Semi-Quantitative IgG and IgM Anti-\textit{Coccidioides} Antibody Assay for Diagnosis of Coccidioidomycosis

Case report. A healthy young woman from California presented with low-grade fever, cough, arthralgias and painful bumps on her legs of two weeks duration. Temperature was 100.6°F and examination showed tender erythematous nodules on both legs. Chest radiograph demonstrated right hilar lymphadenopathy and a patchy infiltrate in the right lower lobe. Pertinent laboratory findings included 12% eosinophilia. Coccidioidomycosis was suspected but the \textit{Coccidioides} antigen and antibody tests (immunodiffusion [ID] and complement fixation [CF]) were negative.

Question. Do negative antigen and antibody test exclude coccidioidomycosis?

Answer. No. The diagnosis was acute pulmonary coccidioidomycosis (APC). Antigen is detected mostly in immunocompromised patients with disseminated coccidioidomycosis\textsuperscript{[1, 2]}. ID and CF are negative in 40-60\% of patients with APC\textsuperscript{[3]}. The diagnosis in this case was based on positive IgG and IgM antibodies in a new EIA\textsuperscript{[4]} (\textit{Journal of Clinical Microbiology} Feb 2017, 55 (3) 893-901). The IgG level was > 80 units and the IgM level were 73 units six weeks after onset of symptoms and declined over the next 16 months (Figure 1).

> READ MORE ON PG. 3

Meet Kairong Li, Ph.D.
Senior Research Scientist

We are pleased to welcome Dr. Kairong Li to MiraVista Diagnostics. He brings over 20 years of experience in life sciences to his new role as Senior Research Scientist, where his talents will be utilized to expand MiraVista’s scope into molecular diagnostics.

> READ MORE ON PG. 5
Do you accept specimens on Saturdays?

ANSWER

Yes, we accept shipments on Saturdays and offer Histoplasma and Blastomyces antigen EIA tests on Saturdays.

What specimen types do you test?

<table>
<thead>
<tr>
<th>Test</th>
<th>Specimen Type*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antigen: Histo, Blasto, Cocc</td>
<td>Urine, serum, BAL, CSF, plasma</td>
</tr>
<tr>
<td>Antigen: Asper</td>
<td>Serum, CSF, BAL</td>
</tr>
<tr>
<td>Antigen: Crpto LA</td>
<td>Serum, CSF</td>
</tr>
<tr>
<td>Antibody EIA</td>
<td>Serum, plasma, CSF</td>
</tr>
<tr>
<td>Antibody ID</td>
<td>Serum, plasma, CSF</td>
</tr>
<tr>
<td>Beta D Glucan</td>
<td>Serum, CSF</td>
</tr>
</tbody>
</table>

How do I ship the specimen?

ANSWER

a. Specimens should be shipped FedEx Priority Overnight or UPS Next Day.

b. 2-day delivery can be selected to reduce shipping costs if the delay in result time is acceptable to healthcare provider. If the client cannot send a specimen in time to meet the test date deadline for assays that are not run daily, (Antibody assay, FID), 2-day shipping may be a reasonable option for cost reduction.

c. Obtain a tracking number from your courier to ensure delivery of your shipment.

d. Schedule delivery:

1. For same day testing, 8:00am –10:30am EST. Use FedEx Priority Overnight or UPS Next Day Air. Note: not all tests are run daily. See chart.

2. Saturday 8:00 am – 10:30 am EST, select Saturday Delivery when creating the shipping request.
The study evaluating the new EIA included 103 patients with pulmonary (70%) or disseminated (30%) coccidioidomycosis. Most had been ill for several months and 75% were receiving antifungal therapy.

Sensitivity of EIA was higher than ID or CF (Table 1) and not affected by disease manifestation (p=0.308), immune status (p=0.498) or antifungal therapy (p=.760).

IgG specificity was 91% and IgM was 97% in healthy persons from areas where 70% are skin test positive. Cross-reactivity occurred in 32% of patients with histoplasmosis and 8% with blastomycosis. In histoplasmosis cases, antibody levels are lower in the *Coccidioides* EIA compared to the *Histoplasma* antibody EIA.

Moreover, IgG and IgM levels are highly reproducible, which is essential for quantification (Figure 2). Quantification facilitates determination of seroconversion and antibody clearance during treatment. **Summary.** The new antibody EIA offers major advancement in diagnosis and management of coccidioidomycosis. Cross reactions can be resolved by comparison of antibody levels to the related fungi. Background IgG levels of 10-20 units occur in about 10% of healthy subjects from highly endemic areas, overlapping those in patients with recent coccidioidomycosis. Repeat testing may differentiate active from past infection. Some cases are negative by EIA but positive by ID, supporting testing by both methods.

**Table 1**

<table>
<thead>
<tr>
<th>Disease</th>
<th>EIA</th>
<th>ID</th>
<th>CF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disseminated-31</td>
<td>84%</td>
<td>71%</td>
<td>68%</td>
</tr>
<tr>
<td>Pulmonary-72</td>
<td>92%</td>
<td>54%</td>
<td>65%</td>
</tr>
<tr>
<td>Immunocompromise</td>
<td>EIA</td>
<td>ID</td>
<td>CF</td>
</tr>
<tr>
<td>Yes-30</td>
<td>83%</td>
<td>50%</td>
<td>65%</td>
</tr>
<tr>
<td>No-73</td>
<td>90%</td>
<td>63%</td>
<td>65%</td>
</tr>
</tbody>
</table>
Reference List


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After earning his Ph.D. degree from Peking University, he moved to the United States to study genetic brain development and genetic disorders using the latest technologies in microbiology, molecular biology, genetics, genomics, biochemistry, etc. During this period, he published nearly twenty research papers in peer-reviewed journals and received many awards, such as the “Youth Investigator Award” from the Children’s Tumor Foundation. Prior to joining our company, he worked at BioGX to design and develop high complexity molecular microbial diagnostic products utilizing real-time PCR and Next Generation Sequencing-based technologies. He took a leading role in multiple cross-departmental teams to improve product transfer, manufacturing, and quality control for new product development.

We’re thrilled to have him join our team!

Progress on our Building Expansion
MiraVista Diagnostics attended:
> Dr. Wheat hosted a dinner with colleagues to discuss “New Developments in the Diagnosis of Coccidioidomycosis” | **June 6, 2019**, Phoenix, AZ

Upcoming events:
> American Association of Clinical Chemistry, 71st AACC Annual Scientific Meeting & Clinical Lab Expo | **August 4-8**, Anaheim, CA.
> Infectious Disease Society of America, ID Week | **October 2-6**, Washington, DC.