

Rhino-orbital Aspergillosis: Changing Trends in the Management?

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Abstract

Purpose: To analyze the results of oral voriconazole following optimum management protocol for invasive sino-orbital aspergillosis.

Methods: It was a prospective study wherein all immunocompetent cases with a final histopathological diagnosis of invasive sino-orbital aspergillosis were included from a period between Jan 2007 till Dec 2009. All cases were evaluated clinically and radiologically for the condition and were classified into four groups on clinical and radiological basis. All cases were subjected to endonasal endoscopic biopsy and were subjected as per the optimum management protocol. These were then followed up for a period ranging from 6 months to 3 years clinically, endoscopically and radiologically.

Results: There were 15 cases enrolled for the study. There were 10 males and 5 females with age ranging from 14 to 43 years. The most common sign was proptosis. The cases in each group were subjected to the treatment protocol decided for the group. Residual disease was seen in 2 cases (13.34%) and recurrence was seen in 1 case (6.67%). One patient (6.67%) died of disease in our series.

Conclusion: Invasive sino-orbital aspergillosis is associated with significant morbidity and mortality. In our study, voriconazole was found to drastically improve the outcome of sino-orbital aspergillosis.

Keywords: Aspergillosis, Sino-orbital, Voriconazole.

INTRODUCTION

Sino-orbital aspergillosis is usually a localized invasive variant of aspergillosis wherein there is invasion of the sinus mucosa by the fungal hyphae and disease also spreads to the orbit. Invasive aspergillosis is a well-known entity in immunocompromised patients, with the primary risk factors being neutrophil defects and corticosteroid use.¹

Other predisposing factors include HIV infection, diabetes mellitus, use of prosthetic devices or trauma, hematological malignancies, etc.¹ Less than a hundred cases have been reported in english literature of invasive aspergillosis in immunocompetent individuals.^{2,7} The indolent variant of invasive fungal sinusitis presents late and most of the times presenting features are due to the extension of the disease to the adjacent regions. The major manifestations are proptosis, double vision, decreased visual acuity or even loss of vision. The rarer manifestations are epilepsy, loss of higher mental function, recurrent syncopes or headaches due to its spread into the cranial cavity.^{5,6} This entity if inadequately treated can give rise to significant morbidity and can be a cause of mortality as well. The usual cause of mortality is cranial extension of the disease. So the

treatment modalities are undergoing significant changes to decrease the associated morbidity and mortality. We conducted a study on 15 cases of sino-orbital aspergillosis over last three years who were managed aggressively and were followed up for associated morbidity and mortality. We used voriconazole instead of itraconazole and this is the first study from India wherein a large number of patients were studied for the effect of voriconazole.

MATERIALS AND METHODS

This is a prospective study conducted in the department of Otolaryngology, Head and Neck Surgery, Maulana Azad Medical College, New Delhi, India from January 2007 till December 2009 wherein all cases with a histopathological diagnosis of invasive sino-orbital aspergillosis or isolated orbital aspergillosis were enrolled. The cases with allergic variant of the condition were excluded from the study. A detailed otolaryngological and ophthalmological examination was done in all the cases. The cases were evaluated for the immunological status and the cases with immunocompromised state were excluded from this study. All the cases were subjected to fungal serology, fungal smear,



Fig. 1: CT Nose and PNS: Axial cuts showing scan and involvement of posterior ethmoids with intraorbital extension



Fig. 2: CT Nose and PNS: Axial cuts showing scan and involvement of anterior ethmoids with intraorbital extension

culture and the radiology in the form of computed tomography (CT) (Figs 1 and 2) and occasionally magnetic resonance imaging (MRI) in patients with intracranial extension or vision loss. The diagnosis was made after subjecting these cases to endonasal endoscopic biopsy. The cases were managed using the “optimum management protocol” as defined by Gupta et al.

These cases were analyzed for the clinical profile, radiological extent of the disease, management given, associated morbidity, mortality and the final outcome.

RESULTS

There were a total of 15 cases enrolled into the study with 10 males and five females. The age group ranged from 14 years to 43 years with a mean age of 31 years. Most common symptom was proptosis and was seen in all (100%). The clinical profile is detailed in Table 1.

Table 1: Clinical profile of the cases

Symptoms and signs	No. of cases (%)
Proptosis	15 (100%)
Nasal obstruction	6 (40%)
Decreased vision	9 (60%)
Loss of vision	3 (20%)
Diplopia	9 (60%)
Headache	3 (20%)
Telecanthus	6 (40%)
Epiphora	2 (13.34%)
Nasal mass	6 (40%)

Fungal serology was positive in 9 cases (60%). The smear was positive in 10 cases (66.67%). All cases were histologically proven cases for invasive aspergillosis with a tissue invasion of the fungus. Two cases (13.34%) required repeat biopsy as the initial biopsy was negative in these cases.

There were six cases in group 1 and were managed with oral voriconazole and endoscopic endonasal debulking of the disease. All these cases had no residual or recurrent disease on follow-up. There were no associated morbidities post-treatment.

Group 2 had four cases and were managed as per group 1 and had no residual disease but one of the cases had persistent double vision post-treatment. There was no recurrence of the lesion in any of the cases.

Group 3 had 3 cases and were managed by external approach and were given intravenous amphotericin B initially followed by oral voriconazole. There was residual disease in one case. The visual deterioration persisted in two of the cases. There was no mortality.

Group 4 had 2 cases and were managed as per group 3 but craniofacial resection was done. One case died during the course of treatment secondary to vascular invasion. The second case had persistent visual loss.

The results revealed only one mortality (6.67%) and morbidity in the four of the cases (26.67%) in the form of persistent diplopia, persistent decrease in the vision and persistent vision loss.

DISCUSSION

Fungal infestation of the sinuses can either be noninvasive or invasive. Noninvasive infections are either allergic sinusitis or sinonasal fungal ball wherein bony erosion may occur due to decalcification but with no histological evidence of invasion of tissue or bone. Invasive infections can either be localized or fulminant. Localized disease often starts in

the sinuses and spreads to adjacent structures like orbital cavity or cranial cavity through focal bony erosion or even through vessel walls, causing double vision, loss of vision or stroke and death. The fulminant form is characterized by multiple organ involvement.¹ In our series, all patients had localized invasive sino-orbital aspergillosis.

Invasive aspergillosis is a well-known entity in immunocompromised patients, with the primary risk factors being neutrophil defects and corticosteroid use.¹ Other predisposing factors include HIV infection, diabetes mellitus, use of prosthetic devices or trauma, hematological malignancies, etc.¹ Rarely has invasive aspergillus infection been described in immunocompetent patients. In our series we had included only the cases with no immunocompromise after evaluating them.

The diagnosis is established by histopathology. Austin et al,² and Heier et al³ reported patients that required a second biopsy, and there are cases where the diagnosis was made at autopsy⁴. If diagnosis is not made on first biopsy and suspicion is high for the fungal pathology, a second biopsy should be performed. The diagnosis was established after second biopsy in two of our patients.

Fungal serology is a useful aid in establishing the diagnosis but it is positive in only 60% of the cases. It was found to be positive in 60% of our cases as well. The main role lies in the follow-up of these cases when the biopsy and the radiology may be inconclusive but a raised titer four times or more makes it strongly suspicious for either the residual or the recurrent lesion. All cases with the residual or recurrent disease were serologically positive in our series.

In our series, the organisms were all identified as aspergillus flavus whereas in the western countries aspergillus fumigatus is found more often.¹

The disease to adjacent structures like orbital cavity or cranial cavity through focal bony erosion or even through vessel walls, causing compromise of the function in the form of double vision or loss of vision as was seen in our cases and is in accordance with the literature. Most often the sinuses affected were ethmoids (anterior followed by posterior), maxillary sinus and then the sphenoid sinus where the intracranial extension was seen more frequently.

The prognosis of invasive sino-orbital aspergillosis is significantly worse than the noninvasive forms of sinus aspergillosis,^{5,6} so far the literature mentions a survival rate of around 30-67%.⁷ We by following the above mentioned

protocol for the management of this condition achieved a significantly higher survival rate of 93.34% but this may be because of limited number of cases with intracranial extension.

There is no uniformly accepted treatment protocol for such clinical entity. We here in our study followed the protocol given by Gupta et al. Voriconazole was used instead of itraconazole. In limited disease, surgical debridement followed by oral voriconazole resulted in excellent outcome and thus in these cases amphotericin B and its associated morbidity could be avoided. In more extensive disease, radical surgical debridement, amphotericin B followed by voriconazole resulted in better final outcome. We by following the above mentioned protocol could achieve a survival rate of 93.34% highlighting the efficacy of voriconazole.

CONCLUSION

The trends in the management of invasive aspergillosis will continue to change. The better drugs would continue to come for the management but in our study we found that patients managed with voriconazole have a significant survival benefit compared with itraconazole. Hence, we recommend universal usage of this drug for the management of invasive aspergillosis.

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