



Diagnosing *Histoplasma* by Antigen Detection

Presented by Lawrence Joseph Wheat, MD

Case Report

A patient with ulcerative colitis who was treated with a TNF blocker presented with respiratory symptoms but denied fever or weight loss. CT chest showed numerous parenchymal and pleural-based nodules and extensive mediastinal and bilateral hilar adenopathy. The patient underwent bronchoalveolar lavage and bacterial, fungal and mycobacterial stains were negative.

Subsequently a needle aspirate of a mediastinal lymph node revealed necrotizing granuloma and the GMS stain showed yeast suggestive of *Histoplasma capsulatum*. The urine antigen was negative but the serum antigen was 3.0 ng/ml.

Most physicians are familiar with the useful role of antigen detection for diagnosis of disseminated histoplasmosis^[1] but are not aware that both the urine and serum must be tested for optimal sensitivity. In an earlier review of histoplasmosis complicating TNF blocker therapy the serum antigen was positive but the urine antigen was negative in one case^[2]. In acute pulmonary histoplasmosis, the sensitivity for antigen detection was 83%, but 38% were positive only in the serum and would have been missed by testing only the urine^[3].

NOTE: These observations apply only to the MVista® Histoplasma Quantitative Antigen EIA performed at MiraVista Diagnostics.

Is There Value in Testing Serum + Urine for *Histoplasma* Antigen?

While many physicians are aware of testing urinary antigen to diagnose histoplasmosis, the practice of testing serum antigen for diagnosis is not as well-known. In fact, many physicians are surprised when they receive negative urine in a patient with disseminated disease. Trials performed at MiraVista Diagnostics' laboratory using the MVista® *Histoplasma* Quantitative Antigen EIA show:

- Testing both urine AND serum provides the highest sensitivity for *Histoplasma* antigen
- 38% of acute pulmonary histoplasmosis cases may not be properly diagnosed if only urine is tested
- 5-10% of progressive disseminated histoplasmosis cases may not be properly diagnosed if only urine is tested

Rationale

Manifestation

Acute Pulmonary

Progressive Disseminated

Limitation

- Urine antigen negative, but serum is positive in 38%
- Antibody requires 4-6 weeks

Urine antigen is negative:

- 5% immunocompromised
- 30% non-immunocompromised

Urine + Serum Antigen in Acute Pulmonary Histoplasmosis

Antigen	Percent
	N=29
Urine Only	3%
Serum Only	38%
Both	41%
Neither	17%



Consequence of Missed Diagnosis of Acute Pulmonary Histoplasmosis

Consequence

Percent

Hospitalization	27%
Acute Respiratory Failure	6%
Death	4%
Progressive Disseminated Histoplasmosis	3%

Outcome of Delayed Diagnosis of Pulmonary Disseminated Histoplasmosis

Delay in diagnosis is likely to contribute to the severity of infection as a result progression of disease in the absence of therapy. 5% to 10% of PDH cases may have antigenemia without antigenuria and may not be diagnosed until the illness has progressed in severity if only urine was tested.

Group	ICU	Death
Transplant (N=152)	32%	10%
TNF Blocker (N=98)	17%	1%
AIDS (N=141)	8%	4%

Assi 2013, Myint 2014, Vergidis IDSA 2011

PDH Cases with Negative Urine but Positive Serum Antigen

Over the past year, 12 patients with disseminated histoplasmosis have been identified in whom the serum antigen was positive but the urine antigen was negative in the MVista® *Histoplasma* Quantitative Antigen EIA.

Condition	Serum Ag-ng	Path/Cult Pos	Comment
Anti-TNF	1.7	none	recovered
Anti-TNF	1.8	ileum	sepsis, nearly died
Anti-TNF	3	node	recovered
Anti-TNF	0.3	none	recovered
Anti-TNF	0.52	lungs	pending
Anti-TNF	0.7	meninges	died
AIDS	0.3	none	pending
AIDS	0.4	skin	recovered
Elderly	1	tongue	recovered
Elderly	1.7	axillary node	recovered
None	0.3	none	recovered
None	4.2	skin	recovered

Summary

Results apply only to testing performed at MiraVista Diagnostics' laboratory using the MVista® *Histoplasma* Quantitative Antigen EIA :

- Testing both urine AND serum provides the highest sensitivity for *Histoplasma* antigen
- 38% of acute pulmonary histoplasmosis cases may not be properly diagnosed if only urine is tested
- 5-10% of progressive disseminated histoplasmosis cases may not be properly diagnosed if only urine is tested

References

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