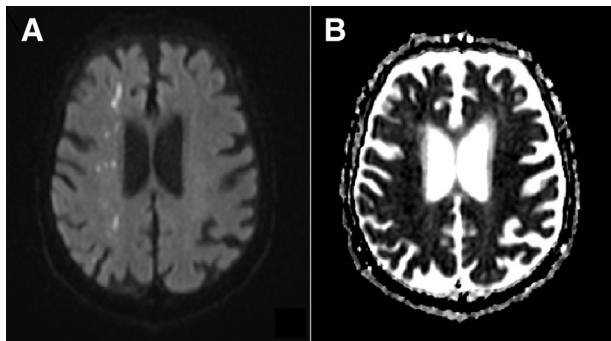


Fig. 5 – Diffusion weighted imaging (A) and Apparent diffusion coefficient (B) sequences demonstrate small foci of restricted diffusion in watershed areas.

Discussion

Fungal SBO is an extremely rare entity, most cases of which are due to *Aspergillus* species [7,8,12]. While fungal SBO has been reported in both the immunocompromised and immunocompetent patients, immunosuppression appears to have a strong association with this disease process. In a literature review of fungal SBO conducted in 2001, 17 out of 24 patients diagnosed with fungal SBO had underlying haematological malignancy or acquired immune deficiency syndrome (AIDS) [4]. *S apiospermum* is a highly resistant fungus which is an uncommon cause of fungal SBO [7,8,12]. The majority of cases involving *S apiospermum* have been reported in patients which are immunosuppressed due to comorbidities, medical therapy, or prior organ transplantation [1,7,8,12]. All 3 cases of fungal SBO due to *S apiospermum* reported in the previously mentioned lit-

erature review had underlying AIDS. In our case, *S apiospermum* led to fungal MOE and SBO in an immunocompetent patient.

Malignant otitis externa and central nervous system infections due to *S apiospermum* have a high mortality rate [3,4,22]. One of the possible causes of the poor outcomes could be due to localized spread of infection and involvement of adjacent vascular structures. Vascular complications including aneurysm formation and occlusion are a rare yet documented potential complication of *S apiospermum* infection. Ong et al. conducted a Medline search which yielded 10 biopsy-proven cases of mycotic aneurysmal formation due to adjacent *S apiospermum* infection [12]. Only two of these involved large caliber vessels (aneurysmal aortic dilation due to vertebral osteomyelitis), while the remainder of the cases involved small to medium sized vessels, nearly all of which were intracranial in location. We note marked similarity between our case and the cases presented by both Ong et al. and Jalava-Karvinen et al., which involved the superior cerebellar artery and internal carotid artery, respectively [2,12]. All 3 cases involved craniocervical vessels secondary to SBO leading to mycotic aneurysm formation and/or vascular occlusion causing stroke in immunocompetent adults [2,12]. While the patient in our case survived, albeit with residual disability secondary to stroke, the other 2 patients died. These cases highlight the risk of vascular involvement as well as the morbidity and mortality associated with osteomyelitis due to *S apiospermum*, even in immunocompetent adults.

There is a wide range of radiological signs associated with SBO across a range of modalities. However, there is no clear consensus regarding the best imaging modality for diagnosis, and a combination of anatomical and functional imaging is required to understand the disease process and progression [18,19]. CT findings in SBO include swelling of the external ear canal, involvement of the middle ear cavity, and bone erosion [17–19]. Bone erosion on CT is only visible post demineralization, and hence not present in early disease and not clearly identifiable in our presented case [17,21]. CT carotid angiogram studies can also demonstrate evidence of vascular involvement due to localized spread of infection as manifested in our case and other cases in the literature. CT carotid angiograms are able to show narrowing, aneurysmal dilatation as well as abnormal enhancing tissue surrounding the involved vessels. Imaging also plays an important role in identifying complications of disseminated disease which include brain abscesses, aortic mycotic aneurysms, and hematogenous spread to the liver, spleen, kidneys, and lungs [1,3,12].

Nuclear medicine studies have also frequently been used in the setting of SBO to aid in the diagnostic process by supplementing radiological findings from other modalities with functional imaging [2,6,7,13,15,18,20]. Gallium-67 (Ga-67) single photon emission computed tomography (SPECT) usually shows increased tracer uptake at the base of skull, with possible involvement of the sphenoid or occipital bones depending on the degree of infection spread [18,19]. However, assessing disease progression and resolution radiologically is often difficult. In a recent survey of 221 otolaryngologists, there was no general consensus regarding the modality of choice for follow up of SBO cases [24]. However, we note the use of Ga-67 SPECT in multiple other cases of SBO as a form of follow up in the literature [6,7,20]. Stokkel et al. assessed the value of Ga-67

as a follow-up modality in 8 patients with SBO by performing Ga-67 at diagnosis as well as post-treatment. Uptake at the disease site was compared with the uptake at the unaffected contralateral side. A lesion to nonlesion uptake ratio was determined. The clinical recovery of all patients corresponded with reduction of gallium uptake to normal levels, with a lesion to nonlesion ratio reduced to 1 ± 0.1 after 6-8 weeks. Based on these and similar findings in other studies, gallium SPECT appears as a potentially useful follow-up modality, however, this area remains debatable and there is need for further research to assess the effectiveness of CT or nuclear studies in accurately identifying signs of resolution [20,23,24].

In conclusion, this is a rare case of *S apiospermum* causing SBO with subsequent development of a mycotic aneurysm, intracranial artery occlusion, and stroke. Such cases are rare in the literature. SBO should be considered in patients with chronic otitis externa and prompt management is necessary. The diagnosis is often difficult partially due to its rarity, with the need for multiple imaging modalities as part of the diagnostic progress. A long course of appropriate IV therapy is needed, however mortality rates associated with this condition remain high. There is not yet a single widely recognized follow-up imaging modality to assess resolution, and this is a potential area for further research in the future.

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