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Different presentations of ophthalmic aspergillosis

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PURPOSE. *Aspergillus species is found worldwide and does not normally cause disease. However, when the immune system is compromised, it can invade many organs and be responsible for severe disease. The authors present cases with both classical and atypical features of ophthalmic aspergillosis.*
METHODS. *Case series of three patients.*
RESULTS. *All patients were female and had a long history of methylprednisolone use. The first two presented with endogenous endophthalmitis. One case was unilateral with a classical presentation of endophthalmitis. The other presented with a very severe bilateral acute retinal necrosis like syndrome. General work-up revealed disseminated disease in both cases. The diagnosis was made by serum immunologic testing in one case and after direct examination and culture from vitrectomy in the other. Despite intense antimycotic therapy, both patients died. The third patient presented with a unilateral progressive painful orbital apex syndrome. An orbital lesion was demonstrated by computed tomography scan and was unresponsive to methylprednisolone. Diagnosis of sino-orbital syndrome was made on biopsy. The lesion responded poorly to different antimycotic therapies, invaded the chiasma, and the patient lost all visual acuity.*
CONCLUSIONS. *This case series illustrates that ophthalmic aspergillosis can present acutely with a devastating intraocular inflammation or more indolently in the setting of sino-orbital aspergillosis. Both forms have a poor visual prognosis and the systemic form is frequently associated with a fatal outcome. (Eur J Ophthalmol 2008; 18: 827-30)*

KEY WORDS. *Mycose, Aspergillus, Endophthalmitis, Acute retinal necrosis, Orbital apex syndrome*

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INTRODUCTION

The saprophytic species Aspergillus is found worldwide. Its high sporulating capacity results in its widespread presence in the air and Aspergillus are thus continuously inhaled by humans. In the immunocompetent host it does not usually lead to important pathologies as they are eliminated by the innate immune system (1). Invasive aspergillosis has thus been extremely rarely described in healthy subjects (2). However, when the immune system and particularly the polymorphonuclear response is impaired, Aspergillus can invade many organs and be responsible for severe disease. Hence, the mortality rate of invasive aspergillosis is between 70% and 90% (3). Ophthalmic presentation can involve different structures and ocular aspergillosis illustrates how the management of

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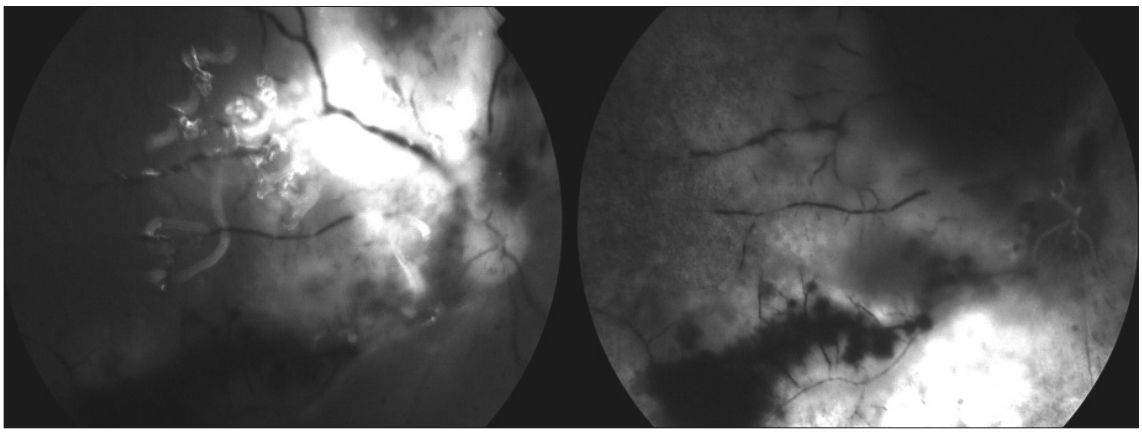

Fig. 1 - *Red-free photograph and middle phase fluorescein angiogram of Case 2 illustrating the absence of perfusion in the right eye (a similar image was found in the left eye).*

Aspergillus infection is difficult (4, 5). In this case series, we describe three patients with two severe forms of ocular aspergillosis: endogenous endophthalmitis and sino-orbital aspergillosis.

Case reports

Case 1

A 49-year-old woman was treated for several months with high doses (0.5 to 1 mg/kg) of methylprednisolone (MPS) for autoimmune hepatitis and presented to our department with decreased vision in the left eye. The patient was slightly disorientated. Visual acuity was hand movement left eye and 10/10 right eye. Slit lamp biomicroscopy showed many inflammatory cells in the anterior segment and a hypopyon. Fundus was not visible. Pulmonary and brain computed tomography (CT) scan demonstrated many multifocal lesions. Her general situation rapidly degraded. Aspergillus galactomannan antigens were detected in her serum (Biorad Platelia Aspergillus EIA) and she was treated with voriconazole and amphotericin B. Intravitreal injection of amphotericin B was also given. However, the situation continued to degrade and the patient died 1 month later.

Case 2

A 36-year-old woman presented to our consultation for sudden and total loss of vision in both eyes. She had been treated for several months with high dose (0.5 to 1 mg/kg) MPS for graft versus host disease in the setting of acute myeloid leukemia. Vision was no light perception in both eyes. Slit lamp biomicroscopy showed an intense inflammatory reaction in the anterior chamber and the vitreous of both eyes. Fundus was barely visible but large white lesions with hemorrhages could be seen all around the fundus. Acyclovir was given systemically and Foscavir intravitreally. Polymerase chain reaction from anterior chamber liquid was negative for herpes virus and toxoplasmosis. A systemic workup revealed multiple brain lesions compatible with the diagnosis of Aspergillus or toxoplasmic abscesses. Vitrectomy was performed bilaterally. Direct examination and culture demonstrated the presence of *Aspergillus fumigatus*. Fundus examination showed a pale retina with large lesions around the optic nerve and many hemorrhages. No retinal perfusion was found during fluorescein angiogram (Fig. 1). Despite systemic treatment with voriconazole the patient died.

Case 3

A 54-year-old woman with a history of systemic sarcoidosis and years of MPS treatment was referred for acute loss of vision in the right eye. Vision was limited to light perception. There were no inflammatory cells in the anterior chamber or vitritis but an important right optic disc edema. Magnetic resonance imaging (MRI) showed an ill-defined lesion at the level of the right optic nerve. MPS, azathioprine, and cyclosporine were given. After a short improvement the clinical picture worsened and she developed a severe hemicranial pain. The right optic nerve became atrophic and visual function was lost. MRI demonstrated an extension of the lesion. A repeated biopsy demonstrated the presence of *A fumigatus*. Immunosuppression was progressively stopped and intense antifungal treatment started. However, 1 month later the patient

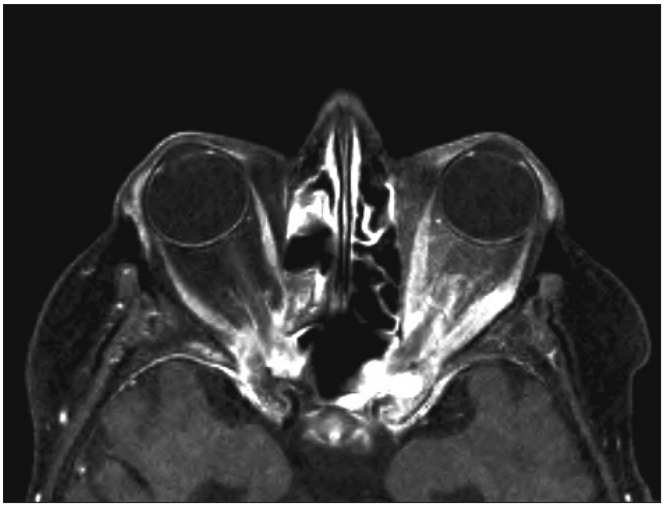

Fig. 2 - *T1-weighted magnetic resonance imaging with gadolinium and fat suppression demonstrating lesions in the sphenoid and ethmoid sinus with extension in both orbital apex.*

complained of a drop of vision in her left eye. Visual acuity was no light perception and 5/10. Slit lamp biomicroscopy was normal, but fundus examination showed right optic nerve atrophy and a left optic nerve edema. MRI showed the presence of a new lesion in the left orbital apex while the lesion of the right orbit was stable (Fig. 2). The situation was not controlled with antimycotic treatment and the patient progressively lost the vision of her left eye.

DISCUSSION

Aspergillus can infect different parts of the eye and can cause conjunctivitis, scleritis, keratitis, canaliculitis, endophthalmitis, and orbital infection (5). Our small case series illustrates how Aspergillus infection can be devastating.

Fungal endophthalmitis represents approximately 60% of all endogenous endophthalmitis and is generally due to Candida rather than Aspergillus species. Aspergillus endophthalmitis is thus a relatively infrequent disease but has distinctive clinical features. As in our cases, it is generally seen in individuals who received immunosuppressive agents for autoimmune diseases or organ transplantation but can also occur in patients with valvular cardiac surgery. Clinical presentation can be fairly unspecific but Aspergillus endophthalmitis can rarely mimic a fulminant retinal necrosis. Pathologic analysis has demonstrated that this funduscopic aspect represents the invasion of the retinal vessels by the fungus (6). The terrible presentation of our second case can be explained by this vascular tropism. Hence, the sudden blindness and the absence of perfusion of the retinal vessels, demonstrated during fluorescein angiography, suggest that the fungus has penetrated into the eyes through the central retinal arteries and occluded them. The last main characteristic of endogenous aspergillosis, also found in our small case series, is its high rate of associated mortality.

Aspergillus species are the most common fungal contaminants of the sinuses and in some circumstances can give rise to sino-orbital aspergillosis which can be noninvasive or invasive. Noninvasive sino-orbital aspergillosis can be in the form of either allergic sinusitis or sinonasal fungal ball. No invasion of tissue occurs in those forms. In contrast, invasive forms are defined by the spreading of the infection to adjacent structures through bone and vessels erosion. Invasive sino-orbital aspergillosis is generally found in immunocompromised patients, but as in our case can also occur in immunocompetent individuals (7). Orbital aspergillosis has a wide variety of presentation and its diagnosis requires a high index of suspicion. Hence many infectious and noninfectious diseases can present as a progressive orbital apex syndrome. However, a key element feature seems to be a persistent and unilateral pain. Unfortunately, resistance to systemic and local treatment is often the rule and the prognosis is poor.

Our cases illustrate that ophthalmic aspergillosis can present acutely with a devastating intraocular inflammation or more indolently in the setting of sino-orbital aspergillosis. Both forms have a poor visual prognosis and the systemic one is frequently associated with a fatal outcome.

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