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Nota

A case of colonization of a prosthetic mitral valve by *Acremonium strictum*

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ABSTRACT

A case of colonization of a prosthetic mitral valve in a 73-year-old Spanish male by the fungus *Acremonium strictum* W. Gams is described. The valve was replaced due to paravalvular leak and severe insufficiency and the patient died of multiorgan failure. The identity of the fungus was determined by morphological studies and it was confirmed by the analysis of the ITS region sequence analysis. Molecular studies seem to demonstrate that *A. strictum* is a species complex. The case emphasizes the potential high risk of fungal infection for patients with prosthetic valves.

Un caso de colonización de una prótesis de válvula mitral por *Acremonium strictum*

Palabras clave:
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Hongos oportunistas
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RESUMEN

Se describe un caso de colonización por el hongo *Acremonium strictum* W. Gams en un paciente varón tras la implantación de una válvula mitral protésica. El paciente falleció a causa de fallo multiorgánico. La identificación del hongo se realizó morfológicamente y se confirmó mediante análisis de las secuencias de la región ITS. Los estudios moleculares demuestran que *A. strictum* constituye un complejo de especies. El presente caso enfatiza el alto riesgo potencial de infección fúngica para los pacientes con prótesis de válvulas cardíacas.

Case report

A 73-year-old Spanish male with prosthetic valve dysfunction showing paravalvular leak and severe insufficiency presented to the Hospital 12 de Octubre on October 14, 2003, for a replacement of his prosthetic mitral valve by a mechanic prosthesis St. Jude no. 27. The patient had a history of severe COPD, treated with bronchodilators and corticosteroids, and mitral stenosis of long duration. In 1979, he underwent a replacement of his mitral valve with a mechanical prosthetic valve. In 1996, after a perivalvular leak, he underwent a second replacement with a new Carbomedics no. 27 prosthetic valve. Upon hospital admission, the patient showed silent ischemic cardiopathy and moderate pulmonary hypertension. His left ventricular ejection fraction was normal (> 59). An echocardiogram revealed the presence of a mass compatible with a thrombus of 16 mm × 7 mm in the auricular region. Within the first 72 h after the operation he developed acute renal insufficiency of multiple origins with oliguria (< 0.5 ml/kg h) and creatinine elevation (maximum 2.35 mg/100 ml). At the same time he presented with respiratory insufficiency with acute pulmonary oedema, and a bilateral neumothorax, probably related to a bronchopleural fistule and massive left atelectasis. A tracheothomy was performed on October 29. Due to a suspicion of preoperatory endocarditis caused by a thrombus on the prosthetic valve, the patient was treated with vancomycin and gentamycin. After the operation, gentamycin was suspended due to its nephrotoxicity and vancomycin was substituted by linezolid. In the histological examination of the withdrawn mitral prosthesis thrombus, a filamentous septate fungus was observed (Fig. 1). Repeat cultures of that material on Sabouraud glucose agar yielded the growth of an *Acremonium* sp. Antibiotic treatment was

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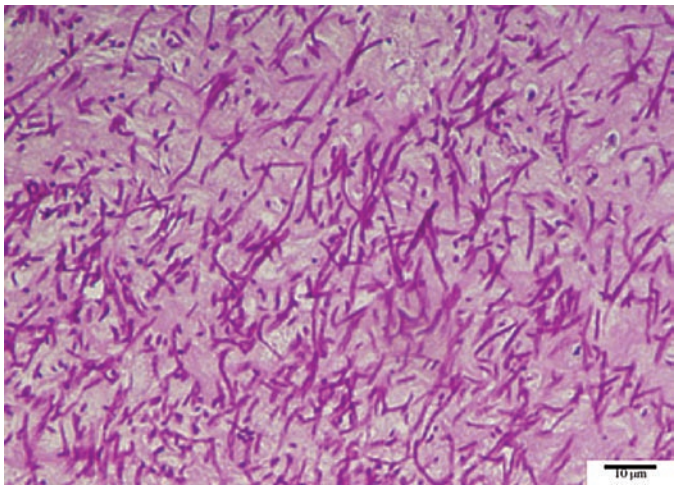

Figure 1. Thrombus from the prosthetic mitral valve stained with periodic acid–Schiff staining showing branched and septate hyphae.

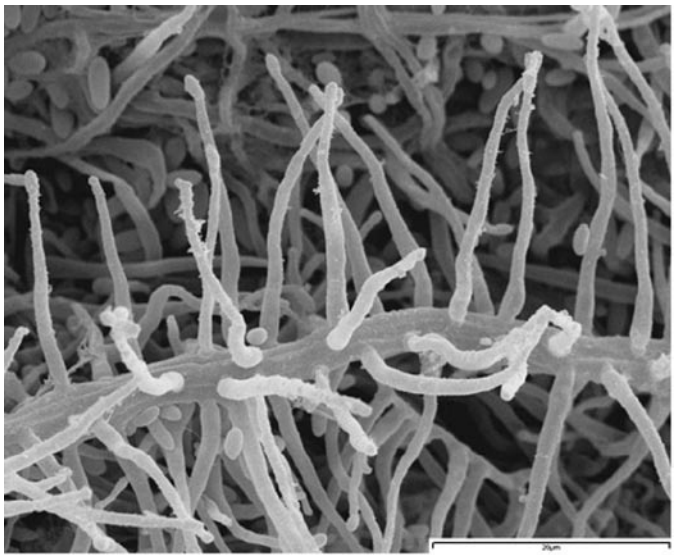

Figure 2. A hyphal strand with numerous conidiogenous cells of *Acremonium strictum* (FMR 8303) under scanning electron microscopy.

suspended and caspofungin was administered i.v. during 5 days (70 mg the two first days and 50 mg subsequently), which was changed to voriconazole (6 mg/kg day the first day followed by 4 mg/kg day) until November 11. Blood cultures were negative. On October 29, nosocomial pneumonia was suspected based on fever, leucocytosis, hemodynamic and respiratory impairment, purulent secretions, and infiltrates seen by radiograph. New empirical treatment with linezolid and ceftazidime was initiated. Over the following days, *Staphylococcus aureus* and *Stenotrophomonas maltophilia* were isolated from respiratory secretions and the patient was treated with linezolid and clotrimoxazole. On November 23, *Klebsiella pneumoniae* was isolated from urine and blood cultures, and the tip of a catheter, and treatment with aztreonam was initiated. Concurrently, treatment with sodium heparin, initiated after the operation, had to be suspended on several occasions due to digestive haemorrhages. As a consequence of all these complications, the patient developed multiorganic dysfunction with polineuropathy and renal impairment, which required assisted venous drainage and furosemida at low doses. On December 17, the patient suffered septic shock and his clinical status worsened progressively with renal, hemodynamic and respiratory impairment. Microbiological cultures were all negative with the exception of bronchial secretion cultures, where *Pseudomonas* sp. was cultured. Believing it to be nosocomial pneumonia, treatment with amoxycillin/clavulanic acid 2 g/8 h was started, which was changed to with levofloxacin. Thoracicradiographs did not reveal the presence of any infiltrate. On December 22, the patient died as a result of respiratory insufficiency and an asystole. Autopsy was denied by his relatives.

Repeat cultures of the thrombus from the prosthetic mitral valve on Sabouraud dextrose agar grew numerous colonies of a filamentous fungus morphologically identified as *Acremonium strictum* W. Gams[2,16]. The fungus was deposited in the Medicine School of the Rovira i Virgili University, Tarragona (Spain), as FMR 8303. This species is characterized by moist to slimy, orange to salmon colonies, with conidiophores usually reduced to simple phialides arising from the submerged or slightly fasciculate aerial mycelium. The phialides are acicular, 20-65 × 1.4-2.5 µm, and produce hyaline, cylindrical to ellipsoidal, 3.3-5.5 × 1-2 µm conidia grouped in slimy heads (Fig. 2). To confirm this identification, a fragment of about 531 bp corresponding to the ITS region of the rRNA genes of this isolate was sequenced (GenBank accession no. AM990178) and compared with sequences of the GenBank. The search revealed a 100% homology with the strain UW 836 of *A. strictum* (AY138844).

Susceptibility testing of the clinical isolate was performed in duplicate using a microdilution test and following the Clinical and Laboratory Standards Institute (CLSI) guidelines[11]. The MICs for the antifungals tested (in µg/ml) were as follows: amphotericin B 2, itraconazole > 16, posaconazole 2, terbinafine 0.25, micafungin > 16, voriconazole 2 and ravuconazole 16.

This report documents only the presence of *A. strictum* colonizing the prosthetic mitral valve. However, considering the virulence of this fungus, it may have had a role in the progressive decline of the patient. It is noteworthy that the sequence of our clinical isolate is identical to that of the strain UW 836, which recently caused a fatal infection in a haematopoietic cell transplant patient in the USA[12]. Those authors found a remarkable genetic diversity among clinical isolates of this species when the ITS region and 28S rRNA sequences were analyzed. This seems to indicate that *A. strictum* may be a complex of phylogenetic species as is seen in many other pathogenic fungi, such as *Pseudallescheria boydii*[6] or *Sporothrix schenckii*[9], previously considered homogeneous species.

A review of the clinical cases of infections by *Acremonium* found eight cases attributed to *A. strictum,* reported up to 2002, and in five of these, the patient died[7,8]. Considering the difficulties in the identification of this fungus and the fact that in numerous cases attributed to *Acremonium* are not identified to the species level, it is likely that disease by *A. strictium* is underreported. In recent years, several new cases attributed to this fungus have been reported, i.e. localized infections affecting immunocompetent patients[1,3,13,15], invasive infections in immunosuppressed patients[5,10] and even some affecting animals[14].

The antifungal susceptibility for this case isolate is similar to that seen in the case of Novicki et al[12]. Both isolates showed an itraconazole MIC of > 8 µg/ml and an amphotericin B MIC of 2 µg/ml. In contrast, response to other azoles was considerably poorer than that indicated by other authors. Miyakis et al[10], reported MICs for voriconazole and posaconazole of 0.25 and 0.03 µg/ml, respectively. These significant differences in MIC data among the isolates of *A. strictum* tested may be explained by the existence of an *A. strictum* species complex, with individual strains displaying different antifungal susceptibilities. In general, however, limited case reports correlating *in vitro* data with clinical efficacy suggest an organism refractory to antifungal therapy. This resistance is similar to that seen in *Fusarium* spp., with which *Acremonium* shares numerous morphological and pathological characteristics. However, it is encouraging to note that on a few occasions, *A. strictum* has responded to voriconazole in an invasive

infection in a bone marrow transplant recipient[10] and to posaconazole in a pulmonary infection in a leukemic patient[8]. Additional studies involving more clinical strains are needed to confirm these promising data. Although *in vitro* data suggest that new azoles may be effective against some *Acremonium* isolates[4], it is unknown against which species, as *A. strictum* most likely represents a species complex of diverse and possibly poorly related species.

This case highlights the fact that a fungus such as *A. strictum*, which is highly resistant to antifungals and has proven ability to invade the debilitated host, can colonize a mechanical prosthetic valve. Such colonization may also constitute an important risk factor for the development of an invasive infection. This fungus should be added to the list of species able to produce fungal endocarditis.

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