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Paranasal sinus aspergillosis

by

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Aspergillus is a fungus of the Ascomycetes class and is world-wide in distribution. It is the commonest fungal infection of the sinuses (Savitskey and Waltner, 1961). However, sinus aspergillosis is an uncommon disease.

Aspergillus fumigatus accounts for 90 per cent of these infections (Miglets *et al.*, 1978), though Aspergillus flavus was responsible for the lesion in all the cases reported by Milosev *et al.* (1969). The pathogenesis of fungal involvement of the sinuses is not fully known. It is believed that, as the spores of aspergilli are inhaled, they settle down in the sinuses, commonly in the ethmoids and the maxillary antra. They become pathogenic when the condition in the sinuses becomes relatively anaerobic. Sometimes they may be introduced into the sinuses during surgical procedures.

This paper describes our experience of nine cases of sinus aspergillosis. The first four cases included in the present series have already been reported elsewhere (Mohandas *et al.*, 1978; Sood *et al.*, 1975).

Illustrative case reports

Case No. 1

S.P.S., a 38-year-old male, was admitted on 18 July 1977 with a history of episodes of nasal obstruction and rhinorrhoea for nearly three years. He also gave a history of swelling over the left maxillary region, and headache for the previous 6 weeks. On examination the swelling was firm and tender. The left eye ball was displaced upwards and there was ptosis of the right eye. An X-ray of the PNS showed opacification with erosion of the left maxillary sinus. An X-ray of the skull was normal. Biopsy from the maxillary sinus revealed an aspergilloma. The patient's level of consciousness deteriorated rapidly and he developed signs of meningitis. Examination of the cerebro-spinal fluid showed 100 lymphocytes/cm^3, total proteins 116 mg/100 ml, and sugar 35 mg/100 ml. He was treated with intravenous amphotericin B therapy. However, he did not recover and ultimately expired.

Case No. 2

V.S., a 58-year-old female, presented to the ENT OPD on 10 February 1975 with complaints of left-sided headache, nasal obstruction and discharge for the previous 36 months. She gave a history of bronchial asthma and was taking steroids. Her general physical examination was normal, but nasal examination revealed the presence of mucoid discharge. An X-ray of the PNS showed haziness of the left maxillary sinus. Repeated antral washings revealed greasy mucopus. However, the washings were negative for fungus on culture. A left Caldwell-Luc operation with antrostomy was performed, and a biopsy showed severe aspergillus infection. The patient continued to have nasal symptoms and she developed a swelling near the medial canthus of the left eye. A later surgical exploration revealed the presence of dark cheesy material involving the lacrimal sac. The biopsy was consistent with aspergillus infection. She was treated intensively with intravenous amphotericin B therapy, in an initial daily dose of 0.5 mg./kg. body weight, added to 450 ml. of 5 per cent dextrose. The dose of the drug was increased to 1 mg./kg. body weight after one week and the treatment was continued for nearly three months, during which she received a total dose of 1,500 mg. of amphotericin B. She improved considerably and her symptoms disappeared.

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Regular recording of the serum electrolytes and blood urea was done during this period. However, there was a recurrence of the lesion 6 months later and she had to be given a second course of amphotericin B therapy. She has since remained free of the disease for 6 years.

Case No. 3

J.C., an 18-year-old female, was admitted to the ENT ward on 14 October 1980 with a history of proptosis of the left eye and rhinorrhoea for the previous 10 months. There was no significant past history. General physical examination was normal, but she had proptosis of the left eye downwards and outwards (Fig. 1). Nasal examination did not reveal any abnormality, and the post nasal space was clear. X-ray of the paranasal sinuses showed opacity of the left maxillary



FIG. 1
Sinus aspergillosis with left proptosis (Case No. 3).

antrum (Fig. 2). X-ray chest was normal. A left Caldwell-Luc operation was carried out, and the sinus mucosa was irregular and darkish in colour. Biopsy revealed a mycotic infection due to aspergillosis. One week later an external ethmoidectomy was performed. A large firm mass was seen occupying almost the whole of the



FIG. 2
X-ray PNS showing haziness of left maxillary sinus and soft tissue mass in left eye (Case No. 3).

medial portion of the orbit, displacing the eye ball laterally. As much of the lesion was excised as possible, while preserving the eye. A small part of the mass which was extending towards the apex of the orbit beyond the posterior ethmoidal cells was left undisturbed. Post-operatively she was treated intensively with amphotericin B for three months, during which she received a total dose of 1,500 mg. of the drug. At the time of discharge from hospital her proptosis had disappeared completely (Fig. 3). There has been no recurrence of the lesion during one-and-a-half year follow up.

The diagnosis in all cases was confirmed by histopathology. The youngest patient in the series was a six-month-old child, whereas the oldest patient was 58 years old (Table I). There were six male and three female patients.

Discussion

Aspergillosis, caused by one or more species of Aspergillus, is an uncommon and ill defined disorder primarily affecting the bronchi, lungs, and external auditory canal and occasionally involving the skin, nails, nose and paranasal sinuses, orbit and meninges.

The Aspergilli are regular inhabitants of the soil and are believed to be widespread in nature.

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FIG. 3
Photograph of the same patient after surgery and amphotericin therapy.

They are common in warm, damp climates. Many species are pathogenic for plants. Birds, especially pigeons and parrots, are particularly susceptible, but some species infect animals and presumably man. It is believed that birds may constitute the medium of exposure (Franks and Guiducci, 1965).

Sinus aspergillosis occurs in two forms: (a) a local process unassociated with any underlying pathology or administration of drugs; and (b) a more common form which is associated with conditions that lower the host resistance or with immuno-suppressive drugs (Young *et al.*, 1970; Meyer *et al.*, 1973; Veress *et al.*, 1973). It is reported that the incidence of fungal infection in the nose and paranasal sinuses has increased because of the use of antibiotics, steroids and other chemotherapeutic agents. However, there was no history of the above factors in eight of our nine patients; only one patient was taking steroids for the treatment of bronchial asthma.

Aspergillosis of the paranasal sinuses has been classified into invasive and non-invasive types (Hora, 1965). The latter type produces features of chronic sinusitis, i.e., rhinorrhoea, nasal obstruction and sinus fullness. X-rays show opacification of the antra without any evidence of bone destruction. The antral washings reveal greasy and darkish material. Cases of the invasive type on the other hand are usually more serious. They often present with a mass involving the orbit, nose and cheek. Pain and blurring of vision may be other symptoms. Features of the invasive type of sinus aspergillosis may simulate those of malignant lesions in this area. X-rays of the sinuses frequently show bony destruction. The clinical features in the nine patients have been summarized in Table I. Except for one (Case No. 6), all our cases belonged to the invasive variety of sinus aspergillosis.

Three patients in the present series had involvement of the brain due to sinus aspergillosis: one case with intra-cranial extension of the disease improved following intensive treatment; the

TABLE I
CLINICAL FEATURES OF SINUS ASPERGILLOSIS

Case no.	Age/sex	Symptoms	Duration of symptoms	Site of lesion
1.	39 yrs F	Pain right side of face and headache	3 months	Sphenoid sinus
2.	34 yrs M	Nasal discharge, headache and vomiting	3 months	Maxillary sinus with intra-cranial involvement
3.	38 yrs M	Nasal discharge, headache and vomiting	40 months	Maxillary sinus with intra-cranial involvement
4.	48 yrs F	Swelling over left cheek and diminution of vision	24 months	Maxillary sinus with intra-cranial involvement
5.	58 yrs M	Nasal discharge, nasal obstruction and headache	36 months	Maxillary sinus and lacrimal sac
6.	50 yrs M	Nasal obstruction with swelling over right side of face	24 months	Maxillary sinus
7.	6 mths M	Proptosis left eye and swelling over left side of face	4 months	Maxillary sinus and orbit
8.	18 yrs F	Proptosis left eye and rhinorrhoea	10 months	Maxillary sinus and orbit
9.	34 yrs M	Swelling over left cheek and proptosis	6 months	Maxillary sinus and orbit

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second case left hospital against medical advice; and the third died despite therapy. The diagnosis of fungal meningitis is based on indirect evidence of antral or systemic infection with pleocytosis and raised protein content in the C.S.F. Direct smear examination of the C.S.F. is more rewarding for the demonstration of the fungus than culture itself (Mohandas *et al.*, 1978). Aspergillus meningitis is rarely encountered; when seen, it is restricted to the base of the brain (Kaufman *et al.*, 1976). Fungal vasculitis or aneurysms are rare (Visudhipan and Bunyatravej, 1973).

The intra-cranial extension of a sinus aspergillus infection may be via the cribriform plate. However, extension of the disease to the orbit may be either via the ethmoids or via the nasolacrimal duct. In one patient with proptosis (Case No. 8), in whom an external ethmoidectomy was carried out, a large firm mass was seen occupying the medial portion of the orbit. A major portion of the mass was excised and the patient subsequently was treated with amphotericin B. The lesion regressed completely. We feel that a small part of the fungal mass can be left behind to preserve the eye and it eventually heals by fibrosis.

One patient with isolated involvement of the sphenoid sinus died despite surgery. Aspergilloma of the frontal sinus has been described by Gupta *et al.*, (1973) and Stevans (1978). However, we have not seen frontal sinus involvement due to aspergillosis in our own patients.

The diagnosis is confirmed by histopathology, which will reveal septate branching hyphae. They are best located in the granulomata, often with marked giant-cell reaction (Fig. 4). Two histological patterns are described (Veress *et al.*, 1973). A proliferative type of lesion is noticed in most cases and is characterized by pseudotubercles in a fibrous tissue stroma, often with thickening of the arterial walls. The second or exudative pathology is seen in a few cases and is characterized by oedematous necrosis. A mixed appearance may also been seen.

Aspergillosis may appear as a localized mass within a thin-walled cavity, as in a chronic granulomatous disease resembling a tuberculous lesion, or as an invasive infection which is characterized by necrosis, haemorrhage and systemic dissemination (Miglets *et al.*, 1978).

A majority of cases in the present series have been treated with local surgery in the form of a Caldwell-Luc operation and antrostomy, in combination with intravenous amphotericin B therapy (Table II). In six cases, the lesion has completely regressed and the symptoms have disappeared. Several authors have reported good results with local surgery and aeration of the sinus (Mcguirt and Harril, 1979; Warder *et al.*, 1975; Iwamoto *et al.*, 1972; Miglets *et al.*, 1978; Milosev *et al.*, 1969; Axelsson *et al.*, 1978). However, it appears from their description that, except for Milosev *et al.*, (1969), probably other authors were dealing with the non-invasive type of sinus aspergillosis. A fatal outcome in two patients in our new series tends to suggest that; first, the invasive variety of sinus aspergillosis may be more common in our country; and secondly, the

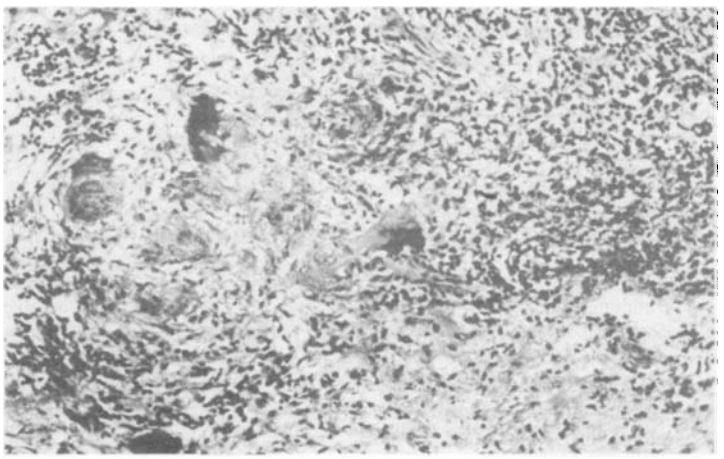


FIG. 4

Microphotograph of histology of aspergillosis, showing a granulomatous response including numerous multinucleated giant cells. Some of the latter contained hyphae of aspergillus in their cytoplasm. A dense mononuclear cell infiltration is also seen. (H&E ×250).

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TABLE II
TREATMENT AND RESULTS

Case no.	Age/sex	Treatment	Results
1.	39 yrs F	Local surgery (exploration of sphenoid sinus)	Died
2.	34 yrs M	Local surgery	Patient was discharged against medical advice
3.	38 yrs M	Local surgery and Amphotericin B therapy	Died due to intracranial extension
4.	48 yrs F	Local surgery and Amphotericin B	Cured
5.	58 yrs M	Local surgery and Amphotericin B therapy	Cured
6.	50 yrs M	Local surgery and Amphotericin B therapy	Cured
7.	6 mths M	Amphotericin B therapy	Cured
8.	18 yrs F	Local surgery and Amphotericin B therapy	Cured
9.	34 yrs M	Local surgery and Amphotericin B	Improved

resistance of patients to invasive mycotic infection is poor.

The precise role of antifungal drugs in the treatment of this condition has not been established. We feel that, whereas local surgery with drainage of the sinus may be adequate in cases of non-invasive sinus aspergillosis, there is a place for amphotericin B (Fungizone) in the treatment of the invasive type of aspergillus infection, in combination with surgery. Of the five patients in the present series who were completely cured, four were treated in this manner; and a child with orbital involvement (Case No. 7) was treated with amphotericin B alone, surgery being limited to taking a biopsy. It is, however, debatable whether the other four cases which received antifungal treatment in combination with surgery would have done as well if they had been treated with surgery alone.

Recurrence of the sinus aspergillosis has not been seen in any patient except one (Case No. 5), in which the lesion recurred within a few months of the initial treatment. She had to be given a second course of amphotericin and has since remained free of the disease for 6 years. All other cases except one (Case No. 9) have been followed for a minimum period of 1 year and have not shown any signs of recurrence. The last mentioned case is still under treatment with amphotericin B after initial surgery, and has shown considerable improvement.

Summary

Nine cases of sinus aspergillosis are presented. The management of the disease is discussed in detail. Emphasis has been placed on the use of intravenous amphotericin B in combination with surgery, in the invasive variety of the disease.

References

AXELSSON, H., CARLSOO, B., WEIBRING, J., and WINBLAND, B. (1978) *Acta Otolaryngologica*, **86:** 303–308.

FRANKS, A. G., and GUIDUCCI, A. (1965) Medical Mycology, edited by R. D. G. Ph. Simons Elesvier Publishing Co: Vol. II. Chapter 35, Pages 384–388.

GUPTA, K. R., UDHAYA KUMAR, B., RAO, P. B., MADHAVAN, M., and DAS GUPTA, L. R. (1973) *Journal of Laryngology and Otology*, **87:** 1007–1011.

HORA, J. F. (1965) *Laryngoscope*, **75:** 768–773.

IWAMOTO, H., KATSURA, M., and FUJIMAKI, T. (1972) *Laryngoscope*, **82:** 903–908.

KAUFMAN, D. M., THAL, L. J., and FARMER, R. M. (1976) *Neurology*, **26:** 484–487.

MCGUIRT, W. F., and HARRIL, J. A. (1979) *Laryngoscope*, **89:** 1593–1568.

MEYER, R. L., YOUNG, L., ARMSTRONG, D., and YU, B. (1973) *American Journal of Medicine*, **54:** 1–15.

MIGLETS, A. W., SAUNDERS, W. H., and AYERS, L. (1978) *Archives of Otolaryngology*, **104:** 47–50.

MILOSEV, B., MAGHOUB, E. L., AAL, O. A., and ELAHASSON, A. M. (1969) *British Journal of Surgery*, **56:** 132–137.

MOHANDAS, S., AHUJA, G. K., SOOD, V. P., and VIRMANI, V. (1978) *Journal of Neurological Sciences*, **38:** 229–231.

SAVITSKEY, S. W., and WALTNER, J. (1961) *Archives of Otolaryngology*, **74:** 695–698.

SOOD, V. P., GOYAL, N. K., and ABROL, B. M. (1973) *Eye, Ear, Nose and Throat Journal*, **54:** 454–456.

STEVANS, M. H. (1978) *Archives of Otolaryngology*, **104:** 153–156.

VERESS, B. *et al.* (1973) *American Journal of Tropical Medicine and Hygeine*, **22:** 765–772.

VISUDHIPAN, P., and BUNYATRAVEJ, S. (1973) *Journal of Neurosurgery*, **38:** 472–476.

WARDER, F. R., CHIKES, P. G., and HUDSON, W. R. (1975) *Archives of Otolaryngology*, **101:** 683–685.

YOUNG, R. C., BENNET, J. B., VOGEL, G. L., and CARBONE, P. P. (1970) *Medicine (Baltimore)*, **49:** 147–173.

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