Case Reports

Successful Treatment of Entomophthoromycosis with Itraconazole

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Entomophthoromycosis is a rare fungal infection involving subcutaneous tissue affecting immunocompetent individuals(l). The disease occurs in tropical belt involving age group 20-60 years; is rarely reported in children below 15 years of age(2,3). The condition is difficult to treat and various drugs have been tried. We report our experience in treating a child for entomophthoromycosis with itraconazole.

Case Report

A 5-year-old previously healthy boy presented with history of low grade fever, weight loss, nasal block, dysphagia to solids and frontal headache for a duration of one month. He also had excessive purulent nasal discharge and breathlessness for last one week.

Physical examination revealed mild malnutrition (weight for age 76% of expected) and pallor. There was facial puffiness and subcutaneous firm, tender, bilateral swellings in submandibular regions extending from the submental region to the angle of mandible. On rhinoscopy, a pale white mass was evident on left side completely obstructing the nasal passage while on the right side a greyish mass covered with mucoid discharge was partially obstructing the right vestibule of nose. Examination of oral cavity showed firm mass measuring 4 x 2 cm over soft palate producing a bulge in the center of the hard palate. No abnormality was detected on systemic examination.

Investigations revealed hemoglobin of 10.9 g/dl and marked leukocytosis (total leukocyte counts 31,300 per mm^3) with predominantly polymorphonuclear response (polymorphs-79%). His renal function test, liver function tests, serum electrolytes were within normal limits. The results of fasting and post prandial blood glucose levels, bone marrow examination, serum immunoglobulin levels and T cell subset counts were within normal limits. HIV serodiagnosis was negative. CT scan of head and nasopharynx revealed a left parapharyngeal mass extending from nasopharynx to the level of epiglottis involving the palate, maxillary sinuses and soft tissue in the neck. There was no intracra-nial extension and no destruction of pterygoid plates. The histopathological examination of biopsy material obtained from the mass showed infiltration of acute and chronic inflammatory cells with

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preponderance of eosinophils *(Fig. 1)*. On hematoxylin and eosin stain, focal granulomatous response was seen around fungal hyphae which were poorly seen. Silver methanamine stain showed a few septate filamentous hyphae of irregular width, and granuloma with fungal hyphae *(Fig. 2)*. *A* diagnosis of *entomophthoromycosis conidiobolae* was made. Fungal cultures could not be done because initial biopsy was taken for a suspected neoplastic mass.

Tracheostomy was done to bypass the airway obstruction. He received fluconazole (5 mg/kg/day), amphotericin B (test dose 0.1 mg/kg, gradually increased to 1 mg/kg/day, anhydrous potassium iodide (1 drop/kg/dose, three times a day) and cotrimoxazole (trimethoprim 8 mg/kg/day in two divided doses by oral route) in succession over a period of 12 weeks but without clinical improvement. After 12 weeks of unsuccessful therapy with various medications, he was started on itraconazole 200 mg/day. All other antifungal medication were stopped. Over the next week there was dramatic improvement with decrease in facial puffiness subsidence of fever and decrease in the size of neck swellings. The child started gaining weight. Itraconazole was continued for next 6 weeks with weekly monitoring of liver function tests and renal function tests. By the end of 6 weeks all the swellings disappeared completely. He continued to remain asymptomatic at follow-up after 18 months.

Discussion

Zygomycosis is a class of fungi which produces infections of respiratory tract and subcutaneous tissues. Within this class are two orders of organisms that are able to produce disease in humans, *i.e., Mucorale* and *Entomophthorale(l)*. Infections due to Entomophthora species have been reported in humans and horses. The cases have been reported from several parts of tropics and subtropics including Nigeria, Ghana, India, Sudan, Uganda and Indonesia(4). The disease presumably develops via inhalation of spore causing sinus disease and subcutaneous infection. It is also called

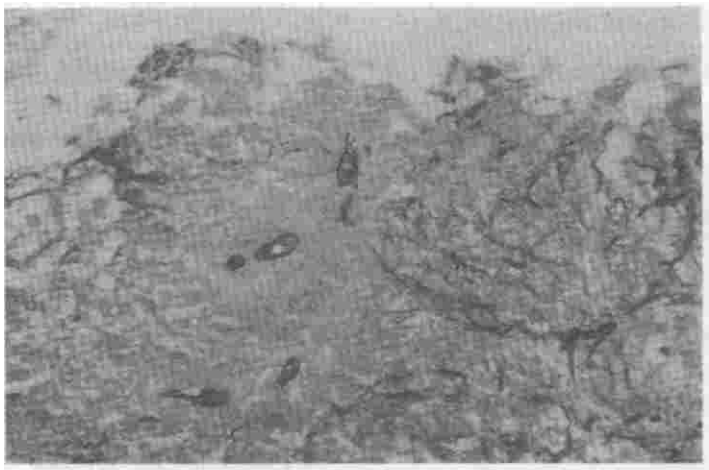

Fig. 1. Silver methanamine preparation showing fungal hyphae lying amidst an acute inflammatory exudate with ill defined granuloma (×10).

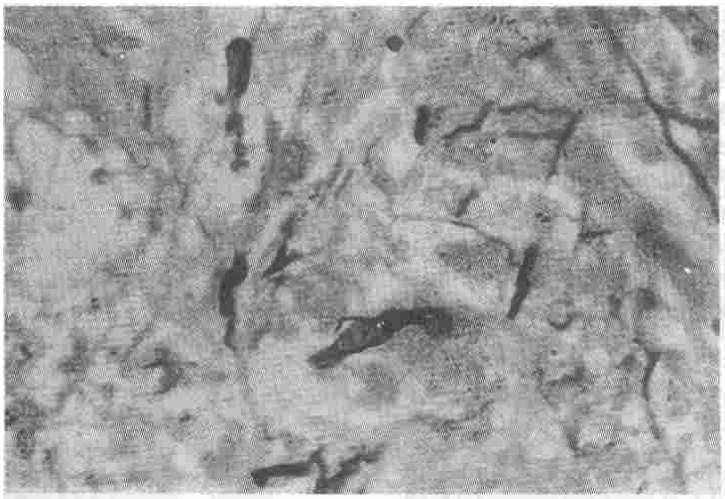

Fig. 2. Silver methanamine preparation showing the septate filaments with irregular width of the wall (×40).

entomophthoromycosis conidiobolae when caused by *Conidiobolus coronatus* and Entomophthoromycosis basidiobolae when cause by *basidiobolus* genera. The classical clinical features include bilateral intranasal swelling eventually progressing to involve paranasal sinuses and soft tissue of the face(3). The entomophthoromycosis basidio-bolus predominantly involve subcutaneous tissue over trunk and extremities(l).

Entomophthoromycosis can often be diagnosed presumptively on the basis of clinical presentation and geographic origin of the patient but usually biopsy showing typical histopathology is required(3). The isolation of fungi on culture from the lesion is difficult and the positivity rate is only 15%(1). Serodiagnosis by immunodiffusion may be available in future(5).

The diagnosis of entomophthoromycosis in our patient was based on the clinical course of illness and typical histopathological findings of thin walled, irregular width, septate hyphae; granuloma formation with absence of vascular invasion. However, there was no eosinophilic sheath around the fungal hyphae (Splendore-Hoeppli phenonmenon) which is described as an important finding. This feature is not pathognomonic of entomophthoromycosis and has been seen in cases of mucormycosis also(3).

The treatment of entomophthoromycosis is difficult. The information available in English literature suggests benefits with the use of cotrimoxazole; ketoconazole, amphotericin B and iodides(6-9). French literature revealed use of itraconazole and fluconazole in adult patients successfully(10,11).

We used itraconazole in our patient considering its high antifungal activity, less propensity to cause side effects, effectiveness in treating cutaneous fungal infections(12,13), and successful use in adults with entomophthoromycosis(10).

After starting itraconazole the child showed marked improvement. We did not see any side effects attributable to itraconazole. A possibility of spontaneous

resolution of entomophthoromycosis has been suggested(14). In our patient a possibility of response due to earlier antifungal therapy or spontaneous resolution is unlikely as the disease progressed even when the child received these antifungals. The resolution began only after starting itraconazole. We conclude that Entomopthoromycosis may affect young children and itraconazole may be one of the effective therapy.

REFERENCES

1. Mortez ML, Grist WJ, Sewell CW. Zygomycosis presenting as nasal polyp in a healthy child. Arch Otolaryngol Head Neck Surg 1987; 113: 550-552.
2. Gugnani HC. Entomophthoromycosis due to conidiobolus. Eur J Epidemiol 1992; 8: 391-396.
3. Wiedermann BL. Zygomycosis. *In:* Text book of Pediatric Infectious Disease, 3rd edn. Eds. Feigin RD, Cherry JD. Philadelphia, W.B. Saunders 1992; pp 1968-1973.
4. Williams AO. Pathology of Phycomycosis due to species Entomophthora and Basidiobolus species. Arch Path 1969; 87: 13-20.
5. Kaufman L, Mendoza L, Standard PG. Immunodiffusion test for serodiagnosing subcutaneous zygomycosis. J Clin Microbiol 1990; 28:1887-1890.
6. Antonelli M, Vignette P, Dahir M, Mohamon S, Favah AA. Entomophthoromycosis due to basidiobolus in Somalia. Trans Royal Soc Trop Med Hyg 1987; 18: 186-187.
7. Davidson T, Sanders R. The surgical correction of residual disfigurement produced by Rhinophycomycosis entomophthorale: A case report. British J Plastic Surg 1985; 38: 97-100.
8. Drouhet E, Dupont B. Laboratory and clinical assessment of ketoconazole in deep seated mycosis. Am J Med 1983; 74: 30-46.
9. Dworzack DL, Pollock AS, Hodges GR, Barnes WG, Agello L, Pahdye A. Zygomycosis of the maxillary sinus and palate caused by *Basidiobolus haptosporus*. Arch Intern Med 1978; 138:1274-1276.
10. Testa J, Vailleeard E, Ravisee P, Dupont B, Gonzalez JP, Georges AJ. Two new cases of rhino entomophthoromycosis diagnosis in the central Africa Republic (French). Bull de la Societ de Patnol, Exohgue et de ses Filialls 1987; 80: 781-791.
11. de Castro e Sourza Filho LG, Nico NM, Salebian A, Heins-Vaccari EM, de Castro LG, Sottom M, *et al.* Entomophthoromicose rhinofacial por conidiobolus coronatus. Registro de um caso tratado com successo pelo fluconazole. Revista do Instituto de Medicina Tropical de Sao Paulo 1992; 40: 483-487.
12. Cauteren HV, Heykants J, Coster RD, Cauwenberga Co. Itraconazole: Pharmacologic studies in animals and humans. Rev Infect Dis 1987; 9: S43-S46.
13. Borelli A. Clinical trial of itraconazole in the treatment of deep mycoses and leishmaniosis. Rev Infect Dis 1987; 9: S57-S63.
14. Taylor GD, Sekhon AS, Tyrrell DLJ, Goldsand G. Rhinofacial zygomycosis caused by Conidiobolus coronatus: A case report including *in vitro* sensitivity to antimycotic agents. Am J Trop Med Hyg 1987; 36: 398-401.