but he had experienced unintentional weight loss and fatigue. His general condition was poor as a result of malnutrition. The neurological examination revealed a ptosis, ophthalmoplegia, and impairment of visual acuity on the right eye. His laboratory results were as follows: white cell count, 9.100/μL; sedimentation rate, C-reactive protein, peripheral smear and biochemical tests were all in normal range. Viral markers were negative. Magnetic resonance imaging (MRI) revealed a mass in the right cavernous sinus, extended to the anterior cranial fossa and the superior orbital fissure with an iso-signal intensity in T1-weighted image. The lesion showed a slightly low signal intensity in T2-weighted sequences and strong enhancement (Fig. 1). Based on these MRI findings, the impression was inflammatory abscess, but meningioma or metastatic tumor were also suspected. The patient underwent a pterional approach craniotomy for pathologic diagnosis and decompression of neural structures. During surgery, a well-encapsulated pus pocket was found, and histopathological examination of the mass resulted in the diagnosis of aspergillosis. Despite appropriate anti-fungal treatment, the patient eventually died from fatal cerebral ischemic change and severe brain swelling. The correct diagnosis of cerebral aspergillosis can only be achieved by histopathological examination because clinical and radiological findings including MRI are not specific. Surgical intervention and antifungal therapy should be considered the optimal treatment. Early diagnosis and aggressive antifungal treatment provide good results.

Key Words: Aspergillosis · Brain abscess · Neuroaspergillosis · Voriconazole.
Fatal Case of Cerebral Aspergillosis | JC Lee, et al.

Inflammatory granulation tissue and micro abscesses containing a large number of hyphae with 45 degree angulations and spores (Fig. 2). The pathology result was consistent with aspergillus infection.

Postoperatively, the patient was treated by systemic administration of antifungal drug (Amphotericin-B and Voriconazole), to which he showed only a minimal response. Despite appropriate medical and surgical treatment, the disease progressed and the patient eventually died from fatal cerebral ischemic change and severe brain swelling on the 23rd postoperative day (Fig. 3).

**DISCUSSION**

CNS aspergillosis is rare. However, the number of reported cases increased significantly in the last decade (Table 1). Aspergillus can reach the CNS by three different routes. The first is by hematogenous spread from a remote extracranial focus. The second is by extension from a contiguous extracranial location, and the third is direct introduction of aspergillus by a neurosurgical procedure iatrogenically.

CNS aspergillosis is very serious, with a mortality of more than 90%. CNS aspergillus presents as menigitis, encephalitis, brain abscesses, subdural abscesses, mycotic arteritis or sellar abscesses.

Preoperative diagnosis of parasellar aspergillus abscess is difficult because clinical presentation and imaging findings in these patients are very similar to the symptoms and imaging results in patients with neoplasms. Headaches and unilateral ophthalmologic signs, including orbital pain, visual deterioration and progressive ophthalmoplegia dominate the clinical presentation of parasellar aspergillus abscess. Ptosis is reported in up to 46% of published reports. MRI is the best technique for the radiological evaluation of a sellar abscess, but the definitive diagnosis is made with histological tests. On an MRI, the sellar abscess usually appears as a hypo-isointense sellar mass on T1-weighted sequences, as a hyperintense mass on T2-weighted sequences, and as a cystic lesion with peripheral ring enhancement after the administration of a contrast medium. In our patients, imaging findings suggested parasellar tumor, but the contrast enhanced rims of the masses and the clinical findings led us to reconsider the preoperative diagnosis.

Patients with aspergillosis have historically been treated with amphotericine B or combined therapy with amphotericine B and flucytosine or itraconazole. The superiority of voriconazole and caspofungin over amphotericin B as initial therapy for aspergillosis infection in terms of response rate, survival rate, and safety has now been demonstrated in a large randomised study. The aim of treatment should be the complete removal of the masses as early as possible. Even with the invasive type, providing intra dural extension had not yet occurred, total excision was curative without systemic use of antifungal agents. However, in patients in whom total removal cannot be achieved or intra dural invasion has already been confirmed, intensive systemic therapy with antifungal agents must be administered postoperatively to prevent subsequent lethal vasculitis or meningoencephalitis developing. In our case, treatment by voriconazole and amphotericine B was effective in patient, but patient died of cerebral...
Table 1. Reported cases of CNS aspergillosis in an immunocompetent patient in the last decade

| Year | Author                  | Nation  | Age  | Sex | Past history | Symptom                      | Treatment                          | Vessel invasion | Outcome |
|------|-------------------------|---------|------|-----|--------------|------------------------------|------------------------------------|-----------------|---------|
| 2012 | Xiao et al.             | Japan   | 57   | M   | (-)          | Headache visual defect       | Biopsy and antifungal (-)          | Expire          |         |
| 2011 | Koshy and Malhotra      | USA     | 71   | F   | DM           | Seizure                      | Biopsy and antifungal (-)         | No deficit      |         |
| 2009 | Hiraga et al.           | Japan   | 74   | M   | (-)          | Headache fever               | Surgery and antifungal (-)        | No deficit      |         |
| 2009 | Ueno et al.             | Japan   | 81   | F   | (-)          | Altered mentality            | Surgery and antifungal (+)        | Expire          |         |
| 2009 | Ueno et al.             | Japan   | 64   | M   | (-)          | Bilateral visual loss        | Surgery and antifungal (+)        | Expire          |         |
| 2007 | Okugawa et al.          | Japan   | 65   | F   | DM           | Headache                     | Biopsy and antifungal (-)         | Expire          |         |
| 2006 | Pinzer et al.           | Germany | 59   | F   | (-)          | Headache                     | Surgery and antifungal (-)        | No deficit      |         |
| 2005 | Palanisamy et al.       | USA     | 42   | M   | Hep C        | Vertigo                      | Surgery and antifungal (-)        | No deficit      |         |
| 2003 | Petrick et al.          | Germany | 74   | M   | (-)          | Third nerve paresis          | Surgery and antifungal (-)        | Improve         |         |

CNS: central nervous system

ischemic change, possibly due to resistance for antifungal agents, or developing vessel invasion.

CONCLUSION

Aspergillus infection is strongly invasive into vessels. It is important to consider the possible occurrence of cerebrovascular disease when treating invasion of aspergillosis into the CNS. CNS aspergillosis is very serious, with a high mortality. A combination of surgical resection and antifungal therapy resulted in good outcomes. The prognosis of the patients depends on early diagnosis and prompt aggressive treatment.

References

1. Alapatt JP, Kutty RK, Gopi PP, Challissery J: Middle and posterior fossa aspergilloma. Surg Neurol 66: 75-78; discussion 78-79, 2006
2. Bodey G, Bueltmann B, Duguid W, Gibbs D, Hanak H, Hotchi M, et al.: Fungal infections in cancer patients: an international autopsy survey. Eur J Clin Microbiol Infect Dis 11: 99-109, 1992
3. Endo T, Numamagi Y, Yokura H, Ikeda H, Shirane R, Yoshimoto T: Aspergillus parassellar abscess mimicking radiation-induced neuropathy. Case report. Surg Neurol 56: 195-200, 2001
4. Gupta AK, Mann SB, Khosla VK, Saxtry KY, Hundal JS: Non-randomized comparison of surgical modalities for parasinal sinus mycoses with intracranial extension. Mycoses 42: 225-230, 1999
5. Haran RP, Chandy MJ: Intracranial aspergillus granuloma. Br J Neurosurg 7: 383-388, 1993
6. Herbrecht R, Denning DW, Patterson TF, Bennett JE, Greene RE, Oestmann JW, et al.: Voriconazole versus amphotericin B for primary therapy of invasive aspergillosis. N Engl J Med 347: 408-415, 2002
7. Hiraga A, Uzawa A, Shibuya M, Numata T, Sunami S, Kamitsukasa I: Neuroaspergillosis in an immunocompetent patient successfully treated with voriconazole and a corticosteroid. Intern Med 48: 1225-1229, 2009
8. Işıklıoğlu AC, Bek S, Bikmaz K, Ceylan D, Gökduman CA: Aspergillus pituitary abscess. Acta Neurochir (Wien) 146: 521-524, 2004
9. Jain KC, Varma A, Mahapatra AK: Pituitary abscess: a series of six cases. Br J Neurosurg 11: 139-143, 1997
10. Koshy R, Malhotra P: Treatment of primary aspergilloma of the central nervous system in a diabetic immunocompetent patient with surgical resection and voriconazole: a case report and review of the literature. Turk Neurosurg 21: 641-644, 2011
11. Okugawa S, Ota Y, Tatsuno K, Tsukada K, Kishino S, Koike K: A case of invasive central nervous system aspergillosis treated with micafungin with monitoring of micafungin concentrations in the cerebrospinal fluid. Scand J Infect Dis 39: 344-346, 2007
12. Palanisamy A, Chao SD, Fouts M, Kerr D: Central nervous system aspergillosis in an immunocompetent patient: cure in a hospice setting with very high-dose itraconazole. Am J Hosp Palliat Care 22: 139-144, 2005
13. Petrick M, Honegger J, Daschner F, Feurerhake F, Zentner J: Fungal granuloma of the sphenoid sinus and clivus in a patient presenting with cranial nerve III paresis: case report and review of the literature. Neurosurgery 52: 955-958; discussion 958-959, 2003
14. Pinzer T, Reiss M, Bourquain H, Krishnan KG, Schackert G: Primary aspergillosis of the sphenoid sinus with pituitary invasion - a rare differential diagnosis of sellar lesions. Acta Neurochir (Wien) 148: 1085-1090; discussion 1090, 2006
15. Stevens DA, Kan VL, Judson MA, Morrison VA, Dummer S, Denning DW, et al.: Practice guidelines for diseases caused by Aspergillus. Infectious Diseases Society of America. Clin Infect Dis 30: 696-709, 2000
16. Ueno A, Hamano T, Fujii A, Matsunaga A, Nagamura S, Yoneda M, et al.: Effects of voriconazole and vascular lesions in invasion of aspergillosis into the central nervous system. Rinsho Shinkeigaku 49: 468-473, 2009
17. Yates GE, Berger MS, Wilson CB: Diagnosis and management of pituitary abscess: a review of twenty-four cases. J Neurosurg 95: 233-241, 2001
18. Walsh TJ, Pappas P, Winston DJ, Lazarus HM, Petersen F, Raffalli J, et al.: Voriconazole compared with liposomal amphotericin B for empirical antifungal therapy in patients with neutropenia and persistent fever. N Engl J Med 346: 225-234, 2002
19. Xiao A, Jiang S, Liu Y, Deng K, You C: Invasive intracranial aspergillosis spread by the pterygopalatine fossa in an immunocompetent patient. Braz J Infect Dis 16: 192-195, 2012

422