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Maxillary sinus fusariosis in immunocompetent hosts

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Abstract
We report the first known cases of Fusariosis of maxillary sinus with granuloma and oro-antral fistula in two immunocompetent hosts. *Fusarium solani* was demonstrated in the direct microscopic examination and isolated in heavy growth from the biopsy materials. Both these patients were successfully treated with oral ketoconazole (200 mg daily) for three weeks followed by a Caldwell-Luc operation. Ketoconazole was continued for two months post-operatively.

Introduction

Disseminated and invasive fusarium infections have been occasionally reported in immunocompromised hosts (Minor *et al.*, 1989; Schneller *et al.*, 1990) and those with extensive burns (Wheeler *et al.*, 1981). However non-invasive infections of the cornea (Liesegang and Forster, 1980; Vajpayee *et al.*, 1990) and nails (Rebell, 1981) caused by fusarium have been reported in otherwise healthy individuals. To our knowledge there has been only three reports in the literature of invasive fusarium infection in previously healthy adults (Jackle *et al.*, 1983; Nuovo *et al.*, 1988; Hiemenz *et al.*, 1990), all of which were secondary to open or penetrating injuries. Though invasive paranasal sinusitis in normal hosts has been reported (Washburn *et al.*, 1988; Hartwick and Baksakis, 1991; Manning *et al.*, 1991), fusarium species have never been isolated. Our two patients are the first known cases of invasive fusariosis of the maxillary sinus in immunocompetent hosts.

Case reports

Case 1

A 36-year-old male farmer presented with history of pain and a very slowly progressive swelling of the right side of the face and upper part of the jaw for about 15 years, following extraction of the upper last molar tooth. He had an associated history of mucopurulent discharge from the right nasal cavity for three years. There was no history of epistaxis, nasal obstruction, headache, eye, ear, throat or laryngeal complaints. He had no other systemic complaints. He was operated upon twice elsewhere and the lesion was reported as chronic inflammatory granulation tissue. Clinical examination revealed a well built young adult, not acutely ill, with a ill-defined swelling involving the right half of the face extending from the infra-orbital area to the inferior border of the mandible and posteriorly to the pre-auricular area. There was local rise of temperature and tenderness. Examination of the oral cavity showed trismus, a 5 mm oro-antral fistula sublabially and missing teeth on the right half of the jaw. Anterior rhinoscopy revealed frank pus through the antrostomy site in the inferior meatus and a polypoidal mass in the middle meatus on the right side. The left nasal cavity and posterior rhinoscopy was normal. There was no other abnormality clinically detected. Since there was clinical evidence of superadded bacterial infection the patient was started on co-trimoxazole and metronidazole for a week after which a 4 mm rigid nasal endoscopy was done under local anaesthesia. Fleshy granulation tissue was seen filling the right middle meatus area occluding the openings of the frontal, ethmoidal and maxillary sinuses. Similar tissue was also seen in the antrostomy site and the maxillary antrum on the right side. The latter was visualized endoscopically via the oro-antral fistula. The rest of the maxillary antral walls were intact. Biopsy was taken and sent for fungal and mycobacterial cultures. Routine blood investigations including ESR were normal. The fungal culture yielded a heavy growth of fusarium species. The patient was started on oral ketoconazole (200 mg) once a day for three weeks followed by a Caldwell-Luc procedure and debridement.

Case 2

A 31-year-old male farmer presented with history of swelling of the right cheek for one year and right-sided nasal discharge, headache and otalgia for two months. He had no associated history of epistaxis, nasal obstruction, vision complaints, ear discharge, hearing loss, throat or laryngeal complaints. He was operated upon (Caldwell-Luc) elsewhere six months previously and the lesion was reported as chronic granulation tissue. However as his symptoms persisted he was referred to us. He had no other significant systemic complaints or past history. Clinical examination revealed a well built young adult who was not acutely ill. There was an ill-defined swelling with induration limited around the right cheek, obliteration of the adjoining naso-labial fold and a 2 mm oro-antral fistula sublabially. Anterior rhinoscopy showed only mucopurulent discharge in the region of the right middle meatus and posterior rhinoscopy was normal.

The throat, larynx and ears were normal. Other systemic examination was normal. A 4 mm rigid nasal endoscopy revealed a polypoidal mass filling the entire right middle meatus occluding the openings of frontal, ethmoidal, and maxillary sinuses. Other areas were normal. Tissue was taken and sent for mycobacterial and fungus cultures. The initial smear was reported as few weakly staining acid fast bacilli and fungal smear showed *Fusarium solani*. A chest X-ray was normal. Routine blood investigations including ESR were normal. Gastric juice for AFB was negative. Based upon the smear report the patient was started on anti-tuberculous therapy and the cultures were awaited. Bacterial culture was negative and fungal culture grew *Fusarium solani*. The patient was then recalled and no clinical improvement was noted following anti-tuberculous therapy. He was then started on oral ketoconazole (200 mg) once a day. Three weeks of therapy showed a remarkable improvement. This was followed by a further Caldwell-Luc procedure and debridement. On opening the antrum it was noted that the

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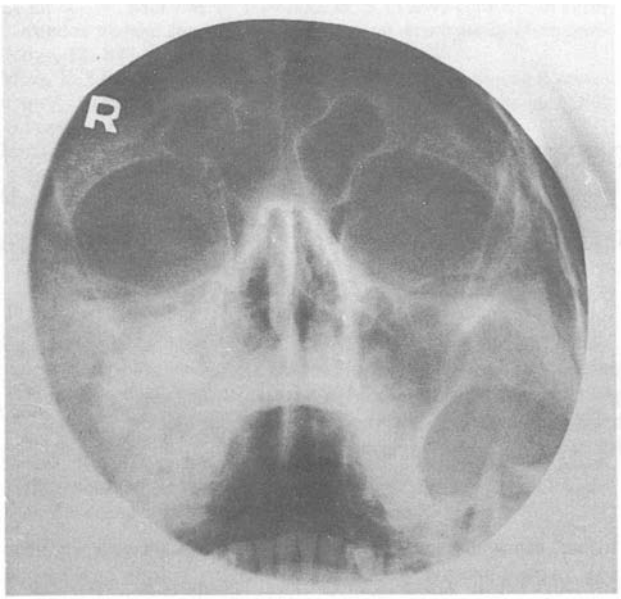

FIG. 1a
Homogenous dense opacity within expanded maxillary antrum with intact walls.

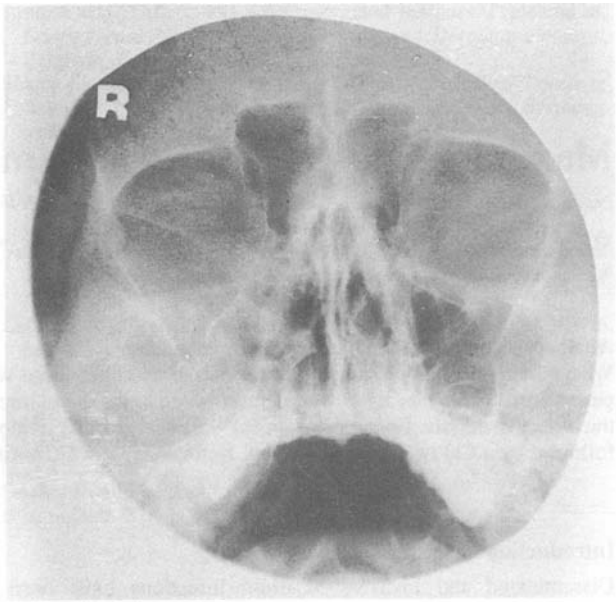

FIG. 2a
Haziness of maxillary antrum with intact walls.

anterior wall and the floor were covered with granulation tissue. The roots of the teeth (premolar and the molars) at the floor were exposed too. All other areas were normal.

Both these patients were on oral ketoconazole for three months post-operatively.

X-rays

Radiographs of the paranasal sinus of the first patient showed a homogeneous dense opacity with ill-defined margins in the right maxillary antrum which was expanded but had an intact roof and floor (Fig. 1a) and in the second case there was haziness of the right maxillary antrum with intact roof, floor and lateral walls (Fig. 2a).

Mycology

Biopsy material from the maxillary antrum and nasal cavity of the two patients was received. A potassium hydroxide (10 per cent) mount of the tissue of Case 1 showed many septate, narrow, branched fungal hyphae with oblong conidia (Fig. 1b). Moderate, septate, narrow, branched fungal hyphae with no spores were seen in case 2 (Fig. 2b), as described by Emmons *et al.* 1977.

The biopsy materials were cultured on two sabouraud dextrose agar plates with (SAB) and without antibiotics (SDA), brain heart infusion agar, beef infusion blood agar with and without antibiotics and a thioglycollate broth. One set of plates was incubated at 37°C and another set at 25°–30°C. The fungal growth appeared after 3–5 days of inoculation. The mature colonies were off-white with a purple tinge. The reverse side of the colonies were purple-brown. Lactophenol- cotton blue of the slide culture in both these patients had numerous macrocoidia and microconidia. The macroconidia were banana shaped, septate with two to four septation and the conidia were arranged diffusely or in slimy masses in both the patients (Figs. 1c & 2c). The microconidia were single to double celled. Rough walled spherical chlamydosphores were also seen in older cultures.

The fungus was identified as *Fusarium solani* as described by Lennette *et al.*, 1980.

Discussion

Fusarium species are common soil saprophytes and plant pathogens *F. solani* has been the most frequently isolated fusarium species from human infections. Non-invasive fusarium infection in otherwise healthy individuals have been reported in

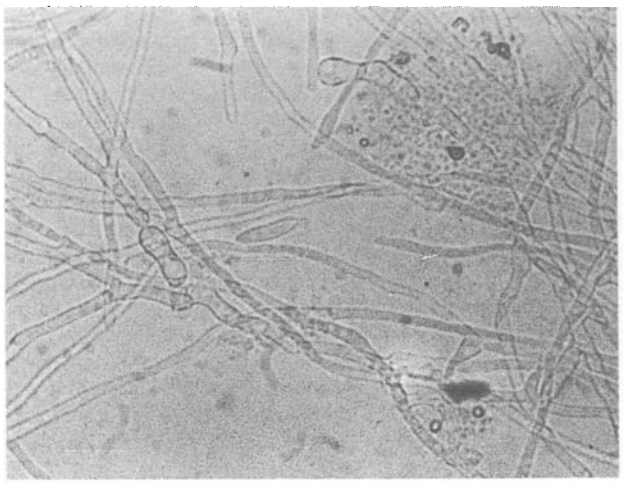

FIG. 1b
Shows many septate branched fungal hyphae with conidia.

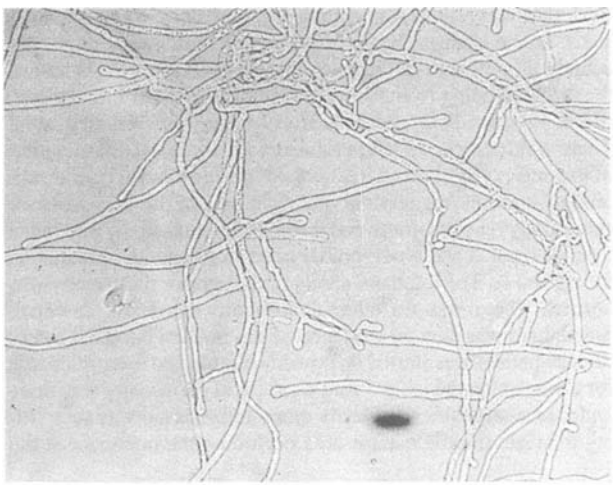

FIG. 2b
Shows moderate septate branched fungal hyphae.

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FIG. 1c
Shows banana shaped macroconidia.

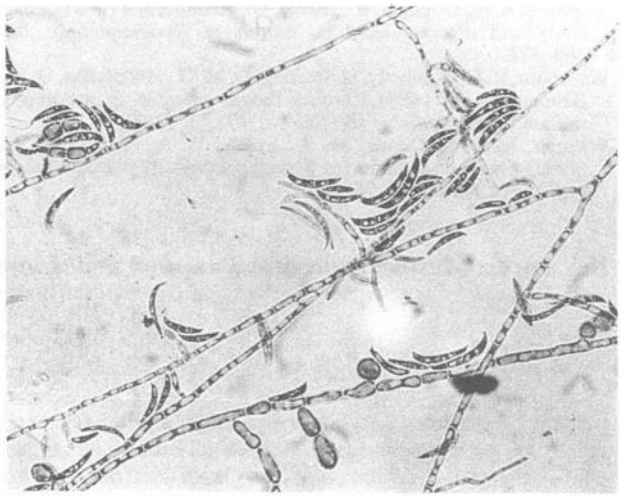

FIG. 2c
Shows banana shaped macro and microconidia with chlamydospores.

the cornea and nails, the largest series being keratomycosis (Liesegang and Forster, 1980; Vajpayee *et al.*, 1990). However only three cases of invasive fusarium infections in previously healthy individuals have been reported in the literature to date (Jackle *et al.*, 1983; Nuovo *et al.*, 1988; Hiemenz *et al.*, 1990). All three were adult males of which two had multiple fractures due to automobile accidents. The first patient developed infection of the second right proximal interphalangeal joint 25 days after the accident and was successively treated with parenteral amphotericin B. The second patient who had undergone several debridements of both lower extremities after the accident developed the infection during the fifth week after hospitalization. He was successfully treated with multiple debridement and topical applications of amphotericin B-soaked dressings. The third patient, who suffered an injury by a sting ray barb on his right hand while he was fishing, developed infection in that site after two weeks even though the embedded barb was surgically removed within five hours of the injury. He was successively treated with debridement and skin grafting in conjunction with oral ketoconazole therapy.

In both our patients, who were otherwise healthy individuals, suspicion of fungal infection was based on the clinical examination and previous history of repeated biopsies being reported as chronic inflammatory granulation tissue. Both of these patients do not recall any traumatic episodes involving contamination with vegetable matter which occurred in cases of mycotic keratitis and has also occurred in the three reported cases of invasive fusarium infections in immunocompetent hosts. The course of infection in both our patients, varying from one to 15 years, reflects that fusarium species may take a longer duration to produce signs and symptoms of infection especially in an immunocompetent host.

The majority of the previous reports (Jackle *et al.*, 1983; Nuovo *et al.*, 1988; Minor *et al.*, 1989) and *in vitro* susceptibility tests (Rotowa *et al.*, 1990) have shown a good response to amphotericin. Unfortunately amphotericin available in India at present is imported and the course of therapy was economically not feasible for both our patients. Ketoconazole was reported successful in one case (Hiemenz *et al.*, 1990) and *in vitro* susceptibility tests have also shown some response to it (Rotowa *et al.*, 1990). Hence these patients were initially started with oral ketoconazole 200 mg daily for three weeks followed by a Caldwell-Luc operation and debridement. The second biopsies of both patients which were sent after the Caldwell-Luc procedure were negative for the fungus. However they were continued on oral ketoconazole for two months following surgery.

Conclusion

The first known cases of invasion fusariosis of the maxillary sinus in two immunocompetent hosts is reported from a tertiary care centre in India. These patients were successfully treated with a combination of anti-fungal therapy and surgical debridement. The importance of suspecting and identifying fungal infection in cases with persisting chronic granulomatous lesions, even if the patients are not immunocompromised, is stressed here. Surgical debridement along with medical therapy is an essential aspect in treatment of maxillary sinus fungal granuloma.

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