Case Report

Journal Of Clinical & Medical Images Case Reports

Open Access, Volume - 2

Successfully treated case of cerebral aspergillosis in sri lanka

Welagedara[1*]; B Devakanthan[2]; Sigera[1]; Jayasekara[1]

[1]Department of Mycology, Medical Research Institute, Colombo 8, Sri Lanka.

[2]Department of Microbiology, Teaching hospital, Kurunegala, Sri Lanka.

Received Date : Feb 14, 2022
Accepted Date : Mar 11, 2022
Published Date : Mar 26, 2022
Archived : www.jcmimagescasereports.org

***Corresponding Author:** Welagedara, Department of Mycology, Medical Research Institute, Colombo 8, Sri Lanka.
Email: isanka784@gmail.com

Abstract

Introduction: Cerebral aspergillosis is a rare condition associated with high mortality. It is reported predominantly in immunocompromised patients. Nonspecific clinical and radiological features may contribute to difficulty and delay in diagnosis resulting poor prognosis. Timely diagnosis with proper specimen is the key to achieve success.

Case report: A 74-year-old female presented with frontal headache for two weeks. She has been diagnosed with low grade lymphoma and had completed chemotherapy with high dose prednisolone four weeks prior to this presentation. Except headache, she denied any other associated symptom. Physical examination and basic blood investigations revealed no abnormality. However, radiological imaging of brain indicated right frontal sinusitis with secondary small cerebral abscess in the right frontal lobe. Accordingly, she was treated with parenteral antibiotics as for a bacterial infection of CNS and discharged. Then again, she presented with headache after three months of initial presentation. Repeat MRI brain suggested a possibility of a cerebral tumour with increased size in the right frontal lobe. Hence, a diagnostic biopsy was performed and direct microscopic examination of the biopsy revealed fungal filaments and culture yielded a pure growth of *Aspergillus fumigatus*. The patient was started on intravenous amphotericin B, followed by oral voriconazole. Headache gradually subsided with antifungal therapy. Duration of therapy was guided by serial radiological imaging and the patient achieved complete recovery at the end of one-year treatment. She remains asymptomatic to date after two years of treatment completion.

Discussion: Immunocompromised patients with cerebral aspergillosis may present with minimal clinical symptoms and signs. Obtaining a proper specimen for laboratory testing is vital to make definitive diagnosis. Radiological investigations may play an important role in the diagnosis and follow up of a patient with cerebral aspergillosis.

Introduction

Fungi of genus *Aspergillus* are ubiquitous in the environment [1]. Inhalation of Aspergillus spores may lead to invasive infection known as aspergillosis, which is commonly seen in immunocompromised population [1]. Cerebral aspergillosis is a grave condition with high mortality [1]. We report a case of cerebral abscess caused by *Aspergillus fumigatus* who was managed successfully with antifungal therapy.

Case report

AA seventy-four-year-old female presented with frontal headache for about three weeks' duration. She had been diagnosed with a low grade lymphoma for which she had recently undergone chemotherapy and high dose prednisolone. The patient complained of a severe frontal headache, which persisted throughout the day with poor response to analgesics. Headache was not associated with vomiting, fever, photophobia, seizures or weakness. Physical examination revealed no abnormality in the nervous system. Her white blood count was 7.5 with 60% neutrophils. C reactive protein was 7mg/L.

Contrast enhanced Computed topography (CECT) scan of brain revealed right frontal lobe meningoencephalitis complicated with a cerebral abscess (1.5cm) due to right frontal sinusitis (**Figure 1**). Right frontal sinus trephination was performed and there was thickening of sinus mucosa. She was treated with intravenous cefotaxime for fourteen days and discharged. Three months later the patient presented again with worsened headache. Similar to previous presentation, there were no other symptoms or signs. A magnetic resonance imaging of brain revealed increase in size of the lesion in right frontal lobe (4.7cm X 2.1cm) and the radiological interpretation was that it's probably a glioma with local invasion. Craniotomy was performed to excise the tumour, but surprisingly an inflammatory lesion (probable fungal abscess) was

Citation: Welagedara, B Devakanthan, Sigera, Jayasekara. Successfully treated case of cerebral aspergillosis in sri lanka. J Clin Med Img Case Rep. 2022; 2(2): 1108.

found intraoperatively. A diagnostic biopsy was taken and sent for microbiological and histopathological examination. The direct microscopic examination with 10% KOH revealed septate dichotomously branched fungal filaments suggestive of *Aspergillus species* (**Figure 2a**). Fungal culture yielded pure isolates which are bluish green colour with velvety surface and pale reverse side (**Figure 2b** and **2c**). Tease mount with lacto phenol cotton blue stain revealed septate hyaline hyphae and conical conidial heads with uniseriate phialides on upper 2/3rd of the vesicle leading to the identification of *Aspergillus fumigatus* (**Figure 2d**). Bacterial culture was negative. Histopathology of the biopsy found no evidence of malignancy.

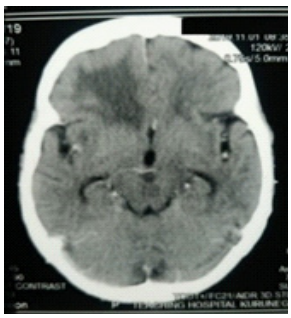

Figure 1: *CECT scan of brain with an abscess in the right frontal lobe.*

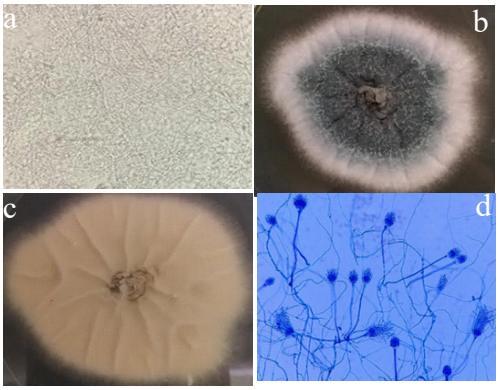

Figure 2a *Direct smear, 2b: A. fumigatus macroscopic appearance, 2c: Reverse side, 2d: Microscopic appearance.*

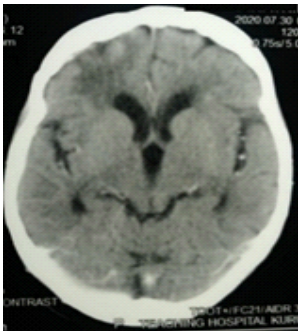

Figure 3: *Resolving abscess.*

Intravenous lyposomal amphotericin B was started due to the unavailability of intravenous voriconazole during that period. Patient's headache gradually subsided and five weeks later, she was asymptomatic and discharged from the hospital with oral voriconazole. CECT brain after three months of total antifungal treatment indicated resolving abscess (1.7 X 1.2 X 1.5cm). (Figure 3) Its size further reduced (5mm X 5mm) after six months. Repeat imaging after completion of one year' treatment revealed complete radiological clear of the abscess.

Discussion

Aspergillus species is an important cause of life threatening infection in immunocompromised individuals. Cerebral aspergillosis is a condition with poor prognosis in the majority of affected patients [1]. Out of all invasive *Aspergillus* infections, cerebral aspergillosis accounts for 10-20% [2]. High prevalence of central nervous system (CNS) invasion by *Aspergillus* sp in tropical and subtropical countries has been reported [3]. According to the literature, three criteria are used to define cerebral aspergillosis [4]. 1) one or more predisposing factors for invasive aspergillosis, Eg: haematological malignancy, immunosuppressive treatment, bone marrow transplantation, prolonged neutropenia; 2) imaging studies (CT or MRI) evidence of localized lesion/s without an alternative diagnosis and 3) brain biopsy, sinus or BAL specimen positive for *Aspergillus* species in culture or direct smear suggestive of Aspergillus species. Our patient fulfilled all three criteria.

The site of abscess indicates the pathogenesis of infection. Frontal lobe involvement is associated with direct extension from the sinuses whereas temporal lobe may be affected secondary to ear infection. Haematogenous dissemination usually results in multiple small abscesses at the grey-white junction [1]. In this patient with right frontal lobe abscess, there was CT evidence of right frontal sinusitis indicating the likely source of infection. Principles of management of cerebral aspergillosis include early diagnosis, proper antifungal treatment, consideration of surgical intervention and reduction of immunosuppression [1]. Diagnosis of cerebral aspergillosis is difficult and even brain biopsy may become negative [5]. Victims may present with seizures or focal neurological signs. But signs of meningeal irritation are rare [1]. Among the patients with brain abscess, headache was present in 60%, fever was documented in 40-50% and only half of the patients had neurological deficits [3]. During early stage of cerebral abscess, there is minimal elevation of blood leucocyte count and CRP level [6]. Accordingly, absence of fever and neurological signs and normal inflammatory markers in our patient with cerebral abscess is understandable.

Neuroimaging is essential for the diagnosis and follow up of patients [1]. Since our patient had only limited clinical features and normal inflammatory markers, (WBC and CRP), radiological evidence played a major role in the diagnosis. However, imaging studies may have a chance of misinterpretation of the condition, as in our patient. After both CT scan and MRI scan, a patient who has presented with focal neurological signs was diagnosed with a brain glioma [7]. Since he was afebrile without peripheral blood leukocytosis, the condition well-matched with a diagnosis of cerebral tumour similarly to our patient. Nevertheless, surgical findings were incompatible with a tumor and histology confirmed as fungal abscess [7]. Therefore, radiological imaging needs careful interpretation. Serial brain imaging was the only option available to monitor our patient and it revealed marked response to treatment.

Recommended primary therapy for cerebral aspergillosis is voriconazole [1]. It is the smallest antifungal agent effective against *Aspergillus* sp and it achieves a fungicidal therapeutic level in CSF and brain tissue as it is the smallest [8]. Penetration of amphotericin B, itraconazole and caspofungin to CSF and brain tissue is negligible [9]. Therefore, amphotericin B is recommended only for patients intolerant or refractory to voriconazole [1]. Our patient was treated for prolonged duration ie twelve months of antifungal therapy. There is a report of three patients with cerebral aspergillosis who were cured following prolonged duration of antifungal therapy [4]. One of them was treated with amphotericin B (mean duration of 33days) and oral azole therapy (mean duration 14months) similar to our patient [4]. Surgical intervention combined with voriconazole therapy has been shown to reduce mortality [1]. Reduction or reversal of immunosuppression is an essential factor determining a good prognosis [1]. Three patients survived in the above study had reversal of their immunosuppression by terminating corticosteroid therapy [4]. Since our patient did not undergo continued immunosuppressive therapy following the diagnosis of abscess, it must have contributed to this good outcome.

Conclusion

Cerebral aspergillosis in immunocompromised patients is associated with poor prognosis. Early diagnosis with identification of pathogen leads to appropriate treatment and may reduce the mortality. Clinical features, inflammatory markers and neuro imaging may not always be helpful and high degree of suspicion in susceptible patients is important in the diagnosis. Appropriate antifungal treatment for prolonged duration, neurosurgical intervention where applicable and reversal or reduction of immunosuppressive therapy leads to good prognosis.

References

1. Patterson TF, Thompson GR, Denning DW, Fishman JA, Hadley S, Herbrecht R, et al. Practice Guidelines for the Diagnosis and Management of Aspergillosis: 2016 Update by the Infectious Diseases Society of America. Clinical Infectious Diseases. 2016; 63(4):e1-60.

2. Bennett JE, Dolin R, Blaser MJ, editors. Mandell, Douglas, and Bennett's principles and practice of infectious diseases. Eighth edition. Philadelphia, PA: Elsevier/Saunders. 2015; 2.

3. Góralska K, Blaszkowska J, Dzikowiec M. Neuroinfections caused by fungi. Infection. 2018; 46(4):443-59.

4. Tattevin P, Bruneel F, Lellouche F, de Broucker T, Chevret S, Wolff M, et al. Successful treatment of brain aspergillosis with voriconazole. Clinical Microbiology and Infection. 2004; 10(10):928-31.

5. Klont RR, Mennink-Kersten MASH, Verweij PE. Utility of Aspergillus Antigen Detection in Specimens Other than Serum Specimens. Clin Infect Dis. 2004; 39(10):1467-74.

6. Oyama H, Kito A, Maki H, Hattori K, Noda T, Wada K. INFLAMMATORY INDEX AND TREATMENT OF BRAIN ABSCESS. :12.

7. Liutkus D, Šilkūnas D, Staškevičius A. Fungal Brain Abscess Mimicking High Grade Glioma. Clinical Case. Sveikatos mokslai. 2016; 26(5):97-100.

8. Schwartz S, Thiel E. Cerebral aspergillosis: tissue penetration is the key. Medical Mycology. 2009;7.

9. Schwartz S. Improved outcome in central nervous system aspergillosis, using voriconazole treatment. Blood. 2005; 106(8):2641-5.