Detection of *Histoplasma capsulatum* in the Peripheral Blood

**Clinical History**

Mr. F. A. was a 27 year old gay Mexican-American male from Arkansas with AIDS and Kaposi's sarcoma of the palate. He had disseminated histoplasmosis, with lymph node and bone marrow cultures, which grew *H. capsulatum*, initially treated in 10/84 with Amphotericin B. Also, he had been recently treated with tobramycin for a Pseudomonas urinary tract infection. He was admitted on 1/24/85 with a five day history of fever to 104°F, shaking chills and nausea. His temperature was 94.0, pulse 100, respirations 30 and blood pressure 90/70. Blood cultures grew Pseudomonas species but no fungi, and he was treated with antibiotics. On 1/29/85 the WBC was 0.6, Hgb 5.7, Hct 17.1, plt 11,000. Rare polys had vacuoles, and metamyelocytes were present. A single poly had cytoplasmic inclusions, consistent with *Histoplasma capsulatum*. Subsequent buffy coat preparations revealed numerous yeasts, and were especially easy to identify at low power with a racked-down condenser viewing the end of the feather edge. The PT was 19.0, PTT 56.5, fibrin degradation products 1:60, and fibrinogen 275. He was thought to have sepsis and DIC, and was treated with fluids and antibiotics. His clinical course had a slight improvement with this therapy, but he subsequently expired 12 days later. An autopsy was not performed.

**Method**

A buffy coat is prepared from peripheral blood, Wright stained and examined at 10X magnification, starting at the tip of the feather edge where the white cells are concentrated. When the condenser is racked down, the *H. capsulatum* organisms occasionally appear as refractile bodies (1). Then the white cells are examined with a high dry or oil lens. One to ten yeast cells are present in the cytoplasm of polys or sometimes in monocytes. They may also be seen extracellularly, but this may be secondary to a ruptured white cell with loss of its contents to the periphery. The yeasts appear as spherical, dark-staining bodies measuring 2-4 μm, surrounded by a halo. This halo is actually a thick wall, not a capsule (2). The dark staining nuclei are usually more concentrated at one end, sometimes having a crescentic shape. These structures, when identified, are virtually pathognomic for histoplasmosis (3). The only other organisms that have a similar appearance are Leishmania species, but these have a brown-black staining kinetoplast (4).

**Clinical Applications**

Human infection with soil fungus *Histoplasma capsulatum* is largely asymptomatic and benign. In heavily endemic areas the entire human population is infected, and may be subjected to repeated episodes of reinfection, the vast majority of which are clinically silent. Symptoms closely associated in time with inhalation exposure
occur only when the inoculum is particularly heavy, causing the syndrome of acute pulmonary histoplasmosis.

A chronic pulmonary disease superficially resembling TB requires for its development the presence of pre-existing emphysematous air spaces, infection of which determines the clinical manifestations and progression of the disease. Rarely, due to some as yet poorly understood and probably transient immunologic defect which seems to inhibit intracellular fungicidal mechanisms on the part of the macrophage, the entire monocyte phagocytic system becomes, to one degree or another, involved with progressive intracellular infection which is fatal if not treated. The latter has come to be known as disseminated histoplasmosis.

*H. capsulatum* is a dimorphic fungus existing in mycelial form at room temperature and in yeast form at the body temperature of mammals. The infecting agent is an airborne spore which may be encountered in small numbers anywhere in the endemic area but occurs in large numbers under dusty circumstances where soil contains bird or bat excreta. It rarely may be transmitted via puncture wound or sexual contact.

The diagnosis of disseminated histoplasmosis depends on either the demonstration of histologically compatible intracellular organisms or a positive culture of blood or viable tissues. Histologic or cultural identification of *H. capsulatum* from caseous foci in the lung indicates only a persisting remnant of the primary infection. Caseous foci containing organisms and well-formed tuberculoid granulomas with very few organisms in the liver, spleen or visceral lymph nodes may represent either residua of the primary infection or chronic disseminated histoplasmosis. A positive blood smear or culture, ordinarily indicative of disseminated histoplasmosis may also represent a transient lymphohematogenous phase of a severe but non-progressive primary infection in clinically compatible circumstances (5,6), although no patients have been known to survive if they have disseminated histoplasmosis with *H. capsulatum* identified in the peripheral blood (2,7,8). A Wright stain smear or culture of the peripheral blood is usually positive in acute disseminated disease. The yield on blood smear may decrease to 50% in subacute disseminated disease and is negligible in chronic disseminated disease. Blood cultures are at times positive in subacute but not in chronic disseminated disease. Use ofuffy coat and silver stains should increase somewhat the positive findings in chronic and subacute disseminated disease (5).

Disseminated histoplasmosis has been recently reported in patients with AIDS (7-10), and rare reports of histoplasma fungemia with the diagnosis established first by visualization of organisms in blood or bone marrow (7,8,11). None of these patients survived.

**Technical Limitations**

There are no good data on the sensitivity of examining the peripheral blood for histoplasmosis, and prospective studies have not been performed (12). Although the estimated sensitivity is probably low, because unless sought for, it is likely that the organisms present in the blood were missed in the past. With a trained eye, however, the specificity may be quite high as only Leishmania species have a similar appearance. Sometimes, as in this case, despite overwhelming fungemia, blood
cultures may not grow the organism (secondary to concomitant Pseudomonas sepsis). In AIDS patients from endemic areas, buffy coats may facilitate the diagnosis of disseminated histoplasmosis.

References

1. Personal observation.


