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REVIEW ARTICLE

Cerebral aspergilloma in a SLE patient: A case report with short literature review

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ABSTRACT

Aspergillosis of brain is very rare, and commonly seen in immunocompromised or immunosuppressed patient. Here, we report a cerebral aspergillosis condition in a late teen girl who is a Systemic Lupus Erythromatosis patient with steroid therapy. She developed headaches, vomitings, and convulsions. On the basis of clinical and neuroimaging, a diagnosis of cerebral tuberculoma was made, and she was put on anti-TB therapy, but she did not respond. Later, surgical partial excision biopsy confirmed the diagnosis. Her cerebral lesions responded with antifungal itraconazole therapy. The case will be presented with short literature review. Such a report in the literature is rare.

Key words: Aspergillosis of brain, cerebral aspergillosis, Systemic Lupus Erythromatosis, steroid therapy

Introduction

Opportunistic infections, particularly fungal infections, are a common complication in bone marrow transplant recipients. Aspergillus is among the most common fungal pathogens, and is responsible for the majority of brain abscesses along with candida in immunocompromised patients.[1,2] Aspergillus spores are commonly airborne and inhaled by the host, causing infection of the respiratory system. Aspergillus may then gain access to the central nervous system (CNS) via hematogenous spread or direct spread from the paranasal sinuses.[3] Invasive aspergillosis is a disease of concern, as it is a leading cause of death in patients with hematological malignancies, immunocompromised patients and transplant recipients. With the use of broad-spectrum antifungal agents for prophylaxis in those high risk patients, the incidence and fatality rates can be declined,[4] but in most of the cases, diagnosis is very late. So, cerebral aspergillosis has a poor prognosis in immunocompromised patients, with the mortality rate approaching 100%.[2] Here, we report a case of cerebral aspergillosis in a young patient of Systemic Lupus Erythromatosis (SLE) who was on steroid and was managed successfully with surgical excision and antifungal therapy. Only a few cases have been reported in the literature.[5-7]

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Case Report

A 19-year-old girl presented with headache, vomiting, and secondary generalized seizure and weakness on left side the body. She was diagnosed of SLE with lupus nephritis for last two and half years. She was getting steroid (Tab. Deltasone) since the diagnosis of SLE. Six months later, she developed headache, nausea, and left sided focal seizure. Magnetic resonance imaging (MRI) of brain showed marginal contrast enhancing lesion in right frontal lobe with perilesional edema [Figure 1a]. Computed tomogrpahy (CT) scan of brain at that time showed two coalescing right frontal cystic lesions with mild marginal enhancement surrounded by huge edema [Figure 1b]. Complete blood count (CBC), X-ray chest was normal. A diagnosis of cerebral tuberculosis was made, and she was put on anti-TB therapy, and advised for regular follow-up with CT scan. She remained unnoticed for two years, but she continued anti-TB drugs. By this time, her severity of headache, frequency of vomiting and seizure increased with gradual development of weakness on left side of body. Initially, her seizure was involving left sided limbs without loss of consciousness, but recently, it converted into secondary generalized with involvement of whole body along with unconsciousness. CBC, X-ray chest remained normal. MRI of brain showed peripheral contrast enhancing lesion in right frontal lobe with huge edema with mass effect. The lesion was isointense in T1W and T2W images. Simultaneously, there was a similar lesion in left occipital lesion [Figure 1c].This time X-ray chest was again normal [Figure 1d]. Orbit and all paranasal sinuses were normal. Through a right frontal craniotomy

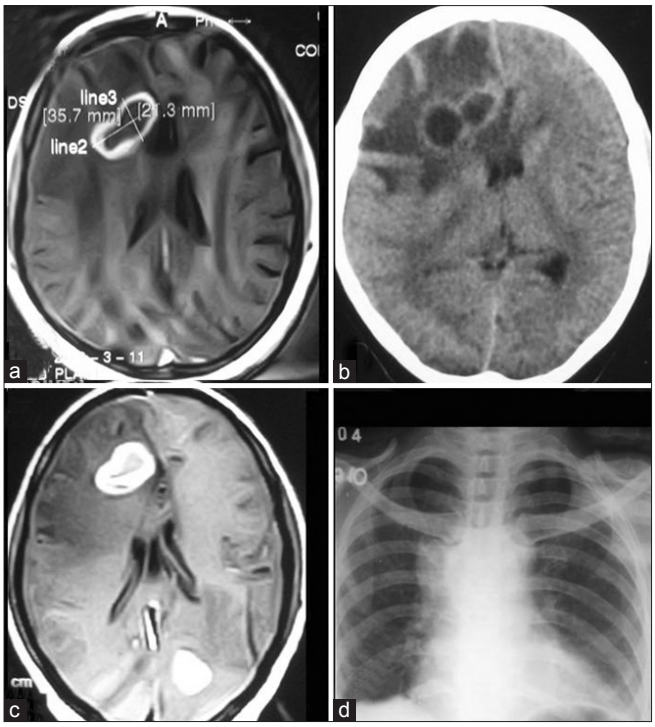

Figure 1: (a) Contrast MRI of brain axial view showing frontal ring enhancing lesion with perilesional edema (at initial presentation). (b) Contrast CT scan of brain axial view showing cystic lesion in right frontal lobe with mild marginal contrast uptake with edema. (c) Contrast MRI of brain axial view (2 years after initial presentation) showing frontal lesion with another lesion in left occipital lobe. (d) X-ray chest P/A view of the patient showing free of lesion

lesion was approached and partial excision biopsy was done. Histopathological report confirmed aspergillosis. Then she was put on itraconazole with phenoytoin for a period of 12 months. Her symptoms gradually subsided within four months. CT scan of brain at the end of three months after operation showed absent frontal lobe lesion and occipital lobe lesion was at stage of resolution with marked edema [Figure 2]. Post operative CT scan after six months showed regression of lesions with scaring at the involved sites.

Discussion

Cerebral aspergillosis may be in the form of isolated cerebral aspergillosis by hematogenous spread or in the form of sino-orbito-cerebral aspergillosis by direct spread. Sino-orbital-cerebral aspergillosis is a highly prevalent disease in tropical countries.[8] It may be in form of invasive fungal rhinosinusitis (FRS) into acute invasive FRS, granulomatous invasive FRS, and chronic invasive FRS.[9]

However, hematological malignancy is the commonly associated underlying disease in acute invasive FRS with higher isolation of A. fumigatus.[10] Granulomatous invasive FRS is described by a time course of 12 weeks with enlargement of mass in the cheek, nose, paranasal sinuses, and the orbit in the immunocompetent host. Histopathologically,

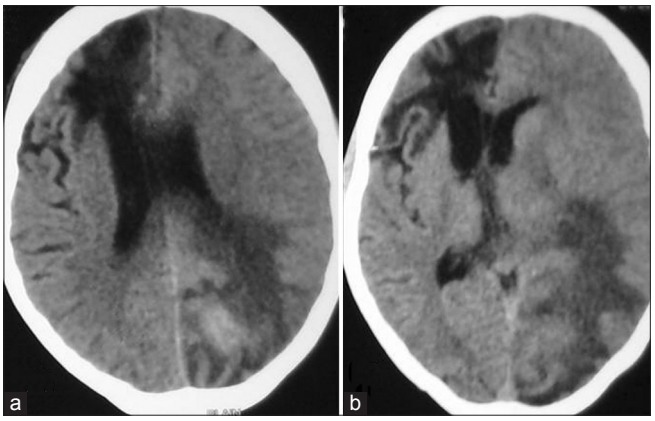

Figure 2: (a and b) CT scan of brain 13 weeks after operation (12 weeks, after initiation of antifungal drug) showing absent of frontal lesion and resoluting of occipital lobe lesion, but there is severe edema in brain in occipital lobe

it is characterized by granulomatous infl ammation and considerable fibrosis, with presence of scanty hyphae, and A. flavus is the primary agent isolated.[11] In contrast, chronic invasive disease is characterized by dense accumulation of hyphae, presence of vascular invasion, sparse inflamatory reaction, and A. fumigatus isolation in patients with diabetes and on corticosteroid treatment.[11] The central nervous system involvement by Aspergillus species is either by hematogenous dissemination or direct inoculation of the agent during surgical procedure or spread from contiguous structures like paranasal sinuses, mastoid, and middle ear. The hematogenous dissemination leads to multiple acute necrotizing purulent lesions commonly in the parietal lobe involving the middle or anterior cerebral artery. In our case, first lesion involved in frontal lobe, then in occipital lobe and dessimination to brain seem to be through blood. Here, lung and paranasal sinus seemed to free of aspergillosis. Contiguous spread occurs from granulomatous lesions in the paranasal sinuses and middle ear leading to the development of chronic granuloma with dense fibrosis in adjacent structures of the brain like the frontal (from paranasal sinuses) or temporal lobe (from middle ear or mastoid).[12] The paranasal source of CNS involvement is common and often results in an orbital apex syndrome or granulomatous disease of the frontal lobe.[12]

The two clinical conditions (rhinocerebral granulomas and intracranial abscess) have different presentations. The former variety occurs commonly in immunocompetent hosts in contrast to intracerebral abscess. Rhinocerebral lesions are usually diagnosed early due to easier sampling from paranasal sinuses and have less mortality. In contrast, intracerebral abscess developed by hematogenous dissemination have high mortality, and are diagnosed late as a clinical surprise because of subtle clinical presentations and absence of any diagnostic characteristics.[10] The clinical diagnosis is difficult to make because the presenting signs and symptoms are non-specific and common for many diseases. There may be

a variety of presenting symptoms such as headache, hemiparesis, dysarthria, lethargy, and seizures with or without fever.[1,13] Aspergillosis has a predilection for invasion of the walls of both small and large blood vessels, resulting in thrombosis and subsequent infarction and hemorrhage.[14] The organism can then spread beyond the vessel walls and form abscesses in the altered brain tissue. Although vascular invasion by Aspergillus species is a common finding, true mycotic aneurysm is rare. Occasionally, intracranial mycotic aneurysms have been reported as a result of direct invasion of the wall of blood vessels either from the luminal or adventitial side.[10,12] Isolated meningitis due to Aspergillus spp. is a rare finding, as also is spinal cord involvement.[10]

The most distinct imaging characteristics at computed tomography or MR imaging are multiple lesions with infarction or hemorrhage in a random distribution due to the angioinvasive nature of the infection.[15] Hemorrhage occurs in approximately 25% of lesions, and contrast material enhancement is usually vague or absent.[16] Low signal intensity is often seen in the periphery of the lesions on T2-weighted MR images. This finding corresponds at least partially to areas of hemorrhage. The zones of low T2 signal intensity is due to the presence of iron, manganese, and magnesium in the fungal concretions.[17] Aspergillus abscesses have been shown to contain a dense population of hyphal elements peripherally with a relative paucity of fungal elements centrally, features that likely contribute to the distinct peripheral T2 hypointensity.[18]

In the present case, the lesions had a central core that was isointense relative to gray matter. Histologic analysis showed this finding to represent coagulative necrosis from vascular occlusion by fungi. The areas of low T2 signal intensity within the core and in a ring around the lesion corresponded histologically to areas of hemorrhage.[1] Polymerase chain reaction can help to diagnose Aspergillosis.[10] But the disease can be confirmed only after histopathological examination or culture of biopsy specimen through a surgical procedure.

The differential diagnosis of multiple brain lesions in an immunocompromised patient includes tuberculosis, lymphoma, metastatic disease, septic emboli, and multiple infarcts.[1] In SLE, patient cerebral aspergillosis can occur due to immunocompromised condition by disease itself, and sometime also by its treating drugs (i.e. steroids, immunosuppressant, dialysis).[6,7] In our case, initially anti-TB therapy was given empirically, as here tuberculosis is common especially in an immunocompromised patient with steroid therapy. But it did not respond rather lesion increased in size and a new lesion developed in occipital lobe.

Though surgery is required to establish diagnosis, but long term medical therapy is the main stay of treatment in cerebral aspergillosis without sinus or orbital involvement. Surgery may be required due to mass effect, compressive effect on vital structures (i.e. cranial nerves), hydrocephalus or lesion not responding to medical therapy.[1,6,7,10] Cerebral aspergillosis with orbital or paranasal sinus involvement, early surgery is needed. Despite the recommendation of Infectious Disease Society of America to use voriconazole as the primary therapy of aspergillosis,[19] and better outcome reported while using voriconazole as compared to amphotericin B,[4] amphotericin B or itraconazole is the first line therapy in the majority of patients with aspergillosis in developing countries possibly due to the higher cost of other anti-Aspergillus effective drugs.[10,20] Use of amphotericin B followed by itraconazole as the mainstay of treatment due to the higher cost of other antifungal agents. Amphotericin B has nephrotoxic side effect in 37.5% cases (nephrotoxicity and renal failure).[21] The response to amphotericin B or itraconazole is good in immunocompetent patients.[10] However, the response in immunosuppressed or neutropenic patients is not encouraging (mortality up to 87.5%).[20] Delay in admission to the hospital, diagnosis, and start of antifungal therapy are the other possible reasons of high mortality in those patients. High mortality (87.5%) was reported in that study in spite of extensive surgery and antifungal therapy in the majority of the patients.[20]

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