

Nonculture Diagnosis of Central Nervous System Coccidioidomycosis

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CASE REPORT

A previously healthy young man from California presented with a one-month history of headache and intermittent fever. Physical examination was unremarkable. CSF contained 123 leukocytes/ μ l, 72% mononuclear cells. Protein was 103 mg/dl and glucose 26 mg/dl. No organisms were seen by cytology. Brain MRI revealed meningeal enhancement.



What is the most sensitive method for diagnosis of *Coccidioides meningitis*?



Answer | Combined *Coccidioides* antigen and antibody detection in CSF

Central nervous system (CNS) involvement occurs in up to half of cases of disseminated coccidioidomycosis (unpublished). Manifestations include meningitis, abscess, vasculitis, hydrocephalus and increased intracranial pressure. Diagnosis may be challenging.

Culture and cytopathology of CSF are rarely positive ⁽¹⁾ (Table). Detection of antibody by immunodiffusion (ID) and complement fixation (CF) have been the basis for diagnosis in most earlier studies. Others have reported sensitivities in CSF of 62% ⁽²⁾ and 83% ⁽³⁾ by CF and 73% by EIA ⁽²⁾. More recently detection of antigen was the most sensitive method ⁽¹⁾. Ongoing unpublished studies support these findings.

Test	Sensitivity (n= 42)	Specificity (n=88)
Antigen	93%	100%
Antibody-ID	67%	99%
Antibody-CF	70%	100%
Antigen & Antibody	98%	99%
Culture	7%	100%
Cytopathology	0%	100%

Deresinski opined in his review of the Kassis study ⁽⁴⁾ that two questions remained. First, he asked about cross-reactivity in other endemic mycoses. We have observed cross reactivity in CSF, but the number of observations is insufficient to provide percentages. We can provide data in serum: low level cross-reactivity occurs in 10% of patients with histoplasmosis or blastomycosis ⁽⁵⁾ (Figure 1). However, antigen concentration for the causative organism is higher than for the cross-reactive organism, facilitating correct diagnosis.

Second, Deresinski asked if antigen testing be used to monitor response to treatment ⁽⁴⁾. Antigen clearance from CSF is shown in two patients, one who responded

Figure 1

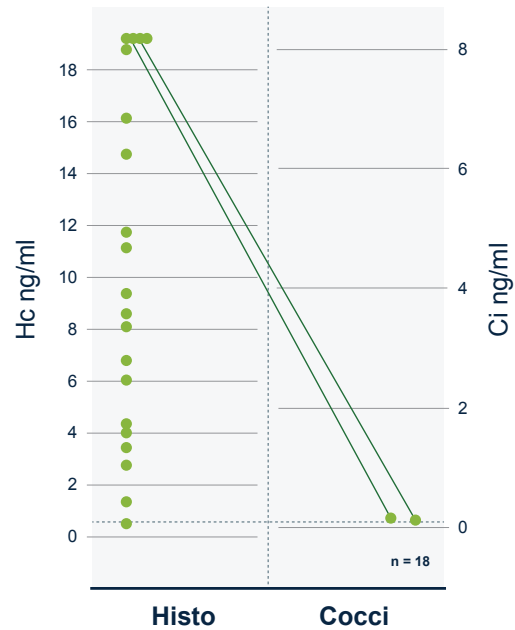
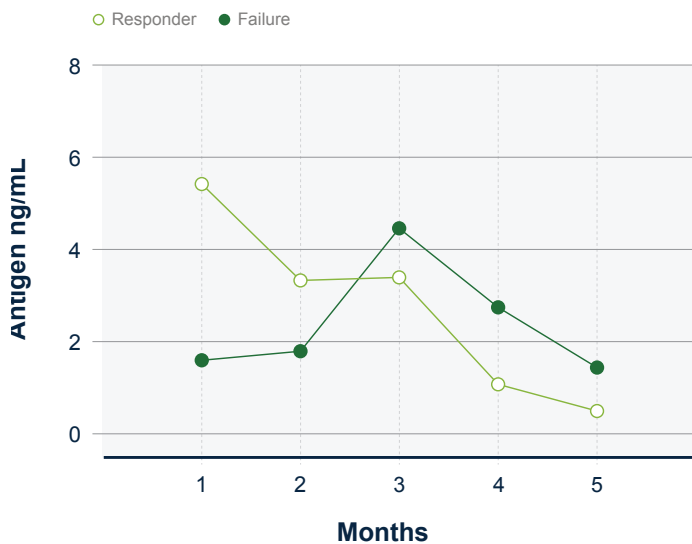


Figure 2



and another who failed treatment (Figure 2). The failing patient did not improve and subsequently progressed with the first treatment regimen, reflected by increasing antigen. Clinical improvement and reduction in antigen occurred following a change in treatment. A study of antigen clearance is in progress.

In summary, combined CSF antigen and antibody detection offers the most sensitive method for diagnosis of CNS coccidioidomycosis. Cross-reactivity among the endemic mycoses can be resolved by comparing antigen and antibody concentrations. Ongoing clinical experience supports antigen testing for monitoring outcome.

Reference List

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- (3) Bouza E, Dreyer JS, Hewitt WL, Meyer RD. Coccidioidal meningitis. An analysis of thirty-one cases and review of the literature. Medicine (Baltimore) **1981 May**;60(3):139-72.
- (4) Deresinski SC. Coccidioidal Meningitis: Diagnosis by Antigen Detection. Clin Infect Dis **2016**;62(1 January 2016):iii.
- (5) Durkin M, Connolly P, Kuberski T, et al. Diagnosis of Coccidioidomycosis with Use of the Coccidioides Antigen Enzyme Immunoassay. Clin Infect Dis **2008 Oct 15**;47(8):e69-e73.