Short report

Aspergillus granuloma of the trigeminal ganglion

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SUMMARY A patient is described with aspergillus flavus granuloma of the trigeminal ganglion. The patient was effectively treated by surgical excision of most of the infected tissue followed by intensive chemotherapy with amphotericin B and flucytosine.

Aspergillosis in man commonly presents as localised disease of the outer ear, lungs¹ or paranasal sinus.^{2–6} Invasive disease including nervous system involvement occurs less frequently,⁷ often in patients debilitated by neoplastic or collagen disorders,^{8–10} drug addiction,¹¹ alcoholism¹² or immunosuppression.^{13–15}

The CNS becomes infected either by haematogenous spread from the lungs or gastrointestinal tract⁸ or by direct invasion from the paranasal sinuses^{5, 18} or orbit.^{12, 19} The organism may colonise heart valves¹⁶ or major vessels¹⁷ during surgery or may be implanted during neurosurgical procedures.^{20, 21} Frequently, however, there is no clear source of infection.^{22–24} Recently there have been reports of successful treatment of CNS aspergillosis^{18, 20, 25} and we describe a further such case.

Case report

A 38-year-old man from Saudi Arabia presented with an 18 month history of left periorbital headaches and progressive numbness of the left side of the face starting on the upper lip. He had had diplopia on looking to the left for six months. Two years before he had had nasal polyps cleared and bilateral ethmoidectomies for sinusitis. His general health had been good. Physical examination showed a generally fit man with a complete lesion of the left trigeminal nerve involving the motor and all sensory divisions and a left lateral rectus palsy. Routine blood tests and chest radiograph were normal. Tomography of the paranasal sinuses showed post-surgical defects in the ethmoid air cells and marked mucosal thickening in

the left ethmoid and sphenoid sinuses but no frank bony erosion. Computed tomographic (CT) scanning of the head showed a small mass lesion in the region of the left petrous apex extending into the posterior fossa which enhanced following the administration of contrast medium. Angiography showed medial displacement of the left carotid siphon, without narrowing, and normal filling of the cavernous sinus. The cerebrospinal fluid (CSF) contained two lymphocytes/mm³, a protein of 0.56 g/l and a glucose of 3.0 mmol/l. Review of the histological slides prepared from material obtained at the time of ethmoidectomy showed no evidence of fungal infiltration or neoplasia. Exploration by craniotomy revealed a firm tumour replacing the trigeminal ganglion and infiltrating the main trigeminal nerve divisions. The tumour was entirely removed apart from the extensions along the trigeminal nerve divisions.

Pathology The surgical specimen consisted of numerous irregular fragments of firm, grey-yellow tissue. Paraffin sections were stained with haematoxylin and eosin, haematoxylin-van Gieson, PAS and methenamine silver impregnation (Grocott). Histological examination showed the sensory ganglion to be extensively infiltrated and replaced by confluent granulomata (fig 1a). Some ganglion cells were still recognisable but many of them showed advanced degenerative changes. The granulomata consisted of epithelioid cells, lymphocytes, plasma cells, eosinophils and numerous Langhans' type giant cells. Foci of necrosis and microabscesses were scattered in the tissue. Blood vessels were surrounded by the inflammatory infiltrate but they showed little endothelial reaction. Numerous septate hyphae could also be seen, singly or clustered together, and were particularly well seen after silver impregnation (fig 1b). They were of variable length and many of them were branched. An occasional swelling, usually at the end of a hypha, could be seen. On direct immuno-

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(a)

(b)

Fig 1 (a) Most parts of the trigeminal ganglion are replaced by granulomatous tissue that included foreign body giant cells. Occasional ganglion cells can be found (Haematoxylin and eosin $\times 120$). (b) Septate hyphae are present in large numbers inside the granuloma. Some of them are branched while others terminate with a club-like swelling (Methenamine silver impregnation $\times 300$).

Aspergillus granuloma of the trigeminal ganglion

fluorescent staining hyphae were positively labelled with antisera to aspergillus species. Counter-immunoelectrophoresis of concentrated serum and CSF for aspergillus flavus antibody was positive. (Professor D W R MacKenzie, Mycological Reference Laboratory, London School of Hygiene and Tropical Medicine.)

Subsequent management (fig 2) Because tumour removal had been incomplete the patient was treated with amphotericin B and flucytosine. Amphotericin B (up to 1 mg/kg) was given by daily intravenous infusion and into the lumbar theca (up to 0.4 mg twice weekly). Mannitol infusions were used concomitantly to prevent excessive renal impairment.^{26 27} Flucytosine

Discussion

Aspergillosis of the CNS may occasionally manifest as single solid granulomata²³ as in the present case. In disseminated disease, however, it more commonly causes multiple abscesses and necrotic lesions.^{7 28 29} The organism exhibits a predilection for blood vessels sometimes causing subarachnoid haemorrhage from mycotic aneurysms^{17 18 24 30 31} or thrombosis^{25 32} and may also cause a granulomatous leptomeningitis^{22 33} giving rise to a parasellar or orbital apex syndrome.¹⁹ In our patient it seems probable that the

Fig 2 Drug treatment, main clinical events, lumbar cerebrospinal fluid pressure and composition (□—total white cell count/mm³, ■—eosinophil count as a percentage of total) during management of the patient.

was given orally in a dose of 10 g per day. During treatment the patient developed pyrexia which persisted until drug treatment was stopped. Following an initial total dose of 1 g of amphotericin the patient was well and was discharged although the CSF remained active with a preponderance of eosinophils (fig 2). He returned three months later with recurrent headache and mild papilloedema. The lumbar CSF pressure was elevated and the fluid contained 1450 wbc/mm³ of which 78% were eosinophils, the protein being 1.8 g/l (23.9% IgG) and the glucose 2.3 mmol/l. A CT scan showed a new enhancing lesion in the chiasmatic cistern. A further course of amphotericin B and flucytosine was started. The proportion of eosinophils in the CSF steadily declined to 12% of 100 wbc/mm³. Persistent raised intracranial pressure was treated with a course of dexamethasone. When discharged from hospital the patient was well with a normal CSF pressure and CT scan showed that the lesion in the chiasmatic cistern had disappeared.

aspergillus spread from the sphenoid sinus to the region of the trigeminal ganglion possibly along vascular channels. Experimental intranasal administration of aspergillus spores in mice indicates that direct venous vascular spread may occur from the nasal region to the brain and that this spread is enhanced by concomitant steroid administration.³⁴

Treatment of localised sinus disease is by surgical excision of infected tissue and adequate aeration of the sinuses.^{3 4} With invasive aspergillosis amphotericin B and flucytosine in combination remain the drugs of choice³⁵⁻³⁷ and the pharmacokinetics of both drugs are known in considerable detail.^{38 39} During treatment the patient developed a marked CSF pleocytosis composed mainly of eosinophils and had high levels of CSF IgG. The eosinophilia was confined to the

CSF and settled with further chemotherapy suggesting that it did not represent allergy to the therapeutic agents. This cellular reaction may represent a local immune response to aspergillus antigen within the blood brain barrier perhaps analogous to the transient pulmonary infiltrates and peripheral eosinophilia which can occur with this organism.¹ Preliminary results on serial specimens of concentrated CSF from this patient during treatment showed a reduction in specific aspergillus precipitins as the eosinophilia resolved (MacKenzie—personal communication). The episodes of meningism and raised intracranial pressure occurring during treatment (fig 2) are unexplained but could reflect an inflammatory response either secondary to an immune reaction or to the shedding of necrotic material from residual granuloma into the CSF.

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C M Wiles, R S Kocen, L Symon, and F Scaravilli

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