Case Report

Rhinocerebral aspergillosis cripple: High oral doses of Itraconazole was the solution

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Abstract

Two cases of intracranial fungal infection, crippled with the recurrence of the fungal infection even after excisional surgery followed by intravenous Amphotericin B and oral Itraconazole are presented.

Introduction

Fundal and moulds are silent opportunistic invaders in our environment. They rarely invade central nervous system especially in immuno-competent patients. The infection may take the form of parenchymal granuloma or abscess, thrombophlebitis or rarely meningitis.[1-3] In majority of cases, the diagnosis is based on clinical presentation, radiological findings and histopathology, then fungal culture. Treatment of cerebral aspergillosis usually consists of surgical excision followed by administration of intravenous Amphotericin B and then oral anti-fungal drugs for long duration. Even with the more aggressive therapy, most cases of fungal abscess or granuloma are fatal. Two cases of intracranial fungal infection are presented.

Case Report

Case No.1

A 57 years old male with no remarkable medical history presented with altered consciousness for 1 day. He had an ongoing headache, nasal discharge and left nasal blockage on and off for 6 months and right sided hemi paresis for 1 month. CT scan brain revealed an enhancing mass in left frontal lobe with midline shift along with opacification of sinuses bilaterally. The mass was excised and the patient made an uneventful recovery. Histopathology revealed septate fungal hyphae consistent with aspergillosis. Parenteral Amphotericin B was started but had to be stopped because of incapacitating itching, urticaria and renal toxicity. Oral Itraconazole was started at low dose initially as 100mg twice daily and then increased to 200mg twice daily.

During the next 16 months he underwent Caldwell Luc operation for nasal blockade, Ventriculoperitoneal shunt for dilatation of left ventricle and excision of recurrent right frontal lobe fungal granuloma. After two years of last surgery he developed monoplegia of right upper limb due to recurrent left frontal lobe granuloma. After all these crippling recurrences we put him on a high dose of Itraconazole at 16/mg/kg i.e. 400mg b.i.d. which cured him of the disease and at the last follow-up (five years post first presentation), he was not seen to display any residual weakness.

Figure 1. CT scan with contrast showing enhancing left frontal lobe fungal granuloma with midline shift.

Case No.2

A 38 years old male patient had complaint of headache and focal seizures involving right upper and lower limb on and off for one year. According to history available from a referring secondary care hospital, he was admitted with right sided hemiparesis of recent onset and a space occupying lesion was diagnosed on CT scan in left fronto-parietal region which was excised. There was no histopathological evidence regarding the nature of the lesion. After four months of surgery right sided weakness had progressed to hemiplegia with intractable headache. CT scan with contrast revealed ring enhancing lesion in left parietal lobe which was again excised. Histopathology revealed septate fungal hyphae consistent with aspergillosis. He was put on Itraconazole 200mg twice daily. Two months after this surgery he developed aphasia due to which Itraconazole was increased to 400mg twice a day. As

Figure 2. Post- op CT scan after excision of left frontal lobe fungal granuloma.

a result his speech improved and power in right upper and lower limb became 2/5. At present patient is much better with no more disease progression.

Discussion

A myriad of antifungal agents that have been used for fungal infections include Amphotericin B, liposomal Amphotericin B, Itraconazole, flucytocine, voriconazole[4] etc. It is conventional to treat disseminated or localized rhinocerebral fungal infection either in the immunocompetent or immunocompromised host with intravenous Amphotericin B, as the largest therapeutic experience is with this drug and is considered as the gold standard for fungal infection.[5]

Several complications have been reported with the use of Amphotericin B like febrile reactions, hypotension, arrhythmias, renal toxicity and, in addition, it does not cross the blood brain barrier significantly.

Liposomal Amphotericin B is a relatively new preparation that safely allows the attainment of significantly higher tissue level with less toxicity than conventional Amphotericin B as has been studied extensively by Walsh et al.,[6] but is an expensive alternative to Amphotericin B particularly for patients in this part of the world. Itraconazole has been studied extensively in systemic fungal infections but to a lesser extent in cerebral aspergillosis particularly in high doses.[7-9]

In our cases Amphotericin B had to be stopped because of the side effects like itching, urticaria and renal toxicity. In these patients Itraconazole was started at low dose initially (100 mg twice a day) and then maintained for long period at a dose of 200 mg twice daily. Although progression of the disease was slowed but these patients were crippled with recurrence of the fungal infection contrary to the results shown by Giman et al. with low dose Itraconazole.[10] These patients were started on high dose Itraconazole as has been emphasized by Imai and Sanchez.[11,12] High dose Itraconazole was continued for 6 months. Among these patients we did not observe any side effects or drug reactions associated with oral Itraconazole.

It was this high dose Itraconazole that led to a remarkable improvement in neurological deficit in these patients with radiological evidence of cure of the disease. Observations in these patients made us believe that there may be a definite role of high dose Itraconazole in immunocompetent patients affected with rhino-cerebral aspergillosis. Despite very encouraging results in our patients, due to a relative rarity of the condition, a large cohort of such patients is difficult to be assembled and a multicentre study needs to be conducted to establish the role of high dose Itraconazole in cerebral fungal infections.

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