Case Report

Post-Surgical Intraventricular Dissemination of Aspergillus Infection: A Case Report and Literature Review

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Abstract

Invasive intracranial aspergillosis is a rare disease with high morbidity and mortality that occurs most commonly in immunosuppressed patients. However, intracranial Aspergillus infections have also been reported in immunocompetent hosts after brain trauma or neurosurgery. Neurosurgical intervention combined with aggressive anti-fungal treatment is effective in treating cerebral aspergillus granuloma or abscess, and recurrent abscess in situ is the most frequently reported complication after surgical debridement. Here, we describe a 39-year-old male who developed an intracranial aspergillus abscess after a posterior fossa craniectomy following brain trauma. Aspergillus infection disseminated intraventricularly after surgical debridement. Ventriculoperitoneal (VP) shunting surgery in conjunction with anti-fungal medications was used to successfully treat the ventriculitis.

INTRODUCTION

Despite the rapidly increasing incidence of invasive intracranial aspergillosis among immunocompromised patients, this disease remains relatively rare in individuals with healthy immune systems [1]. Among patients who contract invasive intracranial aspergillosis, the difficulties in diagnosis and treatment of this disease has led to a high morbidity and mortality [1,2]. According to Schwartz et al., even when patients receive proper diagnosis and treatment with voriconazole, the mortality rate remains higher than 35% [3]. A combination of antifungal medications and surgical excision has been proposed to improve the outcome of patients with cerebral aspergillus granuloma or abscess [4], moreover, recurrent abscess in situ has been described as the most frequent post-surgical complication [4].

Here, we provide a literature review and describe a case of post-craniectomy aspergillus infection. This case describes a fungal infection that extended from the posterior fossa pseudomeningocele to the ventricular system after surgical debridement of an aspergillus abscess, which was subsequently cured with prolonged anti-fungal treatment and multiple VP shunting surgeries.

ABBREVIATIONS

VP: Ventriculo Peritoneal; CSF: Cerebro Spinal Fluid; MRI: Magnetic Resonance Imaging; q.d.: Once a Day; t.i.d.: Three Times a Day; CT: Computed Tomography

CASE PRESENTATION

A 39-year-old male with no underlying medical conditions was hospitalized because of a left frontal lobe contusion and right posterior fossa epidural hematoma following a traffic accident. A posterior fossa craniectomy was performed immediately following admission (day 0), and the patient was discharged from the hospital without any neurological symptoms on day 7. On day 14 post-operatively, the patient was re-admitted with a mild headache and slight neck stiffness. On clinical examination, a bulge localized over the cranial window was discovered, but no neurological decline or fever was detected. Samples of cerebrospinal fluid (CSF) and blood were taken at multiple time points for bacterial cultures, but none of the samples yielded positive findings. Magnetic resonance imaging (MRI) was conducted after the second hospitalization and revealed the formation of a pseudomeningocele (Figure 1A). Following this finding, antibiotics (cefuroxime 1.5u intravenously every 8 hours for 7 days and gentamicin 20000u intrathecal injection every other day for 6 days) and oral anti-tuberculosis medications (isoniazid 1.0 once a day (q.d.), rifampicin 0.15 three times a day...
(t.i.d.), ethambutol 0.25 t.i.d., and pyrazinamide 1.5 q.d. for 33 days) were prescribed empirically.

On day 56 post-operatively, the patient became unconscious (Glasgow Coma Scale: 12/15). An immediate MRI demonstrated an enlarged hydroma accompanied by contrast-enhanced signal in the surrounding tissues (Figure 1B), which suggests cerebral infection. A second posterior fossa craniectomy was performed to explore the nature of the hydroma. During this surgical procedure, we debrided the white floc found in the pseudomeningocele and the surrounding tissues, and we removed the infected dura and the adhered arachnoid between the cavity and the cisterna magna.

On day 63, *Apergillus fumigatus* was identified in the fungal culture of the white floc (Figure 3), and the patient was administered Amphotericin B liposome intravenously (150 mg, q.d.). Oral itraconazole (0.2g twice a day) was added to the patient’s treatment regimen on day 66; however, on day 70, the patient began to lose consciousness. On day 72, the regimen was switched to intravenous administration of voriconazole (6 mg/kg every 12 hours on the first day followed by 3 mg/kg every 12 hours for 7 days), and then oral administration (200 mg every 12 hours) for 6 months. Normothermia and decreased headache were observed within 24 hours of voriconazole administration.

On day 82 (10 days after voriconazole treatment), the patient developed afebrile headache. A computed tomography (CT) scan revealed expansion of all four ventricles, which suggest hydrocephalus. Consequently, an external ventricular drainage was conducted on day 83. The catheter was removed 7 days later (day 90) and replaced by local drainage of the posterior fossa pseudomeningocele.

CSF was collected from the ventricles via insertion of an external ventricular drainage catheter, and *Aspergillus* was found in both smears and cultures of these samples. We continued to sample intracranial CSF through the drainage catheter in three-day intervals (beginning on day 85 and ending on day 98). Blood was also collected on days 85, 88, and 91 (13, 16, and 19 days after voriconazole treatment). No pathogen was detected in blood or CSF. However, hydrocephalus still remained in the CT image on day 97 (26 days after voriconazole administration) (Figure 2A).

Negative cultures indicated that the aspergillus infection was under control, so we conducted a right VP shunt surgery on day 97 to relieve hydrocephalus. On day 130 (58 days after voriconazole treatment), the patient complained of headache and drowsiness; however, pathogens were not identified in CSF smear or culture. An MRI revealed an obvious contrast-enhanced lesion in the left ventricle and narrowing of the right ventricle, as well as significant expansion of the third and fourth ventricles (Figure 1C, 2B). Thus, the patient received a left VP shunt surgery on day 136 and was discharged on day 143. On day 252 (6 months after voriconazole treatment), an MRI showed normal ventricular morphology with minor contrast-enhanced signal in the ependyma (Figure 1D). After voriconazole withdrawal, the patient was able to gradually resume normal daily activities. On day 2435, the patient was admitted to the hospital for a third time with the chief complaint of a headache. An MRI demonstrated signs of hydrocephalus, but no observable intracranial contrast-enhanced signal (Figure 1E, 2C). Moreover, fungal cultures of blood and CSF were negative.

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**Figure 1** MRI features at different stages. (A) - On day 14, repeated Enhancing MRI showed posterior fossa pseudomeningocele without obvious contrast-enhanced signal. (B) - On day 56 enlarged posterior fossa pseudomeningocele was found. White arrow indicates contrast-enhanced signal in surrounding tissue. (C) - On day 130 white arrow points to the contrast-enhancing lesion in the left ventricle with hydrocephalus. (D) - On day 252 (6 months after voriconazole) MRI revealed normal ventricular morphology with only slight contrast-enhanced signal in the ependyma. (E) - On day 2435, MRI showed only hydrocephalus.
A third VP shunt was conducted on day 2442, after which the patient recovered rapidly and remained healthy.

**DISCUSSION**

Neurosurgery combined with aggressive anti-fungal therapy has been proposed as an effective method of treatment for invasive intracranial aspergillus infection [4]; meanwhile, recurrent abscess is the most frequently reported post-operative complication of this condition [5]. In this case, the ventricular infection was determined by the positive identification of aspergillus in the CSF, whereas the contrast-enhanced ventricular signal (observed via MRI) suggested an intracranial infection. To the best of our knowledge, this is the first case report of ventriculitis in an immunocompetent patient after surgical treatment of invasive intracranial aspergillosis.

On one hand, surgical intervention removes most fungi and infected tissue and thus improves the efficacy of medication [6,7]. On the other hand, surgery could also facilitate the release of aspergillus into the ventricular system, leading to the spread of fungal infection [8]. In the current case, infected dura and adhered arachnoid was removed during the debridement surgery, and the flow of CSF between the pseudomeningocele and the cisterna magna diluted the post-operative pathogen concentration. Although these two events prevented the recurrence of infection, the procedure enhanced fungal spread. In this case, the lesion was adjacent to the cisterna magna, which may also have contributed to the spread of the fungal infection. It remains unclear why aspergillus was more likely to invade the ependyma; we hypothesized that a higher concentration of pathogens in the ventricular system could have resulted from a larger accumulation of CSF around the ependyma.

Delayed diagnosis and treatment appear to be other factors that contributed to the spread of aspergillus. As we have already mentioned above, intracranial aspergillosis is rare and usually occurs in immunocompromised patients. Thus, despite of advances in diagnostic technology, the rarity of the disease tends to interfere with clinical judgment. Moreover, misdiagnosis could result from a combination of the lack of typical clinical manifestations and radiologic imaging features, as well as the low positive rate in fungal cultures of CSF obtained through lumbar puncture [4,9-11]. Additionally, the pre-operative use of antifungal medications is seldomly considered before a pathogen...
is identified. Finally, obtaining results from regular pathological examinations and cultures can take days to weeks, which further delay post-operative diagnosis and increase the opportunity for aspergillosis to spread. To overcome the detrimental effect of a delayed diagnosis, early identification of a fungal infection could be achieved through obtaining frozen sections during an operation or through a stereotactic biopsy before an extensive resection. Application of certain biochemical tests, such as the galactomannan enzyme immunoassay and polymerase chain reaction, may also be useful in early diagnosis [10-13].

In the current case, the patient suffered hydrocephalus three times over a span of eight years, which is similar to what has been reported for other types of ventriculitis [14]. The repeated hydrocephalus episodes increased the difficulty of treatment and resulted in prolonged hospitalization [14]. From this case, we found that it is essential to prevent the spread of aspergillus into CSF during surgical treatment of invasive intracranial aspergillosis, especially when lesions are close to cisterns or ventricles. Therefore, an alternative approach to treatment would have been to perform radical surgery and to repair the dura with autologous fascia in order to reduce the opportunity of fungal spread after surgical debridement. Even though this approach could increase the risk of infection relapse in situ, it would be easier to manage in comparison to ventricular infection with subsequent repeated episodes of hydrocephalus.

Similar to other types of fungal ventriculitis, MRI revealed that aspergillus ventriculitis manifested as contrast-enhanced signals in the affected areas. A VP shunt was conducted twice to alleviate hydrocephalus even when there were contrast-enhanced signals in the left ventricle. However, VP shunt did not spread the infection, suggesting that the contrast-enhanced signals in the ventricles were not a contraindication for the shunting approach.

Although a majority of the literature recommends prolonged exposure to anti-fungal medicine in patients with fungal ventriculitis [15], it is difficult for clinicians to decide when to stop antifungal therapy. In the current case, we stopped voriconazole administration when the patient's ventricles appeared normal on an MRI. Using this approach, the patient had no incident of relapse during an 8-year follow-up period. Therefore, the disappearance of contrast-enhanced signals in the ventricles could serve as an indicator for termination of antifungal therapy.

CONCLUSION

In this report, we described the first case of ventriculitis that occurred as a complication of the surgical treatment of invasive intracranial aspergillosis. Furthermore, we found that aspergillosis located adjacent to subarachnoid cisterns or ventricles may spread into the ventricular system after surgical debridement, leading, ultimately, to ventriculitis and later recurrent hydrocephalus. Early diagnosis and appropriate antifungal treatment could prevent the spread of Aspergillus. Moreover, after the ventricular infection is controlled, VP shunting can be applied to relieve hydrocephalus. Finally, MRI features can be used to determine the appropriate length of antifungal therapy.

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REFERENCES


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