Diagnostic Importance of Hyphae on Heart Valve Tissue in Histoplasma Endocarditis and Treatment With Isavuconazole

Zanthia Wiley, Emory University
Michael H. Woodworth, Emory University
Jesse Thomas Jacob, Emory University
Shawn R. Lockhart, Centers for Disease Control and Prevention
Nadine Rouphael, Emory University
Jonathan C. Gullett, Southern California Permanente Medical Group Regional Reference Laboratories
Jeannette Guarner, Emory University
Kimberly A Workowski, Emory University

Journal Title: Open Forum Infectious Diseases
Volume: Volume 4, Number 4
Publisher: Oxford University Press (OUP) | 2017-11-24, Pages ofx241-ofx241
Type of Work: Article | Final Publisher PDF
Publisher DOI: 10.1093/ofid/ofx241
Permanent URL: https://pid.emory.edu/ark:/25593/s7tph

Final published version: http://dx.doi.org/10.1093/ofid/ofx241

Copyright information:
© The Author(s) 2017. Published by Oxford University Press on behalf of Infectious Diseases Society of America. This is an Open Access work distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Accessed December 17, 2018 4:49 PM EST
Diagnostic Importance of Hyphae on Heart Valve Tissue in Histoplasma Endocarditis and Treatment With Isavuconazole

Zanthia Wiley,1,* Michael H. Woodworth,2,** Jesse T. Jacob,3 Shawn R. Lockhart,4 Nadine G. Rouphael,5 Jonathan C. Gullett,6 Jeannette Guarnier,7 and Kimberly Workowski8

1Division of Infectious Diseases, Department of Medicine, Emory University School of Medicine, Atlanta, Georgia, USA; 2Division of Infectious Diseases, Department of Medicine, Emory University School of Medicine, Atlanta, Georgia, USA; 3Division of Infectious Diseases, Department of Medicine, Emory University School of Medicine, Atlanta, Georgia, USA; 4Fungal Reference Laboratory Mycotic Diseases Branch Centers for Disease Control and Prevention, Atlanta, Georgia, USA; 5Division of Infectious Diseases, Department of Medicine, Emory University School of Medicine, Atlanta, Georgia, USA; 6Microbiology, Southern California Permanente Medical Group Regional Reference Laboratories, Greater Los Angeles Area, California, USA; 7Pathology and Laboratory Medicine, Emory University School of Medicine, Atlanta, Georgia, USA; 8Division of Infectious Diseases, Department of Medicine, Emory University School of Medicine, Atlanta, Georgia, USA

A patient who never resided in an endemic area for dimorphic fungi was diagnosed with *Histoplasma capsulatum* endocarditis. His diagnosis was suggested by yeast and hyphae on cardiac valve tissue pathology. Isavuconazole was an optimal therapeutic option due to renal dysfunction and anticoagulation with warfarin for mechanical valve replacement.

**Keywords.** fungal endocarditis; *Histoplasma capsulatum*; histoplasmosis; hyphae; isavuconazole.

**CASE**

A previously healthy 56-year-old male construction worker from rural Georgia presented with 1 year of subjective fevers, malaise, and dyspnea. He was in a monogamous relationship with his wife and denied history of travel outside Georgia or animal exposure. He had fever, systolic and diastolic murmurs, and hepatosplenomegaly. Transesophageal echocardiogram revealed severe eccentric aortic insufficiency, an aortic root fluid collection, and a large aortic vegetation.

His serum creatinine was 2.36 mg/dL, white blood cell count was $3.5 \times 10^9$/L, and platelet count was $96 \times 10^9$/L. HIV polymerase chain reaction and fourth-generation screen were negative. Blood cultures were obtained, and empiric ceftriaxone and intravenous vancomycin were administered. He underwent mechanical aortic valve replacement and aortic root reconstruction. Intraoperatively, a $4 \times 2$-cm aortic valve vegetation was found with extension of abscess into the annulus and myocardium.

**DISCUSSION**

*Histoplasma capsulatum* is one of the most common thermally dimorphic fungi, and though classic areas of endemicity along the Ohio and Mississippi River Valleys have been described, there is increasing recognition of histoplasmosis outside of these areas [1, 2]. *H. capsulatum* is a rare cause of infectious endocarditis, with only 58 previously described cases [3, 4]. In this case, yeast and hyphae were seen in excised cardiac valve tissue before results were available by fungal culture, urine *Histoplasma* antigen, and serological and molecular testing. In tissue sections, *H. capsulatum* is usually seen as phagocytosed clusters of yeasts; however, endocarditis is the exception to the rule as the intracellular yeasts can show hyphal structures more typical of the histopathology of *Candida* spp. or hyaline molds [5].

There are limited data to guide *H. capsulatum* endocarditis treatment, and no specific recommendations in the 2007 Infectious Diseases Society of America Histoplasmosis
Guidelines or the 2015 joint IDSA/American Heart Association Infective Endocarditis Scientific Statement. Expert opinion recommendations include surgical debridement or valve replacement followed by an initial period with amphotericin, then a prolonged or lifelong course of itraconazole [4]. Although an off-label use, isavuconazole may be effective treatment for *H. capsulatum* endocarditis. It does not appear to interact with warfarin, which may be important for patients undergoing mechanical valve replacement, and, where other azoles can cause QTc prolongation, isavuconazole has been associated with QTc interval shortening. Isavuconazole also does not require renal dose adjustment.

Acknowledgments

The authors wish to thank Colleen Lysen at the Centers for Disease Control and Prevention for her excellent laboratory skills.

Financial support. This work was supported by the National Center for Advancing Translational Sciences of the National Institutes of Health under grant number UL1TR000454 to M.H.W. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Centers for Disease Control and Prevention or the National Institutes of Health.

Potential conflicts of interest. All authors: no reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References