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Case report/Cas clinique

First endogenous fungal endophthalmitis due to *Fusarium dimerum*: A severe eye infection contracted during induction chemotherapy for acute leukemia

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INFO ARTICLE

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ABSTRACT

Endophthalmitis is a rare infection of the vitreous and/or aqueous. It can be bacterial or fungal. Exogenous endophthalmitis is the most common form and results from direct inoculation of a pathogen after eye surgery or penetrating trauma. Endophthalmitis can also be endogenous, secondary to disseminated infection. Fungal endophthalmitis is associated with poor prognosis and treatment is difficult given the low penetration of most of the antifungal agents available and the emergence of resistant filamentous fungi like *Fusarium*. To our knowledge, we describe the first endogenous fungal endophthalmitis due to *Fusarium dimerum*, a ubiquitous pathogen found in soil and plants. A 71-year-old woman, diagnosed with acute myeloid leukemia, was hospitalized for surveillance after induction chemotherapy. Prophylaxis by antibiotics and posaconazole was ongoing when she complained of pain and decreased vision in the left eye. A voluminous chorioretinal abscess developed and after multiple sterile aqueous humour samples, only vitrectomy allowed diagnosis with fungal hyphae seen on May-Grünwald Giemsa stained smear and positive cultures. The fungus was identified as *Fusarium dimerum*. The treatment, that included intravitreal injections of voriconazole and amphotericin B associated with systemic administration of voriconazole, allowed complete control of the infection. The source of this infection could not be confirmed despite the discovery of several possible infection sites including a periungual whitlow on the left hand and a lesion on a nail, from which samples were negative in microbiology laboratories. Unfortunately, damages of the retina were too important and the patient did not recover sight of her left eye.

Introduction

Endophthalmitis is a rare and readily sight-threatening infection of the vitreous and/or aqueous. Exogenous endophthalmitis is the most common form and results from direct inoculation of a pathogen after eye surgery or penetrating trauma for instance [1]. It can also be endogenous, frequently in intravenous drug users and immunocompromised patients with predisposing factors such as organ transplantation, haematologic malignancies, autoimmune disorders or HIV infection [2–5]. Germs involved are mainly bacteria or more rarely fungi, associated with poorer prognosis [3,6]. Endophthalmitis due to *Fusarium* are uncommon. To our knowledge, no case of endogenous endophthalmitis due to *Fusarium dimerum* was reported in the literature.

Report

A 71-year-old woman diagnosed with acute myeloid leukemia was hospitalized in the department of Oncology-Haematology for induction chemotherapy (idarubicin, cytarabine) and given broad-spectrum antibacterial and antifungal (posaconazole, 300 mg once daily) prophylaxis. Three and a half weeks later, during the expected phase of aplasia following induction, the patient complained of pain and decreased vision in the left eye. On the third day of symptoms, visual acuity was 20/400 and the fundus examination showed a macular chorioretinal abscess surrounded

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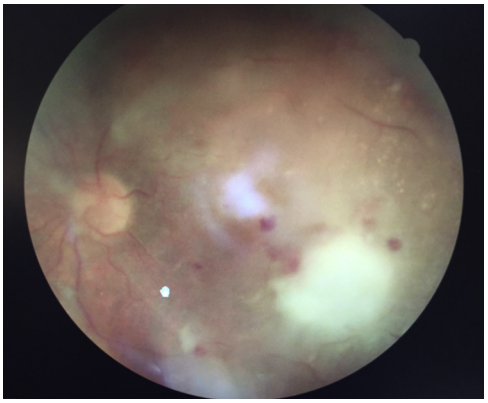

Fig. 1. Fundus of the left eye at day 3 of visual loss, showing a dense vitreous haze, a white mass localized in the inferior macular area with blurred edges, surrounded by deep retinal hemorrhage. There is also a diffuse occlusive arterial vasculitis, predominant in the region of the abscess.

by hemorrhages and vasculitis (Fig. 1). Then, a dense vitreous haze quickly prevented further examination of the fundus and the patient examination revealed only light perception and visual hallucinations on the seventh day after the onset of symptoms. At this stage, we suspected viral retinal necrosis and bacterial endogenous endophthalmitis. Virological, bacteriological and mycological examinations of five successive anterior chamber samples (obtained on day 3, 5, 7, 8 and 9) were negative. Empirical treatment by intravitreal injections of vancomycin, ceftazidime and ganciclovir was initiated. Serological tests for herpes viruses, toxoplasmosis and syphilis were negative. The Aspergillus galactomannan antigenaemia was also negative (Platelia Aspergillus antigen kit®, Bio-rad, Marnes-la-Coquette, France). On day 15, a periungual whitlow was discovered on the third finger of the left hand, suggesting endocarditis with Osler's felon. The echocardiography performed was normal and the blood culture bottles containing a special media for bacteria, fungi/yeasts and mycobacteria (BacT/ALERT®, bioMérieux, Marcy l'Etoile, France) were negative. The whitlow was surgically treated and bacteriological examination of the pus was negative. After this episode and by questioning the patient, she described symptoms compatible with early paronychia that started about a week before the onset of ocular symptoms. Besides, one month after that, the nail of the same finger was thick and unstuck, suggestive of an onychomycosis, but the mycological analysis (microscopic examination and culture) was negative. It is important to note that the patient never presented pulmonary involvement (no abnormality on the chest-abdomen-pelvis CT-scan) or skin necrotic lesions which might be suggestive of disseminated fusariosis.

The evolution of the patient was bad despite the end of the drug-induced myelosuppression. Eye examination revealed hypopyon and the appearance of a cyclitic membrane on the lens, witness of the beginning of cataract. Moreover, daily ocular ultrasound controls showed persistence of the retinal abscess and major vitreous inflammation.

Twenty-five days after onset of symptoms, the patient's vision was limited to light perception. Because of the clinical worsening, a diagnostic vitrectomy was performed, associated with cataract surgery (without implantation). No vitreous needle aspirate had been performed before this date so the vitreous body was sampled for bacteriology, virology, mycology, parasitology and haematological cytology to anticipate as many differential diagnosis as possible. Besides the voluminous abscess seen previously, the peroperative aspect of the fundus showed many whitish retinal spots with presence of diffuse occlusive vasculitis, suggesting fungal infection. Peroperative intravitreal injections of amphotericin B, vancomycin and ceftazidime were performed and intravenous therapy with voriconazole was initiated (loading dose of 2 × 400 mg the first day followed by 200 mg twice daily).

The cytological examination of the vitreous sample showed presence of septate hyphae on May-Grünwald Giemsa stained smear (Fig. 2). The culture on Sabouraud agar was positive. The colonies grew slowly and were deep apricot coloured after ten days at 28 °C (Fig. 3). The microscopic examination of the culture showed septate hyaline hyphae and conidiophores loosely branched with short phialides (10–18 × 4–5 μm). Typical macroconidia (5–23 × 2–4 μm) were strongly curved and pointed at the apex, mostly one to three-septate (Fig. 4). There was no microconidia. The fungus was identified as *Fusarium dimerum* with MALDI-TOF Mass Spectrometry (Bruker, Wissembourg, France).

The Minimum Inhibitory Concentrations (MICs) (Etest®, bioMérieux, Marcy l'Etoile, France) were 0.38 μg/ml for voriconazole and 3 μg/ml for posaconazole. As there is no clinical breakpoints to interpret the MICs of *Fusarium* spp., we can only see that it is a low value for voriconazole and a noticeably higher one for posaconazole. These results could explain why endophthalmitis developed in spite of antifungal prophylaxis. Intravenous administration of voriconazole was stopped after 10 days and voriconazole per os was started (200 mg twice daily) as well as voriconazole eye drops (eight times daily). The patient received three more antifungal intravitreal injections, one of amphotericin B and two of voriconazole.

Treatment helped to completely stop the infection. During the follow-up, the patient presented a clinical improvement with the disappearance of the hypopyon and the slow re-establishment of the transparency of the vitreous. Although, a PET scan was

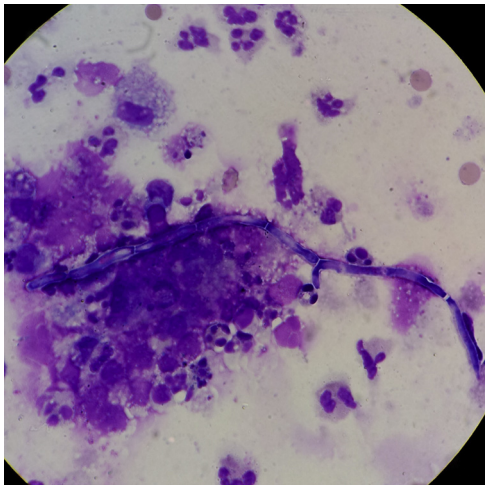

Fig. 2. Fungal septate hyphae in vitreous humour sample (May-Grünwald Giemsa, ×1000).

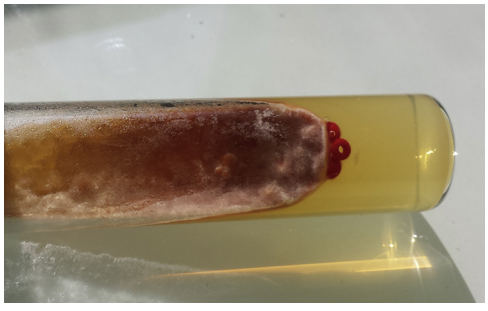

Fig. 3. Culture on Sabouraud agar after 10 days.

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