

Introduction

Histoplasma capsulatum (HC) is a dimorphic fungus that grows as a mold in the environment and as a yeast in human tissue. The incidence is highest within the Mississippi and Ohio River Valleys of North America, and as parts of Central and South America. Patients typically present with symptoms such as weight loss, diaphoresis, chills, malaise, and fatigue. The most common clinical manifestation is pulmonary histoplasmosis, which can mimic community-acquired pneumonia, tuberculosis, and sarcoidosis. Histoplasmosis is often underdiagnosed due to its nonspecific symptoms, leading to the progression to disseminated disease. In rare cases, disseminated histoplasmosis can lead to infective endocarditis (IE) of both native and prosthetic heart valves. From 1940 to 2020, only 80 cases have been reported in the medical literature. Risk factors for fungal endocarditis include the presence of prosthetic valves, history of cardiac interventions, injection drug use and travel to endemic areas.

Case

This is a case of a 59-year-old female with past medical history of paroxysmal atrial fibrillation, sick sinus syndrome (status post pacemaker placement), hepatomegaly, splenomegaly and chronic immune thrombocytopenic purpura (ITP), who presented to the emergency department with nausea, vomiting, fever, and leukocytosis, concerning for possible sepsis. The cardiology team was consulted due to an abnormal transthoracic echocardiogram, which revealed a 2.1 x 1.3 cm echo-density on the aortic valve. A transesophageal echocardiogram demonstrated a large, bulky mass on the aortic valve along with moderate aortic stenosis. Given the clinical presentation, it was essential to rule out an infectious etiology. Further investigation using microbial cell-free DNA testing revealed a high minimum pathogenicity marker for *Histoplasma capsulatum* and *Streptococcus mitis*. Based on case reviews, the clinicians believed that the mass was a vegetation secondary to histoplasmosis. The patient was given IV antibiotics and antifungals and scheduled for an aortic valve replacement. The native valve was sent for pathological analysis.

Results

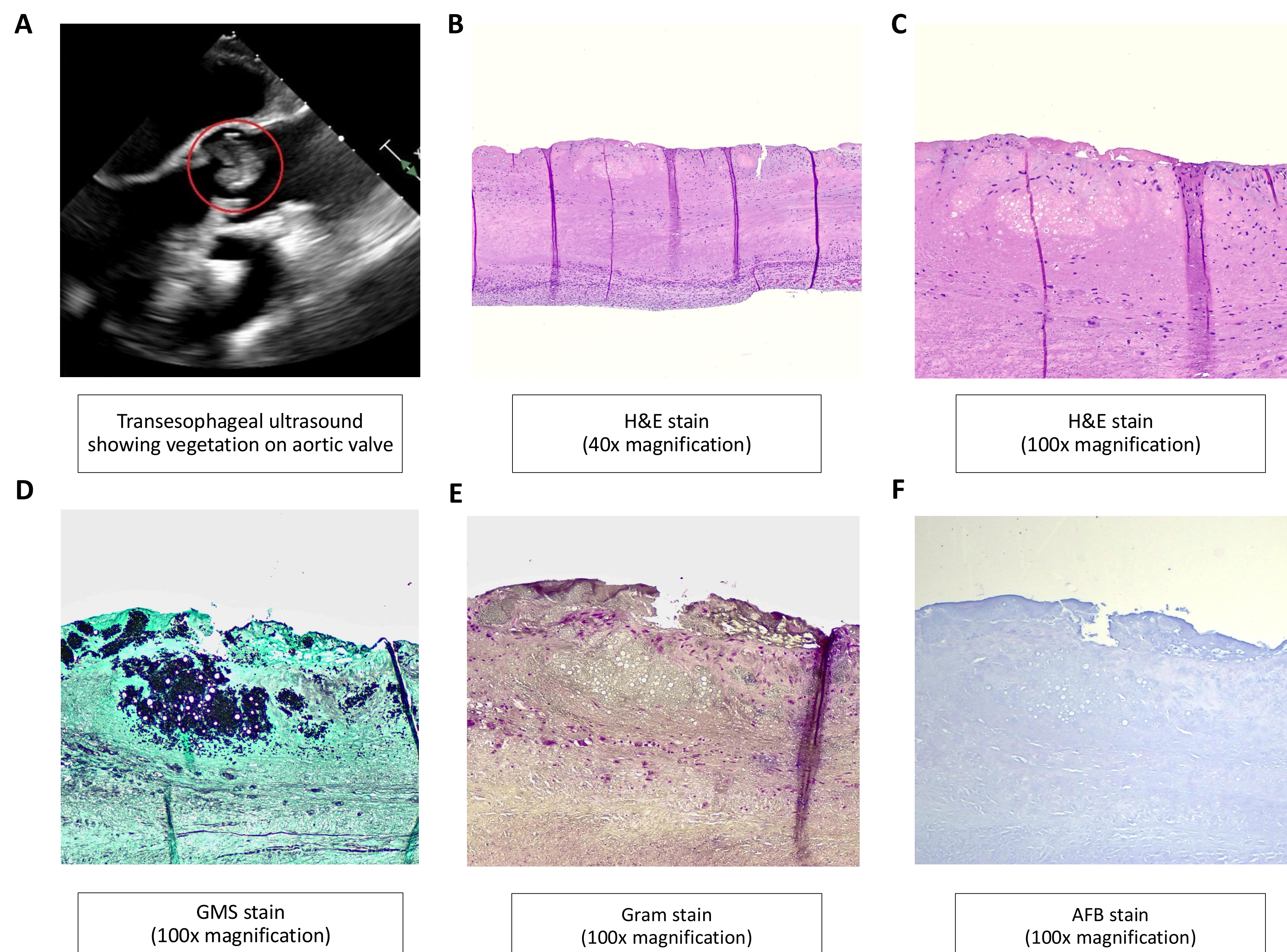


Figure 1. Aortic valve vegetation secondary to disseminated histoplasmosis. A transesophageal ultrasound revealed a bulky mass attached to the aortic valve (figure A). A cross-section of the aortic valve on H&E (figures B and C) reveals the presence of fungal elements. Grocott–Gömöri's methenamine silver stain (GMS) highlights the fungal organisms (figure D). Gram stain (Figure E) and Acid-fast bacilli (Figure F) stain are negative, ruling out bacterial and mycobacterial organisms.

Discussion

Fungal endocarditis accounts for 1% to 3% of all cases of infective endocarditis. The most common causative organisms of fungal endocarditis are *Candida* species, followed by *Aspergillus* and *Histoplasma* species. Given the subacute and non-specific symptoms, it presents with numerous challenges in clinical care, as early diagnosis requires a high degree of clinical suspicion along with the careful use of diagnostic tests. If not diagnosed promptly and treated with a combination of antifungal therapy and surgical intervention, the condition can be associated with a high mortality rate, often exceeding 70%, and with an array of chronic conditions. In the case of this patient, who disclosed that she often travelled to Indiana between 1998 and 2000, the discovery of disseminated histoplasmosis could explain her other chronic illnesses, such as hepatosplenomegaly and ITP. The presence of the pacemaker secondary to her heart disease would have also increased her risk of developing fungal endocarditis. HC can present with atypical forms such as large "globose" yeast and hyphal structure. This poses a diagnostic challenge for inexperienced pathologists or clinical microbiologists, who may mistakenly identify them as *Candida* or other fungal species. These atypical forms are primarily observed in intravascular tissue, emboli and heart valve tissue.

References

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