Letters to the Editor

Rapid Immunochromatographic Assay for Diagnosis of Tuberculosis: Antibodies Detected May Not Be Specific

We read with interest the letter by Grobusch et al. (3) on a rapid immunochromatographic assay for the diagnosis of tuberculosis but wish to present evidence that this test may not be as specific as they portrayed it to be.

It was long thought that the 38-kDa antigen of Mycobacterium tuberculosis (MTBC) (1) was associated with disease in immunocompetent hosts, in distinction to M. avium, which does not possess the antigen. Thangaraj et al. (8) that possession of the antigen may be associated with virulence, demonstrating the presence of a common immunodominant antigen in the three species of mycobacteria (MTBC organisms, M. intracellulare, and M. malmoense) which cause disease in immunocompetent individuals. These findings may have important implications for vaccine studies.

However, it is also clear from our results and those of Thangaraj et al. that the detection of antibodies which react with the 38-kDa antigen of M. tuberculosis cannot be taken to indicate infection or disease due to MTBC organisms alone, since such antibodies may also be evoked by infection or disease with M. intracellulare or M. malmoense.

REFERENCES

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Author’s Reply

Wheeler and colleagues provide interesting in vitro data suggesting that homologues of the *M. tuberculosis* 38-kDa antigen found in *M. intracellulare* and *M. malmoense* also lead to antibody production in humans. However, clinical data to support their findings are lacking so far. If, as speculated by Thangaraj et al. (4), mycobacterial virulence is enhanced by the possession of a homologue of the *M. tuberculosis* 38-kDa antigen, skepticism arises from the lack of demonstration of the antigen and the appropriate gene sequence, at least for *M. kansasii*, another species well capable of causing tuberculosis-like disease in immunocompetent individuals (2).

The sera of immunocompetent individuals investigated in our study (3) cited by Wheeler et al. were from patients with clinical signs and symptoms suggesting tuberculosis, and in all of those who were antibody positive, diagnosis was confirmed by culture—that is, showing that in our small collective seropositivity indicated not merely the presence of the antigen (infection) but overt disease caused by *M. tuberculosis*. In one case, specimens growing non-*M. tuberculosis* mycobacteria stemmed from an immunocompetent seronegative patient with tuberculosis-like pulmonary disease caused by *M. kansasii*. Unfortunately there was no case of *M. malmoense* infection among our patients, which would have given at least anecdotal evidence for or against the notion of Wheeler et al. As reported, Cole et al. (1) and Zhou et al. (5) found specificities of 92 to 93% for the rapid immunochromatographic assay in large trials performed in China, but isolation of mycobacteria other than *M. tuberculosis* in those cases labelled false positive were not reported.

Further research should aim to elucidate whether the 38-kDa antigen homologues identified in various mycobacteria are a common feature of species capable of causing tuberculosis-like disease, and diagnostic trials should allow a judgement on whether human antibody response to the 38-kDa antigen should serve as an indicator for mycobacterial disease requiring treatment, rather than only for tuberculosis, in the nonimmunocompromised patient.

REFERENCES


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