

## Case Report

# Multiple invasive aspergillus brain abscess in an immunocompetent patient without any history of trauma

Akshay K. Barde\*, Pankaj Soni

Department of General Medicine, Max Super Speciality Hospital, Saket, New Delhi, India

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### \*Correspondence:

Dr. Akshay K. Barde,

E-mail: [akki4850@gmail.com](mailto:akki4850@gmail.com)

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## ABSTRACT

Aspergillus is a fungus found in the environment. In an immunocompetent person, inhalation of spores may cause localized infection. In immune compromised patients, these fungi can cause life-threatening invasive infections which has high morbidity and mortality. Invasive aspergillosis has a poor prognosis. Intracranial aspergillosis is an extremely rare manifestation of invasive aspergillosis in immunocompetent individuals. A case of 60-year-old immunocompetent male is reported who had multiple Aspergillus brain abscess.

**Keywords:** Amphotericin B and Voriconazole, *Aspergillus flavus*, Brain abscess, Case report, Immunocompetent

## INTRODUCTION

Brain abscesses are a challenging emergency and any delay in diagnosis or treatment may result in poor health outcomes. The incidence of this infectious disease is approximately 0.4-0.9 per 100,000 individuals worldwide, with much higher rates among immunocompromised patients.<sup>1</sup> Brain abscesses can be caused by bacteria, fungi or parasites.<sup>1</sup> *Aspergillus sp.* is an opportunistic ubiquitous fungus that usually enters the body by inhalation of airborne spores; it can then invade the Central Nervous System (CNS) via the hematogenous route, from direct extension through the paranasal sinuses or by direct inoculation during trauma or surgical procedures.<sup>2,3</sup> Invasive intracranial aspergillosis is unusual, accounting for 10-20% of all cases of invasive aspergillosis.<sup>4</sup>

Most patients with this condition have immune defects, usually in the form of neutrophil or macrophage dysfunction.<sup>5,6</sup> Invasive intracranial aspergillosis is associated with high morbidity and mortality rates; the latter can be as high as 88% in bone marrow transplant

recipients and for those with disseminated or cerebral aspergillosis.<sup>2,7,8</sup> CNS-invasive aspergillosis may present with meningitis, cerebritis, infarctions, abscesses, granulomas or mycotic aneurysms.<sup>9</sup> The exact pathology depends upon the disease pathway and the host's immunity. The most frequent pathological findings are haemorrhage, infarctions and abscesses.<sup>10</sup> Rarely, *Aspergillus* infections present as space-occupying lesions in immunocompetent patients.<sup>3,10</sup> This report describes an invasive *Aspergillus* induced brain abscess in an immunocompetent/ immunocompromised patient with no history of trauma.

## CASE REPORT

A previously healthy 60-year-old male who is farmer by occupation was admitted in the medical ward of Max Super specialty Hospital, Saket, New Delhi in September 2018 with complain of a high-grade intermittent fever, difficulty in breathing, nausea and vomiting and generalized weakness of 5 days. There was no history of chest pain, cough with expectoration, pain in abdomen, loose motion, burning micturition, convulsion or skin rashes. His general physical examination showed

PR108/min, BP-110/60 mmhg, RR-22/min, Temp102F. His systemic examination revealed only bilateral basal coarse crackles and small, rounded, black coloured crusting Eschar on left lower abdomen (Figure 1).



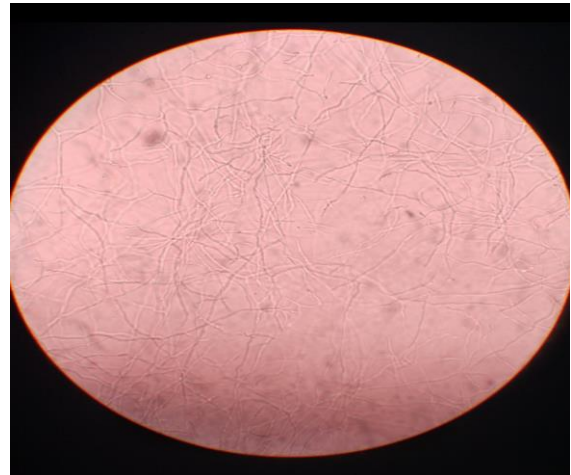
**Figure 1: Eschar on left side of thigh.**

A provisional diagnosis of viral fever/ Typhus fever was made and investigated. Blood examination showed CBC (Hb 11.7 mg/dl, TLC 1000  $10^6$ /ml, and platelet counts 3000  $10^6$ /ml) DLC (PMN-89, Lymphocytes-9, Monocytes-2, Basophils-0, Eosinophils-0).

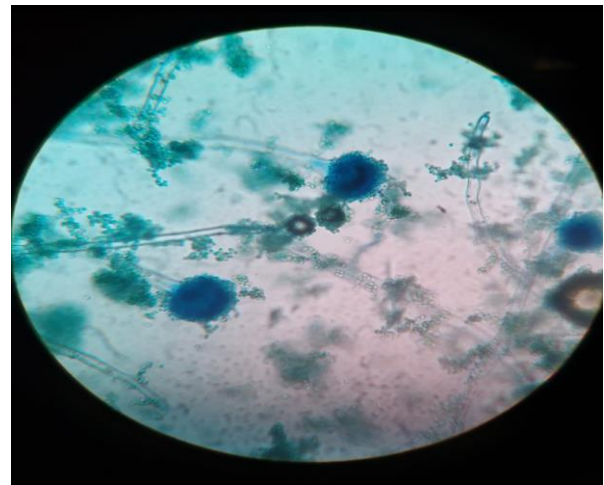
RFT (Urea 55.7 mg/dl, creatinine 1.2 mg/dl, sodium 121 mmol/L, and potassium 4.1 mmol/L), LFT (TP 4.4 g/dl, albumin 1.8 g/dl, globulin 2.6 g/dl, SGOT 340 IU/L, SGPT 108 IU/L, GGT 69 IU/L, ALP 158 IU/L). Leptospira antibody IgG 3.19, IgM 9.94 (Ref range: 11 - Positive), Peripheral smear for malarial parasite, Dengue NS-1 antigen, dengue serology, H1N1 influenza, typhi dot and widal test were negative. Procalcitonin 16.55 ng/ml (Normal range: 0-0.5). X-ray chest PA showed bilateral perihilar alveolar opacities. USG whole abdomen showed mild bilateral pleural effusion.

Urine R/M showed 2-3 RBCs, 3-5 leukocytes and 0-1 epithelial cells. Blood and urine C/S were sterile. Keeping in mind of Eschar, patient was put on Doxycycline and other symptomatic treatment along with 12U of Random donor platelet concentrates.

In view of persistent bicytopenia (TLC and Platelet), Bone marrow examination was done which revealed hemophagocytosis. Thus I/V Dexamethasone was added in his treatment. In spite of evidence-based treatment his condition deteriorated, and he was subjected for CECT chest which revealed extensive consolidation, ground glassing and nodular opacities in bilateral lungs. He was subjected to Bronchoscopy and BAL samples sent for smear for Gram's stain, fungal stain and AFB stain which showed septate fungal hyphae with acute angle branching (Figure 2 and 3). BAL Culture showed *Aspergillus flavus* (Figure 4).



**Figure 2: Septate fungal hyphae with acute angle branching on 10 x film in BAL sample on KOH mount.**

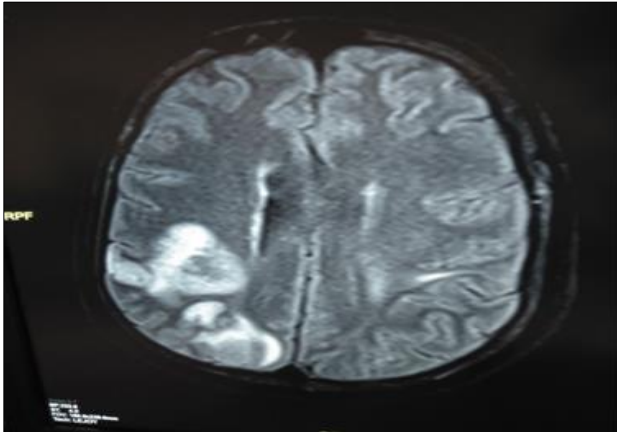


**Figure 3: Septate fungal hyphae with acute angle branching on 40 x film in BAL sample on KOH mount.**

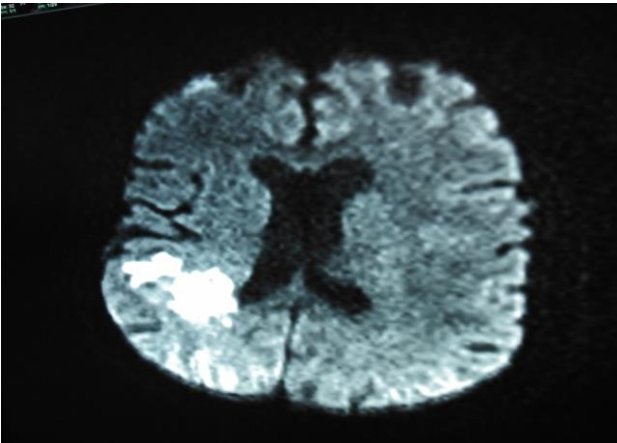


**Figure 4: Parrot green colony on BAL culture s/o *Aspergillus flavus*.**

Galactomannan in BAL was 1.97 (Cut off: 0.5- Sn-78%, Sp-84%, 1- Sn-72%Sp-89%, 1.5- Sn-67%Sp- 93%) and serum Galactomannan was 3.09 (Cut off: 0.5- Sn-78%,Sp-84%, 1- Sn-72%Sp-89%, 1.5- Sn-67%Sp- 93%) . So patient was put on (Initially on Amphotericin B and later on Voriconazole). But patient's condition deteriorated with decreased consciousness prompting an MRI Brain which showed multiple peripherally enhancing rounded thick-walled lesions (abscesses) in left cerebellum, left thalamus, right occipital, left frontal and bilateral parietal regions (Figure 5 and 6).



**Figure 5: MRI Brain showing multiple peripherally enhancing rounded thick-walled lesions (abscesses) in left cerebellum, left thalamus, right occipital, left frontal and bilateral parietal regions showing restricted diffusion and mild peri lesional edema suggestive of abscesses (on diffusion weighted film).**



**Figure 6: MRI Brain showing multiple peripherally enhancing rounded thick-walled lesions (abscesses) in left cerebellum, left thalamus, right occipital, left frontal and bilateral parietal regions showing restricted diffusion and mild peri lesional edema suggestive of abscesses (on contrast MRI film).**

*Aspergillus flavus* in BAL smear examination and high Galactomannan in BAL sample and smear, clinching the

diagnosis of *Aspergillus* brain abscess. Management of fungal brain abscess remain controversial. Antifungal therapy alone poor outcome with mortality of >90% due to poor penetration of antifungal medicines in CNS.<sup>2</sup> Surgical intervention in single lesion reduces mortality to approximately 39%.<sup>2</sup> In case with multiple fungal brain abscess, Voriconazole remain the drug of choice. Early treatment with antifungal can improve the outcome. Since no autoimmune defect was established in this case, the source of fungal infection remains unanswered.

## DISCUSSION

In general, CNS aspergillosis particularly invasive aspergillosis is rarely observed in immunocompetent patients.<sup>2</sup> The brain is remarkably resistant to fungal infections due to its abundant blood supply and the relatively impermeable blood-brain barrier. Nevertheless, despite the existence of anatomical and functional barriers which protect the brain and subarachnoid space, fungal pathogens can breach these barriers under certain conditions.<sup>2</sup> Persistent cerebral *Aspergillus* abscesses in immunocompetent patients may exhibit clinical and radiological features similar to primary or secondary neoplasms or other forms of infection.<sup>10</sup> Only a few cases of invasive *Aspergillus* brain abscesses have been reported; of these, most involved adult rather than paediatric patients.<sup>11</sup> The management of cerebral fungal abscesses remains controversial. Antifungal therapy alone reportedly has a poor outcome for patients with CNS aspergillosis, with a high mortality rate of >90%; this is likely due to the poor penetration of the CNS by the antifungal drugs.<sup>2</sup> Other research has indicated that surgical resection of focal CNS aspergillosis lesions reduces the mortality rate from 64% to 39%.<sup>2</sup> Overall, voriconazole seems to be the drug of choice for the treatment of aspergillosis.<sup>2</sup> In the current case, the patient had multiple brain abscesses without paranasal sinus involvement and with no identifiable immune defects. It is not clear how the patient in the present case developed the brain abscess. Although no immune defects were identified, he may nevertheless have been suffering from a rare form of immunodeficiency, such as an Interleukin (IL)-4 or IL6 deficiency; suppression of monocytes and T helper cells and Interferon-Gamma (IFN- $\gamma$ ) responses can lead to severe *Aspergillus* infections.<sup>12,13</sup>

## CONCLUSION

Persistent cerebral *Aspergillus*-induced abscesses in immunocompetent patients are extremely rare. CNS aspergillosis is very serious condition, 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. Health professionals should therefore be aware of the symptoms of *Aspergillus*-induced brain abscesses, as early detection and appropriate treatment is necessary to ensure positive patient outcomes.

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