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Case Report

Invasive intracranial aspergillosis spread by the pterygopalatine fossa in an immunocompetent patient

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ABSTRACT

Aspergillosis of the central nervous system (CNS) is an uncommon infection, mainly found in immunocompromised patients but rarely seen among immunocompetent patients. Herein we describe a 57 year-old immunocompetent man who suffered intracranial aspergillosis spread by the pterygopalatine fossa (PPF) following a tooth extraction. Based on magnetic resonance imaging (MRI) characteristics, in this report we focus on the spreading routes of CNS aspergillosis via communicative structures of the PPF, the relationship between clinical manifestations and the locations of the lesion, and propose a therapeutic strategy to improve the prognosis.

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Case presentation

A 57-year-old male had suffered from persistent headache for 20 months on the left occipitotemporal side after a tooth extraction, followed by a decrease of his left visual acuity and disordered speech. On neurological examinations, his left eye fixed with light reflex disappeared, the ipsilateral palpebral fissure became narrow in response to his eyelid weakness, and the temporalis and masseter muscles were weak with apparent atrophy. Moreover, his left side hearing declined, his left face felt numb, and his memory deteriorated. On magnetic resonance imaging (MRI) of the head, an enlarged mass with hypo-intense signal on T2WI and T1WI in the left pterygopalatine fossa (PPF) was shown, involving the ipsilateral sphenoid sinus, cavernous sinus, inferior orbital fissure, and temporal and frontal lobes. The left

pterygopalatine canal was obviously enlarged with abnormal signal intensity. The contrast enhanced T1WI showed strong enhancement at the aforementioned regions (Fig. 1). In order to confirm the nature of the mass, a trans-nasal biopsy of the PPF was carried out. The histological result revealed the rare finding of *Aspergillus*. Antifungal therapy was immediately started with voriconazole and amphotericin B. However, his condition was not satisfactorily under control after a long period of antibiotic therapy. A surgical operation was then arranged, and preoperation examinations were completed. The patient underwent a left pterion craniotomy with resection of skull base occupying lesions. The multiple intradural lesions were excised, and *Aspergillus* was proved again by intraoperative biopsy. The lesion had a light yellowish color and a hard consistency that was tightly adhered to the nearby tissue, especially to the left middle cerebral artery. After incision, the

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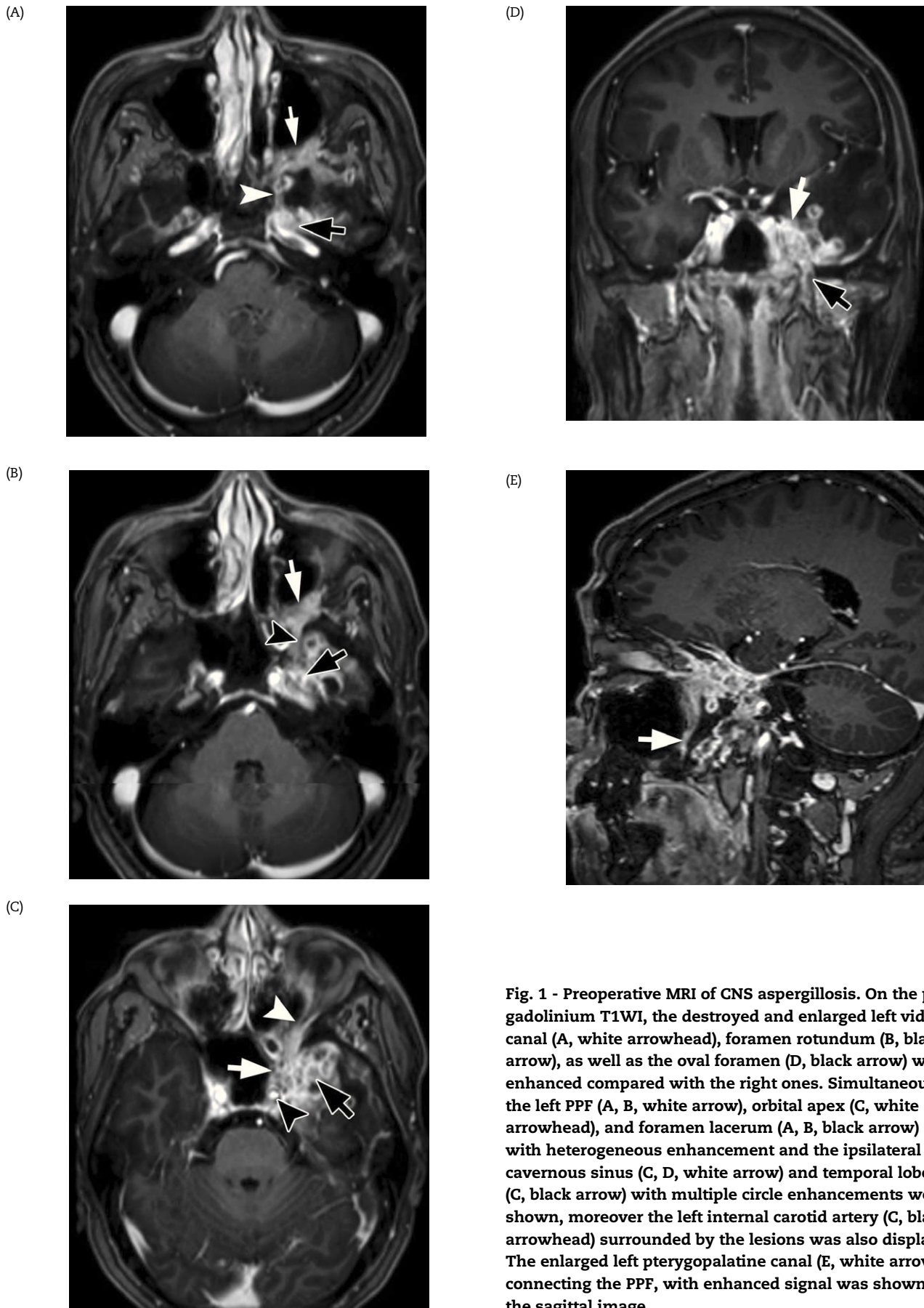


Fig. 1 - Preoperative MRI of CNS aspergillosis. On the post-gadolinium T1WI, the destroyed and enlarged left vidian canal (A, white arrowhead), foramen rotundum (B, black arrow), as well as the oval foramen (D, black arrow) were enhanced compared with the right ones. Simultaneously, the left PPF (A, B, white arrow), orbital apex (C, white arrowhead), and foramen lacerum (A, B, black arrow) with heterogeneous enhancement and the ipsilateral cavernous sinus (C, D, white arrow) and temporal lobe (C, black arrow) with multiple circle enhancements were shown, moreover the left internal carotid artery (C, black arrowhead) surrounded by the lesions was also displayed. The enlarged left pterygopalatine canal (E, white arrow), connecting the PPF, with enhanced signal was shown on the sagittal image.

sticky milky pus was drained. The bone and the dura of the left skull base were partly eroded by *Aspergillus*. Unfortunately, the postoperative MRI (Fig. 2), performed 33 days after surgery, showed further deterioration of the lesion, which enlarged in the anterior left orbit and destroyed the Meckel's cave, entering the Cerebellopontine angle (CPA) and involving the posterior root of trigeminal nerve. As the disease progressed, his condition gradually worsened to a coma, and finally he died on the 42nd day after surgery.

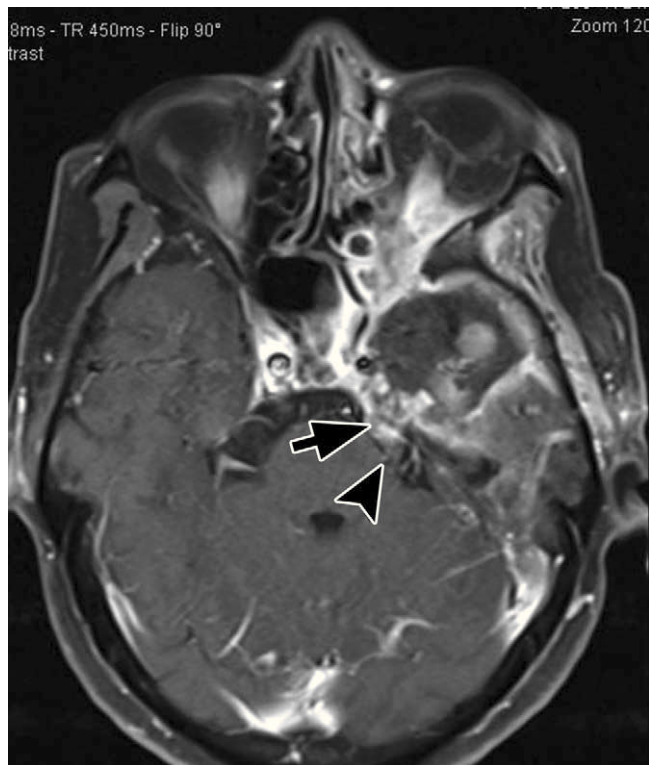


Fig. 2 - Postoperative MRI of CNS aspergillosis on the 33rd day. On the post-gadolinium T1WI, a vast lesion occupying the left orbital apex and orbit was strongly enhanced. The enhanced focus located at the left cerebellopontine angle (CPA) (black arrow) involving the root of trigeminal nerve (black arrowhead) was clearly shown.

Discussion

Aspergillosis is a common opportunistic infection in immunocompromised hosts but quite rare in immunocompetent patients. Intracranial aspergillosis accounts for 5% of all the CNS fungal infections.¹ The overall prognosis of craniocerebral aspergillosis is poor. Mortality is reported to reach 100% in immunocompromised and 67% in immunocompetent hosts.² The lungs and maxillary sinusitis are the most common sites of primary aspergillosis.³⁻⁵ Intracranial spread of *Aspergillus* infection occurs more

frequently by haematogenous routes, and less frequently through direct or contiguous spread.²⁻⁴ Contiguous spread can always be seen in the PPF, which communicates intracranially via channels. As its extent and location are different, clinical manifestations are subtle, frequently presenting features of meningitis, meningoencephalitis, focal neurological signs, or symptoms of raised intracranial pressure.

The PPF is an important anatomic site that communicates with the oral cavity via pterygopalatine canal, nasal cavity via sphenopalatine foramen, orbit via inferior orbital fissure, and middle cranial fossa via foramen rotundum. Infectious and tumor lesions in these regions can disseminate through the PPF, and meanwhile the related channels are always found enlarged or destroyed in the radiologic and pathologic exams. Due to the tooth extraction followed by constant headache and abnormal signals at the pterygopalatine canal on MRI, we propose that *Aspergillus* invaded the pterygopalatine canal, ascending via the greater and lesser palatine canals, and finally reached the PPF in our patient.

Concerning the probable route of this infection, which extended intracranially and perineurally based on the image evidence, we consider that the PPF was a crucial site. The left PPF and foramen rotundum were enlarged, and simultaneously the damaged connected structures, as the inferior orbital fissure and the vidian canal, were clearly shown on MRI. The foramen rotundum is a significant access to the middle cranial fossa from the PPF. The lesions, spreading through the foramen rotundum, frequently invade cavernous sinuses, temporal lobes, and the dura, resulting in the related clinical presentations. The symptoms and signs of our patient, including left facial numbness, decrease of left visual acuity, disappearance of ipsilateral eye fixation with light reflex, and eyelid weakness, corresponded to the involvement of the aforementioned regions. The inferior orbital fissure, the antero-superior cleft of the PPF, runs inferior orbital nerve through which infectious lesion from PPF may invade the orbit. In the present case, the damage to the left inferior orbital fissure and a mass in the orbit were demonstrated on the imaging, indicating that the orbital focus originated the PPF. Also, the lesions of PPF subsequently infected the foramen lacerum via the vidian nerve and were enhanced on the contrast-enhanced T1WI, and the lesion on the foramen lacerum might superiorly involve the posterior part of cavernous sinuses. The PPF communicates with the infratemporal fossa, which contains masticatory muscles and is located underneath the skull base of the middle cranial fossa, via the pterygomandibular fissure. Lesions of either the middle cranial fossa or the infratemporal fossa may communicate with each other by destroying the skull base. In the current case, his left masticatory muscles, dominated by the third division of the trigeminal nerve, which passes through the oval foramen, became atrophied. And the images proved the apparent damage on the skull base of the middle cranial fossa, consistent with its clinical manifestations. On the other hand, abnormal enhanced lesions located at the left CPA and at the trigeminal nerve root were shown on the enhanced-T1WI. Probable causes of the involvement of the posterior cranial fossa might be either the spread from the middle cranial fossa by crossing the petrous apex and Meckel's cave posteriorly, or invasion through the petro-occipital suture superiorly.

Consistent with the literature,² intracranial aspergillosis' typical MRI features appear as hypo-intense signals on T1-weighted and T2-weighted images, and as heterogeneous and multiple peripheral enhancements on post-gadolinium T1-weighted images.

The conventional treatment for invasive aspergillosis used to be amphotericin B. However, amphotericin B alone showed few encouraging results, especially in refractory fungal infections.⁵ Voriconazole has proven to be significantly superior to conventional amphotericin B, and has led to a profound survival improvement in patients with CNS aspergillosis.^{2,6} Combination therapies with two antifungal compounds are the common treatment protocol. Although the surgical treatment of *Aspergillus* infection is still controversial, our experience is that surgery combined with antifungal therapy may improve survival.

The prognosis of aspergillosis is closely related with the location and the extension of the lesion. Once the PPF has been involved, the infectious lesion would be very intractable. Although the vast majority of his intracranial lesions were resected during the operation, the focus of the pterygopalatine fossa and the orbit still remained. In our opinion, his poor prognosis was attributed to his elder age, longtime course, and the widespread infection caused by the rapid progression in size and number of lesions. Based on the literature,⁷⁻⁹ we propose that diagnosing the disease based on radiologic or pathologic findings in the early stage, starting combined antifungal therapies, and even performing surgical treatment if necessary could possibly improve the prognosis of patients with CNS aspergillosis.

Conflict of interest

All authors declare to have no conflict of interest.

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