



FEATURED ARTICLE

Semi-Quantitative IgG and IgM Anti-*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 *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^[1, 2]. ID and CF are negative in 40-60% of patients with APC^[3]. The diagnosis in this case was based on positive IgG and IgM antibodies in a new EIA^[4] (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).

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

Figure 1

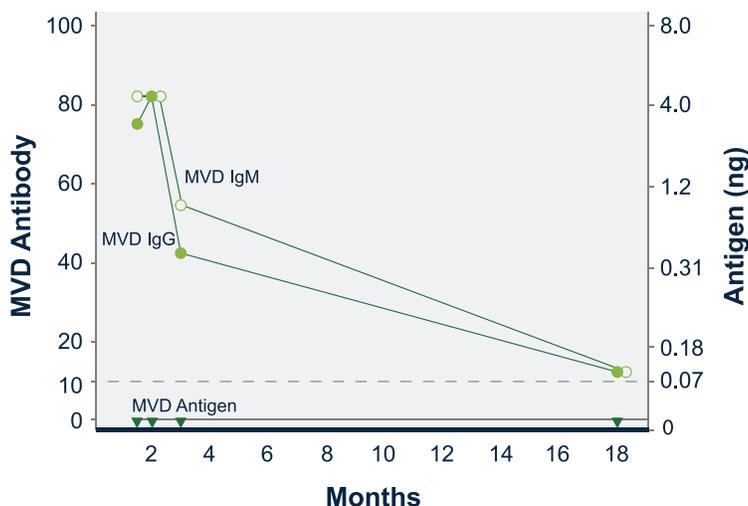


Table 1

Sensitivity Comparing Manifestation and Immunity

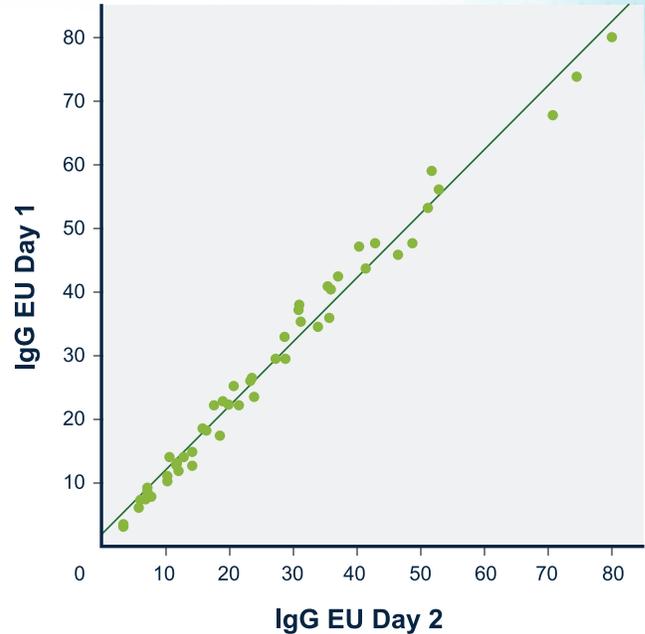
Disease	EIA	ID	CF
Disseminated-31	84%	71%	68%
Pulmonary-72	92%	54%	65%
Immunocompromise	EIA	ID	CF
Yes-30	83%	50%	65%
No-73	90%	63%	65%



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.

Figure 2



Reference List

- (1) 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.
- (2) Durkin M, Estok L, Hospenthal D, et al. Detection of coccidioides antigenemia following dissociation of immune complexes. *Clin Vaccine Immunol* **2009 Oct**; 16(10):1453-6.
- (3) Blair JE, Chang YH, Cheng MR, et al. Characteristics of patients with mild to moderate primary pulmonary coccidioidomycosis. *Emerg Infect Dis* **2014 Jun**; 20(6):983-90.
- (4) Malo J, Holbrook E, Zangeneh T, et al. Enhanced Antibody Detection and Diagnosis of Coccidioidomycosis with the MiraVista IgG and IgM Detection Enzyme Immunoassay. *J Clin Microbiol* **2017 Mar**; 55(3):893-901.