Histoplasma capsulatum Antigen Detection: Comparison of the Performance Characteristics of a New Inhibition Immunoassay to Those of an Established Antibody Sandwich Immunoassay

Dr. Beatriz L. Gomez and colleagues described a new inhibition immunoassay for the diagnosis of histoplasmosis (1). My laboratory developed and extensively evaluated an antibody sandwich immunoassay for this purpose. It is important to contrast the two methods, as their performance characteristics differ.

The characteristics of the assay developed in my laboratory are high sensitivity in disseminated histoplasmosis but less sensitivity in pulmonary and chronic pulmonary histoplasmosis, with greater sensitivity in urine, cross-reactions with Blastomyces dermatitidis, Paracoccidioides brasiliensis, and Penicillium marneffei, but not with Aspergillus spp., Cryptococcus spp., and Mycobacterium tuberculosis (2). The report by Gomez et al. demonstrated cross-reactivity in their inhibition assay with Aspergillus spp. (20.00%), Cryptococcus spp. (10.00%), and M. tuberculosis (22.22%) (1).

Results obtained by using the inhibition immunoassay reported by Gomez et al. differ from ours in several respects. Detection in serum is more sensitive than in urine, and significant cross-reactivity is noted with Aspergillus spp., Cryptococcus spp., and M. tuberculosis. Furthermore, 2.27% of the normal human sera tested false positive for Histoplasma capsulatum. Also, the sensitivity in cases of acute pulmonary histoplasmosis (88.85%) was greater than in cases of disseminated histoplasmosis (non-AIDS, 62.50%; AIDS, 72.72%). In our experience the sensitivity is higher for disseminated disease (urine 92%, serum 82%) than for acute pulmonary disease (44%) (3).

In conclusion, the detection characteristics of the inhibition immunoassay differ considerably from those of the antibody sandwich immunoassay, raising concern about the accuracy and usefulness of the inhibition immunoassay.

REFERENCES

Authors’ Reply

We would like to take the opportunity to respond to Dr. Wheat’s comments regarding the recent publication (1) in which we describe a novel test for the detection of Histoplasma capsulatum antigen in sera. Dr. Wheat has highlighted three variations in the inhibition immunoassay we describe compared to the antibody sandwich immunoassay developed in his laboratory. These are (i) differences in the spectrum of cross-reactivity, (ii) differences in the sensitivity in serum relative to that in urine, and (iii) differences in the sensitivity of the tests as applied to distinct patient groups.

We are somewhat perplexed to find that he uses these differences to conclude that the inhibition immunoassay is of questionable accuracy and usefulness. It seems to us that Dr. Wheat is overlooking the profound differences in the nature of the diagnostic test we described compared to his own assay. The inhibition assay we describe uses a murine monoclonal antibody to detect a 70-kDa protein. This novel antigen is currently being characterized. Dr. Wheat’s test uses a polyclonal serum in a radioimmunoassay to detect polysaccharide antigen.

As the two antigens being detected, the reagents being used, and the methodologies adopted are all vastly different, is it not surprising that there should be differences between the test results? This being the case, is it not disingenuous to then use such differences to conclude that one test is of questionable value? We have now followed up our original observations with a second paper describing the use of this inhibition assay (2), which to us, at least, confirms that there is some merit in the test. We have always believed that there are advantages in developing different approaches to the same clinical problem and feel that our inhibition enzyme-linked immunosorbent assay, while by no means a perfect assay, has something to contribute to the diagnosis of histoplasmosis.

REFERENCES

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