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CLINICAL TREATMENT & MONITORING

Case Study: Blastomycosis Diagnosis

Case Study:

31-year-old man from Wisconsin presented with 4 weeks of respiratory complaints and fever after fishing in the Little Wolf River. Rales were present, respiratory rate was 33 breaths/minute, oxygen saturation 88% and chest CT showed diffuse nodular infiltrates and a mass in the right lower lobe. Testing included negative immunodiffusion (ID) antibody tests for blastomycosis and histoplasmosis but positive urinary antigen tests for both.

Key Questions:

1. **What is differential diagnosis?**
   a. Blastomycosis, histoplasmosis
2. **What further testing could be useful?**
   a. *Blastomyces* and *Histoplasma* IgG antibody detection EIA
3. **What treatment is recommended?**
   a. Itraconazole

Blastomyces dermatitidis is endemic in the Midwest, south-central and south-eastern parts of the US and Canada along bodies of water: Ohio, Mississippi, St Lawrence rivers and Great Lakes [1]. Soil containing bird guano favors growth of *Blastomyces* spp, and disturbances of the soil cause infection in humans and other mammals.

Culture: Culture of respiratory specimens are positive in most cases of pulmonary blastomycosis [2]. However, delays of up to 4-5 weeks can occur waiting for *Blastomyces* to grow [3].

Microscopy: *Blastomyces*' unique features provide for an accurate rapid diagnosis in most cases using KOH preparations or calcofluor white [3].

Antigen: Results using the second generation *Blastomyces* galactomannan antigen detection EIA found the sensitivity to be 90% and specificity 99% in urine [4], table 2. The same galactomannan is present in *Histoplasma* and antigen was detected in 96% of patients with disseminated histoplasmosis. Antigen was detected in serum in 57% of patients with blastomycosis. Other specimens that can be tested include bronchoalveolar lavage fluid (BALf), CSF and other sterile body fluids. Antigen detection is the most sensitive and rapid method for diagnosing most cases of blastomycosis. Sensitivity is highest in urine. Whether testing both serum and urine increases the sensitivity is unknown. In patients who undergo bronchoscopy, bronchoalveolar lavage for bronchial aspirates should also be tested for antigen. Sensitivity was 94% [5].

Antibody: MiraVista Diagnostics recently developed an IgG anti *Blastomyces* detection EIA as an LDT. Validation testing found sensitivity to be 94% (N = 35) and specificity 95% (N = 100). Table 2. The question arises whether antibody detection is warranted for diagnosis of blastomycosis given the high sensitivity of antigen detection. Most publications are biased towards more severe cases accounting for the high-sensitivity of antigen detection. Others reported the sensitivity to be 76% (45/59) [7]. Blastomycosis causes more severe illness than histoplasmosis but may be asymptomatic or self-limited [8]. Antibody detection using this EIA may be the method of choice for diagnosing acute self-limited or mild disease.

Table 1. Antigen Detection

Specimen	Sensitivity % (pos/tot)	Specificity % (neg/tot)
Urine	90% (41/46)	99% (197/199)
Serum	82% (9/11)	Not done

Table 2. Antibody Detection

Assay	Sensitivity	Specificity
IgG EIA	94% (33/35)	95% (95/100)
IgM EIA	Pending	Pending

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MVista® *Blastomyces* Antibody IgG EIA

TEST CODE: 331

CPT CODE: 86612

Clinical Significance

This assay indirectly detects anti-*Blastomyces* IgG by recognizing the BAD-1 repeat surface protein. During validation testing, the sensitivity was found to be 94.29% and specificity 95.00% with an assay cutoff of 14.0 EU. It offers an improvement over the current method of detecting antibodies by FID, where sensitivity has been reported as only 32%. Complement fixation is even less sensitive than FID.

The *Blastomyces* Antibody IgG EIA is useful for diagnosing blastomycosis in patients with negative antigen results. Secondly, when both *Histoplasma* and *Blastomyces* antigen assays are positive, comparing *Histoplasma* and *Blastomyces* antibody concentrations may assist in establishing the correct diagnosis. Additionally, following changes in antibody concentration via repeat testing may determine whether the infection has resolved or if relapse has occurred.

Methodology

Semi-Quantitative Indirect Enzyme Immunoassay (EIA)

Limitations

Specimens positive for *Histoplasma* capsulatum may cross-react with the *Blastomyces* Antibody EIA (IgG detection) and test positive (20% cross reactivity).

Specimen Collection

Serum: Collect serum specimens into a serum separator or red top tube. Allow blood to clot for 30 minutes, then centrifuge. Pipette serum separated from clot into a plastic screw cap vial.

Plasma: Plastic screw cap vial

Minimum Specimen Requirements

Serum: 0.5mL
Plasma: 0.5mL

Specimen Stability

Room Temperature: 30 days
Refrigerated: 30 days
Frozen: 30 days

Specimen Rejection

> 30 days old
> Two unique patient identifiers are required on the specimen container.
> Any specimen type other than serum

For specimen submissions that do not meet these criteria, please call Customer Service.

Transport Temperature

Ambient/Refrigerated/Frozen

Shipping

Ship to arrive Monday–Friday using a next day delivery service. Samples may be shipped on dry ice, frozen ice packs, or ambient.

Turnaround Time

Testing is performed on Mon, Wed, Thu and Fri.
Serum: Reported next day

Reference Range

Negative

Interpretative Information

Negative: <10.0 EU
Intermediate: 10.0 EU - 13.9 EU
Positive: 14.0 EU to ≥80.0 EU
Results should be correlated with clinical presentation and history.

Additional Information

This test was developed, and its analytical performance characteristics determined by MiraVista Diagnostics. It has not been cleared or approved by the FDA; however, FDA clearance or approval is not currently required for clinical use. The results are not intended to be used as the sole means for clinical diagnosis or patient management decisions.

Complete Test Information Available

https://miravistalabs.com/medical-fungal-infection-testing/anti-body-detection/blastomyces-igg-antibody-eia/

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