Detection of *Histoplasma capsulatum* in the Peripheral Blood of an AIDS Patient

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**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 October 1984 with amphotericin B. Also, he had been recently treated with tobramycin for a *Pseudomonas* urinary tract infection. He was admitted on Jan. 25, 1985 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 Jan. 29 the WBC was 0.6, Hgb 5.7, Hct 17.1, plt’s 11,000. Rare polys had vacuoles, and metamyelocytes were present. A single body 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 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. Then the white cells are examined with a high dry or oil lens. One to 10 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 yeast appear as spheroidal, dark-staining bodies measuring 2–4 μm, surrounded by a halo. This halo is actually a thick wall, not capsule. The dark staining nuclei are usually more concentrated at one end, sometimes having a crescentic shape. These structures, when identified, are virtually pathognomonic for histoplasmosis. The only other organisms that have a similar appearance are *Leishmania* species, but these have a brown-black staining kinetoplast.

**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 in 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 nonprogressive primary infection in clinically compatible circumstances, although no patients have been known to survive if they have disseminated histoplasmosis with _H. capsulatum_ identified in the peripheral blood. A Wright stain smear or culture of the peripheral blood is usually positive in acute disseminated disease. The yield on a blood smear may decrease to 50 percent 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 of buffy coat and silver stains should increase somewhat the positive findings in chronic and subacute disseminated disease.

Disseminated histoplasmosis has been reported recently in patients with AIDS, and there have been rare reports of histoplasma fungemia with the diagnosis established first by visualization of organisms in blood or bone marrow. 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. Although the estimated sensitivity is probably low, 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, in this case, despite overwhelming fungemia, blood cultures may not grow the organism (secondary to concomitant _Pseudomonas_ sepsis). In AIDS patients from endemic areas,uffy coats may facilitate the diagnosis of disseminated histoplasmosis.

**References**

1. Personal observation.

**Q & A (continued from page 34)**

bodies as well as nonspecific chromatin was scored on 100 cells per case. DNA values were determined after Feulgen staining using a microspectrophotometer.

The incidence of double Barr bodies showed a significant increase in cases of dysplasia, carcinoma in-situ and invasive carcinoma. Correlated with this, the DNA histograms showed a decrease in the diploid mode and an increase in the tetraploid mode in those cases. Most cases that showed an excessive increase in nonspecific chromatin were early invasive carcinoma of the cervix. The authors concluded that this technique could be used to predict the presence of invasive carcinoma of the cervix, but noted that one cannot ascertain whether cells with two Barr bodies are tetraploid cells with no malignant potential or are malignant cells originating in carcinoma in-situ or microinvasive carcinoma.

**Raymond Schiffman, MD**

**Reference**