Invasive aspergillosis of the brain: Improvement with liposomal amphoterecin B and itraconazole

Sir,

Intracranial aspergillosis is often an extension from paranasal sinuses and is usually resistant to medical or surgical therapy.1,2 We report a case that showed good response to a combination of liposomal amphotericin B and itraconazole after having no response to amphotericin B deoxycholate.

A 43-year-old male presented with fever, diplopia, headache, left focal seizures and weakness on the left half of the body of one month duration and nasal obstruction with difficulty in breathing due to nasoethmoidal mass of two weeks duration. The mass was excised and found to have dichotomously branched septate hyphae with conidial heads suggestive of Aspergillus fumigatus on histopathology. A few years back he had undergone balloon mitral valvotomy for rheumatic mitral stenosis and his cardiac status was stable since then. On admission, he had moderate fever of about 100°F with no lymphadenopathy. On neurological examination patient was drowsy, not responding to verbal commands but localizing the painful stimuli. Proptosis was present on the right side. Neck was supple. There was face-arm-leg weakness (2/5 on MRC scale), spasticity, brisk reflexes and extensor plantar response on the left side. His serology for HIV was negative. The MRI revealed mixed intensity heterogeneous mass lesion on T2 weighted image with thick irregular enhancement on T1 contrast image. The mass extended from the sphenoid sinus to the left frontal and parietal lobe and then through the anterior part of the corpus callosum to the contralateral frontal lobe [Figures 1a and 1b].

Patient was given two six-week courses of amphotericin B deoxycholate. No improvement in symptoms or regression of mass was found on MR imaging. He was then treated with liposomal amphotericin B given intravenously 5 mg/kg per day for six weeks along with oral itraconazole 200 mg daily. There was gradual improvement in his consciousness by third third week and his power improved to 4+ on 0-5 MRC scale with decrease in spasticity. His proptosis improved and he walked without support. Oral itraconazole was continued for four months during which he resumed his office and performed mental work. The MRI showed reduction of lesion to nearly half of its original size on T2 image with only a few specks of enhancing areas seen within the lesion on T1 contrast image [Figures 1c and 1d]. The areas which did not enhance but showed T2 hyperintensities, were presumed largely to be due to healing by gliosis as there was shrinkage of the brain tissue evidenced by prominent cortical sulci.

The mortality is reported to be nearly 100% in immunocompromised patients,3 but some immunocompetent patients have survived this disease with antifungal chemotherapy and surgical resection.4,5 Earlier reports of good response to liposomal amphotericin B4 and itraconazole4,5 prompted us to put our patient on a combination chemotherapy and the response was good as assessed by clinical and imaging modalities. Till a better treatment regimen is found, this combination chemotherapy may be used to treat intracranial aspergillosis with satisfactory outcome.

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Figure 1: T2 weighted (a and c) and T1 weighted contrast (b and d) axial images of the brain showing pre-treatment mixed hypo- and hyperintense mass lesion involving the right fronto-parietal region with spread to opposite frontal lobe (a), which shows thick irregular enhancement (b). Post-treatment images taken six months later showed shrinkage of the mass (c) with only a few small areas of enhancement (d).
An isolated non-dural-based cerebellar aspergilloma in an immunocompetent patient

Sir,

Aspergillus infections in the posterior fossa are either extensions of lesions from the mastoid sinuses or part of multiple fungal masses in the brain.\(^1\,^2\) We report a case of non-dural-based isolated aspergilloma of the cerebellar vermis in an immunocompetent patient. To our knowledge there are only two previous reports of immunocompetent patients with an isolated non-dural-based aspergilloma of the cerebellum.\(^3\,^4\)

A healthy 23-year-old male presented with a one-month history of holo-cranial headache, vomiting and gait ataxia. Nine months earlier he had developed chronic fever with cough and mild wheezing. He was treated with steroids initially for one month, along with anti-tuberculous therapy for nine months with which his symptoms had rapidly resolved. General and systemic examination, including the ear, nose and paranasal sinuses was unremarkable. Neurological examination revealed bilateral papilloedema and cerebellar ataxia.

Enzyme-linked immunosorbert assay for human immunodeficiency virus (HIV) was negative. Chest radiograph showed resolved opacities in the left lower zone with prominent bronchial markings. Magnetic resonance imaging (MRI) of the brain showed a well-defined mass in the cerebellar vermis, iso/hypointense on T1 weighted images and enhancing with gadolinium injection [Figure 1].

Considering the past history of tuberculosis and the radiological features, a diagnosis of tuberculoma was considered. The patient underwent posterior fossa craniectomy and biopsy of the lesion. Histopathological examination revealed a lesion composed of confluent granulomata. Smears from the tissue revealed dichotomously branching fungal hyphae, suggestive of Aspergillus spp. [Figure 2]. The fungal culture grew Aspergillus flavus.

The patient was treated with intravenous amphotericin B and oral itraconazole. Computed tomography revealed no regression in lesion size after treatment with 1.5 g of amphotericin. He thus underwent total excision of the lesion, followed by treatment with 500 mg more of amphotericin B in divided doses. In the postoperative period he developed hydrocephalus and a pseudomeningocele necessitating a ventriculoperitoneal shunt. He required a shunt revision six months later. He was treated with oral itraconazole 200 mg twice a day for one year. One year later, at the time of follow-up, CT scan of the brain showed no recurrence of the mass. However, there was isolated dilatation of the fourth ventricle [Figure 3] for which he refused therapy.