

Two rare cases of *Acremonium* acute endophthalmitis after cataract surgery in a tertiary care hospital

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SUMMARY

This report describes two cases of *Acremonium* sp. endophthalmitis, occurring in two patients who underwent cataract surgery on the same day in the same operating room of our hospital ophthalmology clinic. Diagnosis of fungal endophthalmitis was established by the repeated isolation of the same fungal agent from vitreous washing, aqueous fluid and intraocular lens samples and by its identification on the basis of morphological and molecular features. The cases reported in this study emphasize the need for clinical microbiology laboratories to be prepared to face the diagnosis of uncommon infectious diseases such as exogenous fungal endophthalmitis by *Acremonium*, and to enhance the awareness of surgeons and clinicians of this occurrence.

KEY WORDS: *Acremonium* sp., Cataract surgery, Endophthalmitis.

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INTRODUCTION

Exogenous endophthalmitis is one of the most vision-threatening complications of cataract surgery followed by placement of a prosthetic lens. Typically it is caused by the perioperative introduction of microbial organisms (mainly coagulase-negative staphylococci and *Propionibacterium acnes*) into the eye (Benz *et al.*, 2004; Han *et al.*, 1996; Kunimoto *et al.*, 1999). Mycotic post-surgical endophthalmitis is a rather unusual disease: *Candida albicans*, *Aspergillus* sp., and *Fusarium* sp. are the most frequently isolated or-

ganisms in the fungal cases (Anand *et al.*, 2000; Benz *et al.*, 2004). However *Acremonium* sp. Has also been rarely reported as a cause of post-cataract surgery endophthalmitis (Joe *et al.*, 2010).

The present report describes two rare cases of *Acremonium* endophthalmitis occurring after cataract surgery and intraocular lens (IOL) implantation, with the aim of enhancing the awareness of surgeons and clinicians on the possibility of this risk.

CASE REPORT

Case 1

A 75-year-old man, treated with anticoagulant, antiarrhythmic and antihypertensive drugs for dilated cardiomyopathy, underwent phacoemulsification and IOL implantation in his left eye on December 2010 at the ophthalmologic clinic of the University Hospital of Parma. Two weeks after surgery the patient showed signs and symp-

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toms of post-surgical endophthalmitis with decreased visual acuity and pain. On January 2011 the patient was subjected to 23 gauge needle (23 G) vitrectomy for a suspicion of septic endophthalmitis and topical antibiotics and corticosteroids were administered. After 10 days of this therapy the clinical situation had ostensibly worsened with intense conjunctival hyperemia, corneal edema, ipopyon (2 mm), Tyndall ++ and eye fundus unsearchable. Because biomicroscopic and clinical appearance continued to deteriorate, IOL and capsular remnants were removed. Microbiological cultures, performed on vitreous washing, aqueous fluid and intraocular lens samples using conventional methods for bacteria and fungi, were negative for bacteria. On the other hand, moulds with similar macroscopic

and microscopic features were isolated from all the samples on Sabouraud dextrose agar (SDA) (Figure 1A, B). All colonies, grown within 5-7 days, were white with a colourless reverse, smooth, compact and moist at first, becoming powdery with age (Figure 1A). The vegetative hyphae were hyaline and septate, very fine and narrow; the conidiophores were simple, slender presenting erect phialides arising from vegetative hyphae. The phialides showed tapered apices and conidia were ellipsoidal to short-cylindrical, 1-celled, hyaline and often accumulating in slimy heads (Figure 1B). While no macroconidia were observed, initial observations nevertheless suggested either *Acremonium* or *Fusarium* genus. However, *Fusarium* sp. grows faster and has colonies with a characteristic fluffy appearance.

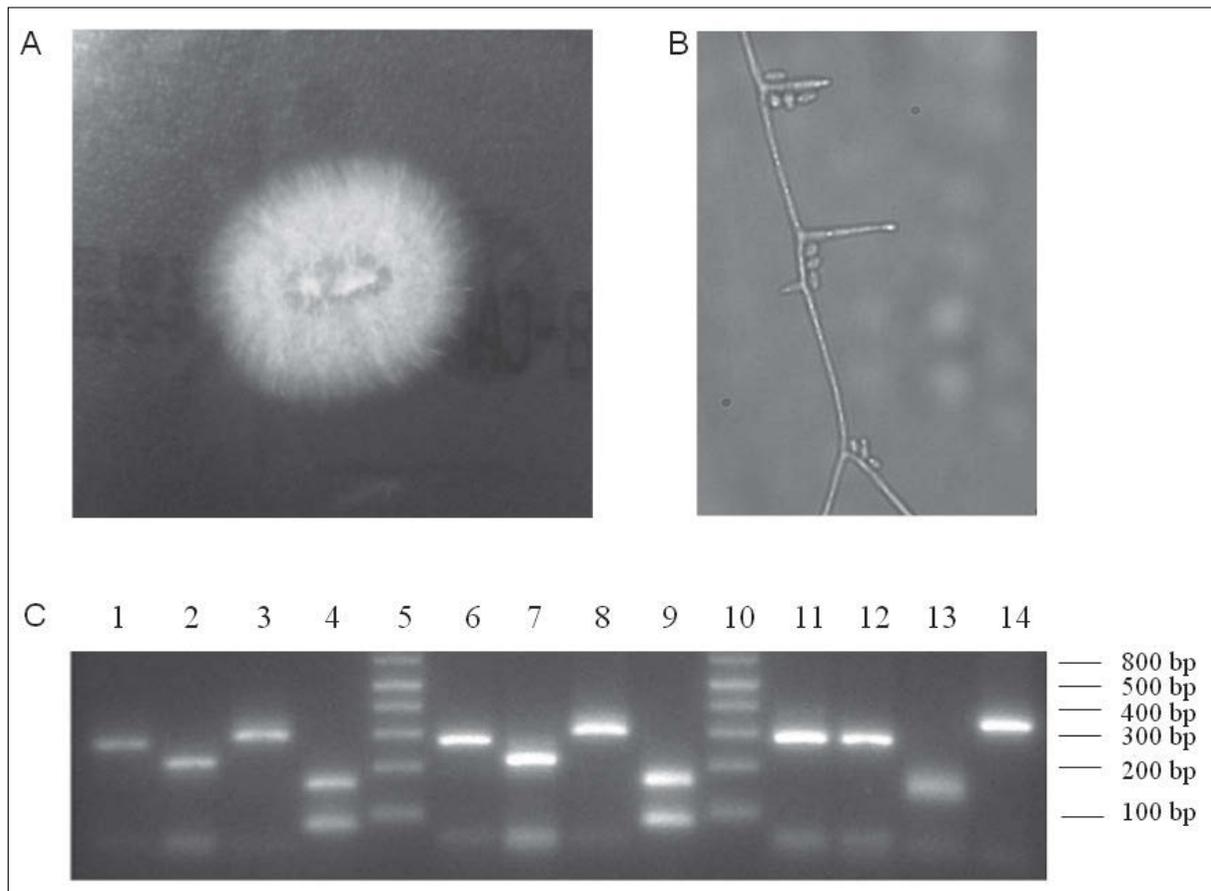


FIGURE 1 - A) Colony grown for 7 days on SDA - Obverse. B) Microscopic observation of slide culture (hyphae with phialides and conidia; magnification $\times 1,000$). C) Single digestion of 5.8S/ITS2 rDNA amplification products. Lane 1-4/6-9/11-14: Digestion of rDNA amplified fragment from aqueous fluid belonging to case 1 and to case 2 and *Acremonium strictum* strain, respectively, with *Hin*I (1, 6 and 11), *Taq*I (2, 7 and 12), *Sau*3 AI (3, 8 and 13); *Msp*I (4, 9 and 14); Lane 5 and 10: 1 Kb Plus DNA ladder (Invitrogen, Italy).

Therefore, moulds were macroscopically and microscopically identified as *Acremonium sp.*

Case 2

A 63-year-old diabetic woman, treated with oral hypoglycemic drugs, underwent surgery for left-sided cataract on the same day and in the same operating room as the patient described in case 1. The patient was referred to the ophthalmologic clinic approximately three weeks after surgery with the same signs and symptoms presented by the patient of case 1: the patient began to experience discomfort and loss of vision, intense conjunctival hyperemia, corneal edema, ipopyon (2 mm), Tyndall ++ and fundus unsearchable. The patient was urgently subjected to 23 G vitrectomy for septic endophthalmitis and treatment with topical antibiotics and corticosteroids was started. The microbiological culture performed on aqueous fluid showed a hyaline mould with macroscopic and microscopic features similar to that identified from the first patient. Voriconazole susceptibility testing for *Acremonium sp.* was not performed in both cases 1 and 2.

For a better evaluation of the reported cases, an RFLP-PCR assay was carried out: DNA for molecular analysis was extracted from moulds grown on SDA for 5 days as previously described (Calderaro *et al.*, 2007). Purified DNA was used for amplification of the ribosomal DNA 5.8S/ITS2 regions, using the universal fungal primer set ITS3 and ITS4 (Borazjani *et al.*, 1998). The enzymatic digestion of the amplicons, performed with *HinfI*, *TaqI*, *Sau3AI* and *MspI* (Figure 1C), showed the same restriction patterns for both the clinical samples analyzed.

Amplicons sequences, compared to DNA sequences in the BLAST alignment program of the Genbank database, confirmed that the fungal species implicated in the endophthalmitis cases was the same in case 1 and in case 2 and showed 100% identity with *Acremonium sp.* J-11 (accession no. HM535388.1).

DISCUSSION

Endophthalmitis secondary to cataract surgery is a rare but serious condition affecting vision. Previous studies have shown that fungi are responsible for 8.6-18.6% of all post-operative in-

fectious endophthalmitis cases (Anand *et al.*, 2000; Benz *et al.*, 2004; Kunimoto *et al.*, 1999). In particular, *Candida albicans* is implicated in endogenous endophthalmitis that usually occurs secondary to dissemination of organisms from a distant focus to the eye via blood: 2-15% of all endophthalmitis cases are estimated to occur in this way (Caldwell *et al.*, 2009; Schiedler *et al.*, 2004; Sallam *et al.*, 2006). On the other hand, *Aspergillus sp.* and *Fusarium sp.* are responsible for exogenous fungal endophthalmitis (Wykoff *et al.*, 2008) that is known to occur in a variety of clinical settings including contiguous spread of fungal keratitis, after penetrating keratoplasty, after retinal detachment surgery, with intraocular inoculations from irrigation solutions or infect IOL implantation and air conditioning systems, mainly during construction activities in hospitals (Fridkin *et al.*, 1996; Narang *et al.*, 2001).

Herein two cases of *Acremonium* endophthalmitis are described for the first time at the tertiary care University Hospital of Parma. *Acremonium* is a large fungal genus that comprises approximately 150 species, most of them being saprophytes in soil and pathogens of plants, insects and other fungi. Some species are considered opportunist of humans and other mammals (de Hoog *et al.*, 2000; Guarro *et al.*, 1997). Infections in humans develop following traumatic inoculation of the fungus, with mycetoma (Geyer *et al.*, 2006) and keratitis (Read *et al.*, 2000) being the most common. Locally invasive infections such as osteomyelitis (Keynan *et al.*, 2007), sinusitis (Durbec *et al.*, 2011), arthritis (Buchler *et al.*, 2003), peritonitis (Khan *et al.*, 2011; Sener *et al.*, 2008) are described.

The initial symptoms of *Acremonium* endophthalmitis are similar to those of most delayed-onset fungal endophthalmitis, including mild pain, redness, floaters, and slightly decreased visual acuity (Fridkin *et al.*, 1996; Scott *et al.*, 2005; Vescia *et al.*, 2002).

The diagnosis of fungal endophthalmitis in the reported cases was established by the demonstration of the fungus in the intraocular fluid samples of the patients. This was carried out by traditional microbiological methods for fungal agents. Because *Acremonium* species are morphologically very similar to one another and at best can only be distinguished on the basis of subtle differences, making their identification diffi-

cult, we reported the isolated strains as *Acremonium sp.*

Molecular methods application was essential for a better evaluation of the reported cases. The major difficulty encountered when using the molecular identification of *Acremonium* species lies in the target used: the nuclear 5.8S and internal transcribed spacer (ITS2) regions of the ribosomal DNA are too conserved to allow a species differentiation. However, the fact that the RFLP analysis showed a restriction pattern identical for both the fungal strains isolated from the two patients but different from that of *Acremonium strictum* control strain, confirmed that the fungal agent involved in both cases was likely the same as demonstrated also by sequence analysis of the amplicons.

Previous studies have shown that exogenous fungal ocular infection has a long latent period, lasting for weeks, even months after intraocular inoculation with a mean latent period of 7 weeks (Narang *et al.*, 2001; Pflugfelder *et al.*, 1988) and do not respond to the usual antimicrobial therapy. The time interval between cataract surgery and endophthalmitis ranged, in our cases, from 14 days and 21 days: the early presentation of clinical signs suggests that a large amount of inoculum was introduced at the time of the surgery. As the two patients developed endophthalmitis by *Acremonium sp.* after cataract surgery, performed in the same day and in the same operating room, it is possible to speculate that the source of inoculum resulted from irrigating fluids or from contamination of the air vent system. Therefore, strict asepsis during the procedure, both of the instrumentation and the operating room, is very important to avoid serious complications.

The rapid identification of the fungal agent belonging to the *Acremonium* genus in all the clinical samples of each of the two patients allowed prompt voriconazole topical, oral and systemic therapy with the resolution of infection in both cases.

In conclusion, the cases described in this study emphasize the need for clinical microbiology laboratories to be prepared to face the diagnosis of uncommon infectious diseases such as exogenous fungal endophthalmitis by *Acremonium* and to enhance the awareness of surgeons and clinicians of this occurrence.

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