Medical Mycology Case Reports 2 (2013) 152–155

Contents lists available at ScienceDirect

Medical Mycology Case Reports

journal homepage: www.elsevier.com/locate/mmcr

Thermomyces lanuginosus infective endocarditis: Case report and a review of endocarditis due to uncommon moulds

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ARTICLE INFO

Article history:
Received 20 July 2013
Received in revised form
31 August 2013
Accepted 12 September 2013

Keywords:
Thermomyces lanuginosus
Endocarditis
Antifungal therapy
Moulds
Emerging moulds

ABSTRACT

We describe a case of *Thermomyces lanuginosus* endocarditis, the first reported in a living patient, and review the literature to delineate the clinical characteristics, investigations and management of endocarditis due to such rare but emerging mould pathogens.

1. Introduction

Fungal endocarditis, which accounts for less than 10% of all cases of infective endocarditis, is most often due to *Candida* and *Aspergillus* species [1]. *Thermomyces lanuginosus*, on the other hand, is an example of a diverse group of previously rare or emerging mould pathogens with protean clinical manifestations, including cardiac valve infection. The first report of *T. lanuginosus* endocarditis was made postmortem over 20 years ago in a patient who had prior valvular surgery for *Staphylococcus aureus* infective endocarditis [2]. There have been no published reports of *T. lanuginosus* endocarditis in a living patient. In this report, we highlight the clinical course and management of a patient with *T. lanuginosus* endocarditis whose illness spanned more than 9 years. We also review the literature for endocarditis caused by this, and other uncommon but emerging non-*Aspergillus* moulds.

2. Case

A 31-year-old lady, 10 weeks postpartum, developed fever, chills and lethargy after a caesarean section in July 2003 (Day 0). The temperature was 39.3 °C and there was a vasculitic lesion on the right great toe. Cardiovascular examination revealed new ejection systolic and diastolic murmurs. Blood cultures grew *Enterococcus faecalis* and a transoesophageal echocardiogram (TOE) showed a 12 mm vegetation on the aortic valve with aortic regurgitation. A porcine aortic valve prosthesis was inserted. Microscopic examination of the native valve revealed gram positive cocci but no microorganisms were cultured. She received 6 weeks of intravenous ampicillin and gentamicin with clinical response.

Twelve months later (Day 365), she represented with fever and embolic lesions to the left great toe and sole of foot. Multiple blood cultures were negative. A transthoracic echocardiogram (TTE) demonstrated 13 mm × 5 mm vegetation at the left coronary cusp. She underwent radical debridement and replacement of the bioprosthetic aortic valve with another (bioprosthetic valve) and had the ascending aorta reconstructed with autologous pericardium.

Culture of intraoperative specimens inoculated onto blood and chocolate agars grew a white fluffy fungus within 4 days of incubation at 35 °C in air. Unusually, the fungus was thermophilic, growing better at 42 °C than at 30 °C or 35 °C. The fungus was identified as *T. lanuginosus* by conventional morphology [3] (Figs. 1–3) and the species identity was confirmed by DNA sequence analysis of the internal transcribed spacer (ITS) 1 and 2 regions of the fungal ribosomal RNA gene using published primers and standard sequencing methodologies [4]. The isolate's sequence was compared to those in the GenBank database using the BLASTn search tool. The PCR product showed 100% identity to

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2211-7539
http://dx.doi.org/10.1016/j.mmcr.2013.09.001

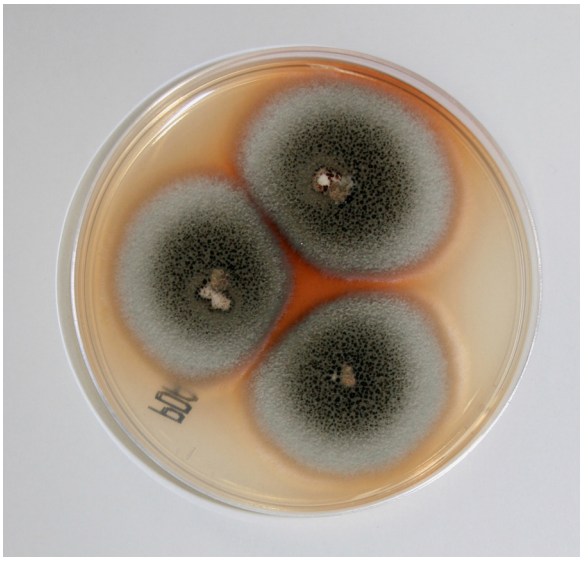

Fig. 1. *Thermomyces lanuginosus* colonies growing on Potato Dextrose Agar (PDA) at 5 days at 42 °C demonstrating greenish grey colonies with a pink vinaceous pigment diffusing into the agar.

Fig. 2. *Thermomyces lanuginosus* colonies on Sabouraud agar at 5 days at 42 °C.

GenBank sequence JN106393 and >99% identity to GenBank sequence AF096278. Antifungal susceptibility testing was performed using Etest strips (AB Biodisk, Solna, Sweden) after incubating plates in air for 4 days at 42 °C. The longer incubation time was necessary to allow sufficient growth of the fungus and 42 °C rather than 35 °C was selected as the better temperature for growth. The following MICs (in mg/L) were observed: amphotericin >32, itraconazole 0.032 and voriconazole 0.006. She was treated with intravenous liposomal amphotericin (LAMB: 6 mg/kg daily) for 2–3 weeks followed by oral voriconazole (4 mg/kg daily after a loading dose of 6 mg/kg daily).

However, she developed severe back pain six weeks later (Day 407) with discitis and osteomyelitis at the T10–11 and L2–4 vertebral levels evident on magnetic resonance imaging (MRI). An abdominal computed tomography (CT) scan showed a left common femoral artery mycotic aneurysm, later repaired with a venous patch. CT guided core biopsy of the spine were unrevealing. A TOE showed no vegetations. She had empiric ceftriaxone

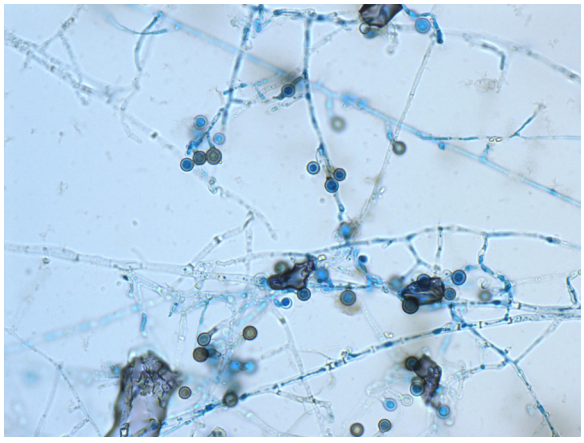

Fig. 3. Microscope slide (×400 magnification) from a subculture (PDA) stained with lactophenol cotton blue showing short, unbranched conidiophores bearing solitary thick-walled, dark brown conidia.

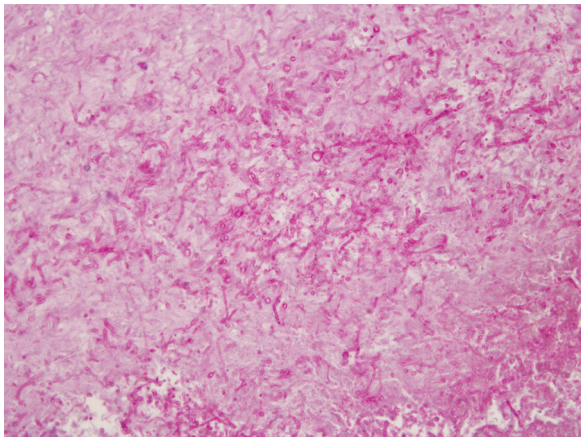

Fig. 4. PAS stain of valvular tissue (x400 magnification) demonstrating abundant fungal hyphae and conidia.

and vancomycin for 6 weeks. Voriconazole 4 mg/kg twice daily was continued and was ceased after a total of 18 months of therapy in July 2005 (day 954). Her history was complicated by two further episodes of endocarditis. In December 2007 (day 1784), she was treated with a course of intravenous penicillin (6 weeks) and gentamicin (2 weeks) for *Streptococcus acidominimus* endocarditis. She subsequently had ceftriaxone and vancomycin for an additional episode of presumed culture negative endocarditis associated with vasculitic lesions to the foot in June 2009 (Day 2229).

In October 2010 (Day 2714), she re-presented with acute onset of bilateral cold and pulseless lower limbs. A CT angiogram demonstrated bilateral common iliac artery occlusive thrombi. TOE revealed the prosthetic aortic valve to be dehisced from the aortic root, with dilatation of the root and presence of large thrombi. She had an urgent aorto-iliac thomboembolectomy, followed by a mechanical aortic valve replacement as well as insertion of a permanent pacemaker for complete heart block. Histopathological examination of tissue from the valve (Fig. 4) and embolus demonstrated numerous branching fungal hyphae, and *T. lanuginosus* was grown on culture.

Antifungal susceptibility testing using the Sensititre YeastOne (TREK, Thermo Scientific, USA) colorimetric broth microdilution method and incubated at 42 °C for 4 days revealed the following MIC results (in mg/L): amphotericin 4, posaconazole 0.25 and voriconazole 0.06. She was commenced on voriconazole 4 mg/kg twice daily following a loading dose of 6 mg/kg twice daily and