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Clinical Case Report

Mycobacterium fortuitum prosthetic valve endocarditis: a case for the pathogenetic role of biofilms

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Abstract

Background: Prosthetic valve endocarditis presents unique challenges for both diagnosis and treatment. A potential role of biofilm has been hypothesized in the pathogenesis of these infections. **Methods:** A patient with infective endocarditis involving a stentless (Freestyle) porcine prosthetic aortic valve with annular abscess and paravalvular leak 8 months after implantation is reported. **Results:** The infected valve did not show vegetations or perforations, but histiocytic inflammation was seen along the endocardial surfaces of the valve. Auramine–rhodamine staining revealed many acid-fast organisms associated with the inflammation. There was also an acellular matrix material with ultrastructural features of biofilm. Blood cultures grew *Mycobacterium fortuitum*, a biofilm-associated microbe. **Conclusions:** The role of biofilm in prosthetic valve endocarditis is discussed. The importance of microscopy for prosthetic valves, even when no vegetations are present, is highlighted along with correlation of pathologic findings with culture results. © 2012 Published by Elsevier Inc.

Keywords: Biofilm; Prosthetic valve; Endocarditis; *Mycobacterium fortuitum*

1. Introduction

Prosthetic valve endocarditis poses a unique set of diagnostic and clinical challenges for pathologists and clinicians. The spectrum of etiologic microbes is shifted toward less common agents compared to native valve endocarditis. The pattern of valve damage is altered due to lack of circulation and exposure to the immune system in the valve tissue. The prospect of reimplanting another foreign body into an infected field is also problematic. Surfaces of foreign materials are prone to formation of so-called biofilm—composed of bacteria that have undergone a physiologic and phenotypic shift to a stationary and matrix-producing state, rendering them highly resistant to antimicrobials. The case presented here illustrates an unusual *Mycobacterium fortuitum* infection of a porcine valve without vegetations, but with evidence of biofilm formation on the valve leaflets. The potential pathogenetic implications of this finding are explored, and the importance of thorough evaluation of prostheses is underscored.

2. Case report

2.1. History and presentation

A 72-year-old Caucasian man with a mechanical aortic valve (Medtronic-Hall) prosthesis for stenotic bicuspid valve placed 6 years ago underwent a second aortic valve replacement surgery with implantation of a Freestyle stentless porcine bioprosthetic valve. A tissue valve was selected because of difficult anticoagulation management.

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Eight months later, he presented with fever, shaking chills, and drenching sweats and reported several months of progressive fatigue, malaise, and myalgias. A rapidly growing mycobacterium was isolated in multiple blood cultures and eventually identified as *M. fortuitum*. A transesophageal echocardiography (TEE) demonstrated periannular thickening and an echo-lucent space adjacent to the porcine aortic prosthesis. No vegetations were seen on the prosthetic or native valves. Combination empiric antibiotic therapy with levofloxacin, clarithromycin, and tobramycin was initiated, but later changed to a combination of intravenous amikacin, oral trimethoprim/sulfamethoxazole, and oral moxifloxacin based on microbial sensitivity results. Repeat blood cultures on combination antibiotics did not grow mycobacteria.

The patient's symptoms improved, but he continued to note weakness and reduced exercise tolerance. A third TEE showed enlargement of the periannular space and a new fistulous communication between the aorta and subvalvular left ventricular outflow tract. The communication was filled with echo-lucent material; there was no blood flow on color Doppler. He again was taken to surgery for valve replacement and aortic root reconstruction. A cryopreserved aortic valve and root homograft was implanted.

2.2. Pathologic examination

Grossly, the infected FreeStyle aortic prosthetic valve showed no vegetations or other apparent features of active or healed endocarditis. A portion had been removed for cultures. Inconspicuous thickening of one cusp over an area roughly 0.7 cm in diameter was also noted. No tissue from the annular abscess was submitted to pathology.

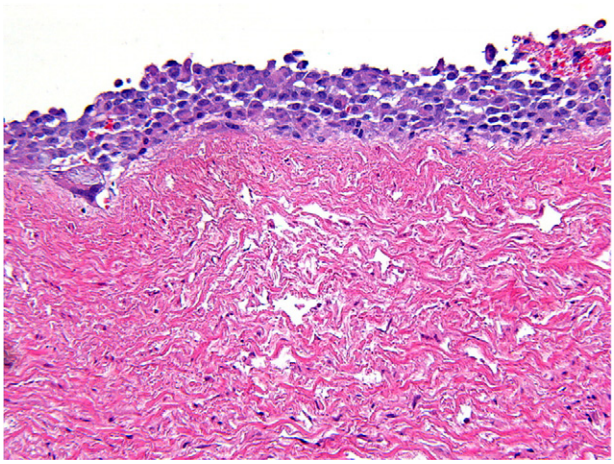

Fig. 1. Macrophage-rich inflammation coating the valve surface. Photomicrograph showing porcine aortic root tissue with wavy eosinophilic elastic fiber layers. The endocardial surface is coated with macrophage-rich inflammation that does not invade the aortic tissue or form mass-like excrescences protruding from the surface (vegetations) (H&E, ×200).

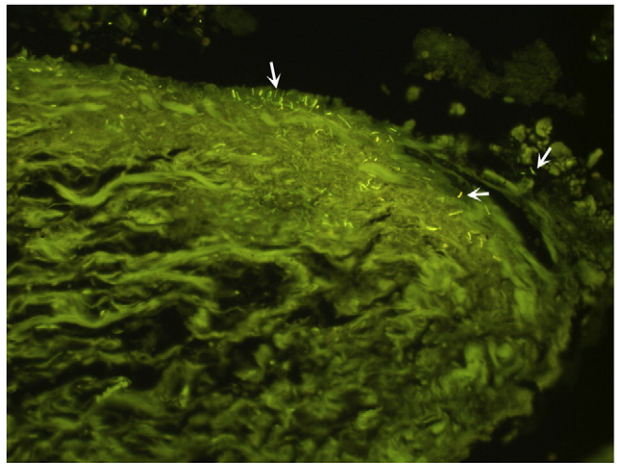

Fig. 2. Acid-fast bacilli on tissue auramine–rhodamine stain. Fluorescence photomicrograph showing numerous bacillary microorganisms (arrows) staining positively (pale yellow) with auramine–rhodamine. Porcine aortic root tissue with autofluorescing elastic fibers is seen in the lower half of the image (×400).

Microscopically, the valve cusps demonstrated mild fibrotic thickening but no bulky fibrin deposition or purulent acute inflammation. Two of the submitted leaflets showed compact aggregation of macrophages (CD68 positive) along the surface of the cusps (Fig. 1), focally associated with a thin layer of fibrin matrix. Gram and silver stains were negative, but auramine–rhodamine staining revealed many acid-fast organisms on fluorescence microscopy (Fig. 2). Organisms were confined to the macrophage layer and superficial aspects of the valve cusp and aortic intima.

Samples of the grossly thickened valve leaflet were subsequently submitted for transmission and scanning electron microscopy. Definitive microbes were not seen by transmission electron microscopy, but the macrophages appeared to be infiltrating through a matrix material with a nondescript fibrillar and finely granular appearance consistent with biofilm matrix (Fig. 3). This was largely devoid of typical fibrin tactoids, and only rare platelets were seen, suggesting that this material was not simply adherent fibrin-platelet thrombus. By scanning electron microscopy, the macrophages appeared to be matted in a three-dimensional lattice that showed both globular and fibrillar features. Rare entrapped platelets were seen, but again, the appearance was distinct from platelet-fibrin thrombus (Fig. 4).

2.3. Postoperative course

Mycobacterial cultures of all tissue and valve specimens were negative. Following surgery, he completed a total of 12 months of multiagent antimicrobial treatment, but continued prolonged (possibly lifelong) suppression with doxycycline. He is alive and well at