HISTOPLASMOSIS ENDOCARDITIS: A MASQUERADING ENIGMA

William L. Winters, Jr.
From Methodist DeBakey Heart Center, Houston, Texas

CASE REPORT

In September 2002, an 87-year-old, white, nonsmoking married rancher from west Texas developed recurrent, relapsing fever to 105°F with diaphoresis, generalized - at times severe - myalgia, weight loss of 40 pounds, anorexia and loss of smell and caste. He had been in good health, but his past history included coronary artery bypass in 1970 and again in 1993. Initial evaluation uncovered a pancycopenia, splenomegaly, a small infrarenal abdominal aortic aneurysm {4.8 cm), cholelithiasis without cholecystitis and benign renal cysts. An initial presumptive diagnosis of brucellosis was entertained. He started doxycycline therapy, which provided only transient control of the symptoms and fever.

In March 2003, he was referred to a physician in another city who confirmed the previous findings but also detected, by echocardiography, a vegetation on the anterior mitral valve leaflet. Multiple blood studies were negative. Lymph node biopsy was normal. He was transferred co Methodist DeBakey Hean Center on April 8, 2003. The vegetation was confirmed by transthoracic and transesophageal echocardiography and measured (13 x 8 mm) (Figure 1). All previous pathology was confirmed. Multiple studies conducted by infectious disease, hematology and gastroenterology consultants failed to provide the source of the vegetation and fever. All manner of serologic, antibody, antigen and culture studies were normal. Bone marrow and lymph node biopsies were unrevealing. Multiple blood cultures for fungi, AFB, Brucella and fastidious organisms were negative, as were urine and serum Histoplasma antigens tests. Ir was concluded that the vegetation most likely represented maramic endocarditis. A PICC line was placed, and, with some misgivings, the patient was discharged on May 4, 2003, on a six-week course of vancomycin as empiric treatment for culture-negative endocarditis.

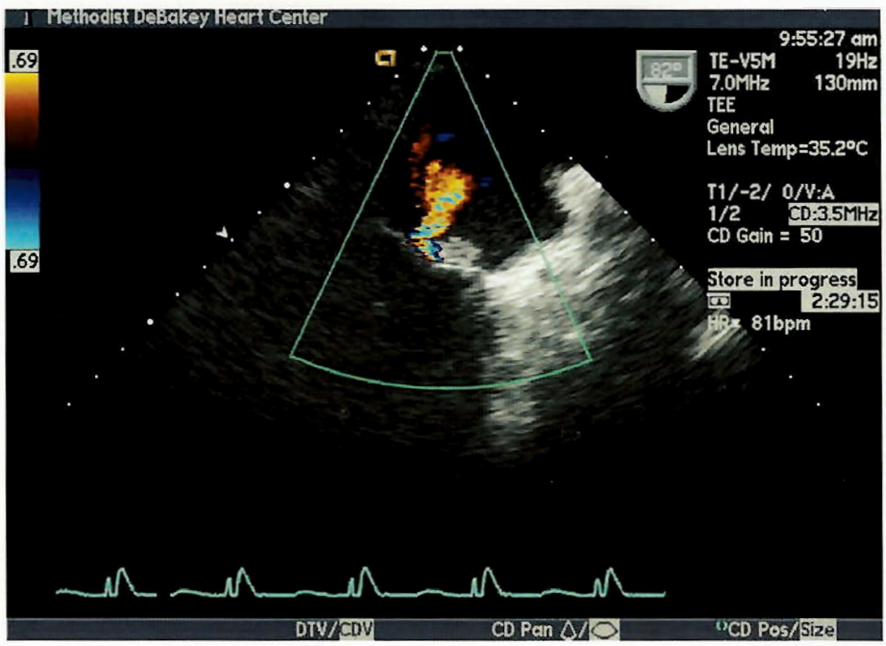

Figure 1
Echocardiography of mitral valve vegetation

On May 9, the patient developed acute pain in his left upper arm with evidence of diminished blood flow distally. He was readmitted to Methodist the next day, and on May 12 an embolectomy successfully removed a thrombus from his left axillary, subclavian and brachia! artery. The patient was discharged on May 16 to cominue his antibiotic course of vancomycin. Prior to discharge, a subsequent TEE showed a vegetation remaining on the amerior mitral valve leaflet, albeit smaller in size (10 x 6 mm). As yet, no clear-cut etiology was forthcoming. The initial culture and staining characteristics of the thrombus failed to provide an answer.

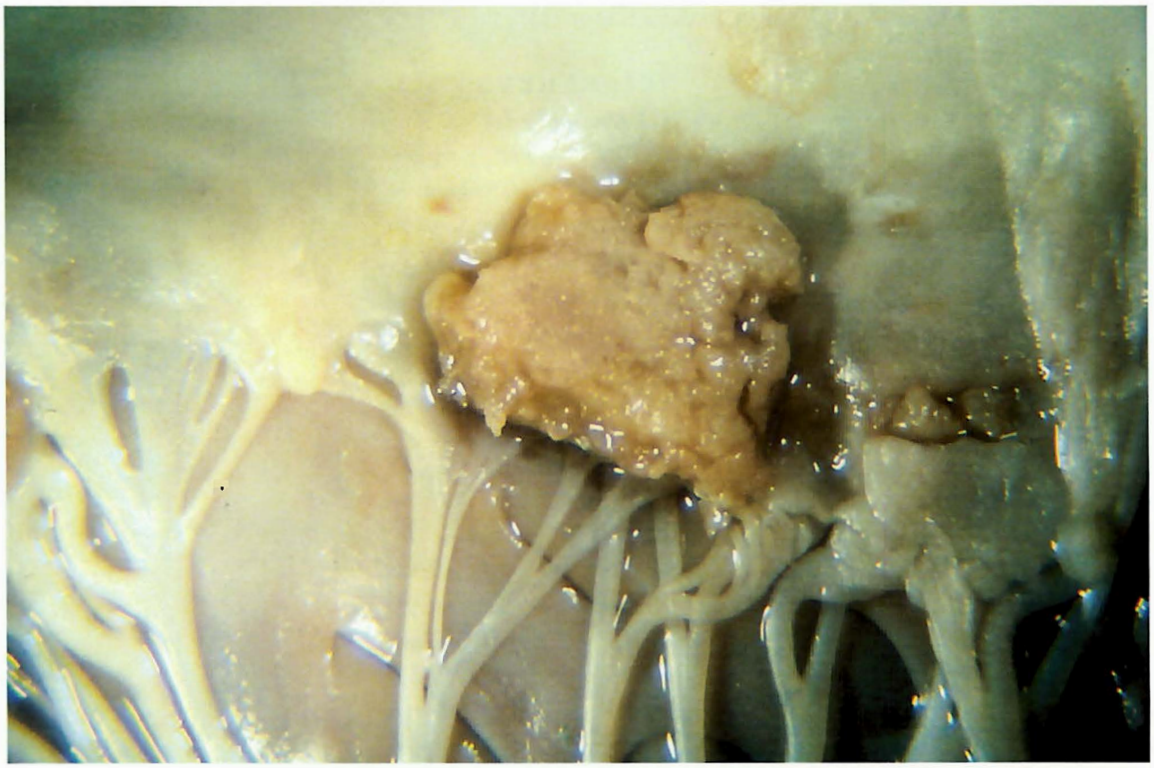

Figure 2
Mitral valve vegetation

As was previously planned, the patient returned to Methodist on May 27 to undergo splenectomy and cholecystecromy, which was accomplished uneventfully. His spleen contained multiple embolic infarcts containing fungal organisms consistent with Histoplasma capsularum. Subsequent restaining of che thrombus removed from the left axillary artery also showed similar fungal organisms. Culcure of the thrombus eventually grew Hisroplasma capsulatum. The preferred treatment for fungal endocarditis recommended by the infeccious disease service was parenceral amphotericin B and then micral valve surgery; however, his general condition and prior bypass surgeries made him an unsuitable candidate for the latter. Therefore, he was initially treated with amphotericin B and subsequently placed on oral itraconazole (Sporanox) 400 mg daily. He has since remained afebrile, regained his weight and appetite and returned co his pre-illness health and accivities. He is being maintained on lifelong icraconazole treacment of 200 mg daily. The mitral valve vegetation disappeared and has not recurred.

EPIDEMIOLOGY

Histoplasmosis capsulatum is endemic in the Ohio and Mississippi valleys bur exhibits worldwide distribution. Exposure occurs when mold forms (microcondia) that grow in soil, commonly enriched by bird and bat droppings, are dispersed into the air, causing pneumonitis and mediastinal adenitis. Hematogenous dissemination occurs within two to three weeks thereafter. The magnitude of exposure and the host's immune status and underlying health may dictate the clinical manifestations. In endemic areas, over half of the population may be infecced, but most remain without symptoms.1.[2]

CLINICAL MANIFESTATIONS

Pulmonary manifescations are the hallmark of hisroplasmosis. These may include acuce or chronic pulmonary syndromes, broncholithiasis, mediastinal granuloma and fibrosing mediastinitis (rare). Pericarditis may be associated with mediastinal granuloma (rarely with the disseminated disease) and usually resolves with anti-inflammatory drugs and without ancifungal therapy. Constrictive pericarditis is rare, but hemodynamic compromise may occur in 40% of patients. Endocarditis has been observed in disseminated histoplasmosis in about 4% of patients, and isolated endocarditis also has been seen.3-5 Hisroplasmosis infection of left atrium myxoma[6] and prosthetic valves[7,8] has been reported.

Blood cultures are commonly unrevealing as in the present case.

Disseminated histoplasmosis rends co occur ac the extremes of age and in immune-deficient patients, especially chose wich HIV-1 infections, and may involve any of che bodily tissues. Sarcoidosis and histoplasmosis share a number of clinical similarities, and ic is imperative that the correct diagnosis between the two is established to direct the appropriate therapy.

LABORATORY DIAGNOSIS

Diagnostic tests commonly employed include cultures, fungal stains, serologic tests for antibodies and antigen studies - although tests vary according to the hose, infection and mycologic conditions. Urine Hisroplasma antigen is positive in 80% of disseminated histoplasmosis cases. The incidence of antigen positivity in Histoplasma endocardicis is unknown but is thought to be low because of small overall body fungal burden. In this case, all such studies were negative until fungal staining techniques were applied co the thrombus and splenic samples and the thrombus culcure eventually became positive.

TREATMENT

Antifungal agents are employed for chose with chronic pulmonary or disseminated infections. Mose, however, are asymptomatic or self-limited and require no treatment. The following references provide guidelines.

CONCLUSION

This case is of interest in that histoplasmosis endocardicis is uncommon and diagnosis is often difficult, as manifest in chis patient whose course lasted six to eight months before a diagnosis was established - and only then when a peripheral thrombus and subsequent spleen became available for analysis (Figure 1).

REFERENCES

1. *Wheat LJ, Dewey C, Allen SD, Blue-Hnidy D, Loyd J Pulmonary histoplasmosis syndromes: Recognition, diagnosis and management. Seminars in Respiratory and Critical Care Medicine. 2004;25(2}:129-44.*
2. *Wheat L], Kauffman CA. Histoplasmosis. Fungal infections, part II: recent advances in diagnosis, treatment, and prevention of endemic and cutaneous mycoses. Inf Dis Clin ofNAmer. 2003;17:J-19.*
3. *Goodwin RA Jr., Shapiro JL, Thurman GH, Thurman SS, des Prez RM. Disseminated histoplasmosis: Clinical and pathologic correlations. Medicine (Baltimore} 1980;59:1-33.*
4. *Bradsher RW, Wickre CG, Savage AM, Harston WE, Alford RH. Histopl.asma capsulatum endocarditis cured by amphotericin B combined with surgery. Chest. 1980 Nov,-78(5):791-5.*
5. *Blair TP, Waugh RA, Pollack M, Ashworth HE, Young NA, Anderson SE, et al. Histoplasma capsulatum endocarditis. Am Heart J 1980 Jun:99(6):783-8.*
6. *Rogers EW, Weyman AE, Noble Rj, Bruins SC. Left atrial myxoma infected with histoplasma capsulatum. A m] Med. 1978Apr;64(4):683-90.*
7. *Alexander WJ, Mowry RW, Cobbs CG, Dismukes WE. Prosthetic valve endocarditis caused by histopl.asma capsulatum. JAMA. 1979 Sept 28;242(13):1399-400.*
8. *Konawaty DS, Stalker MJB, Munt PW Nonsurgical treatment of histoplasma endocarditis inwo/11-ing a bioprosthetic valve. Chest. 1991:99:253-6.*