Whipple’s DNA Is Not Whipple’s Disease

Sloan et al. report a real-time PCR method using the hsp65 gene of Tropheryma whipplei for a target sequence as a new and rapid diagnostic test for Whipple’s disease (7). We and others have already published real-time PCR-based methods for the detection of T. whipplei DNA using 16 rRNA or other gene target sequences (2–4, 9).

The problem with diagnosing Whipple’s disease, however, lies beyond the sensitivity or speed of the PCR test used. DNA of T. whipplei has repeatedly been shown to be present in human samples from healthy people without Whipple’s disease (8, 9). In our study, 4 out of 10 healthy individuals harbored DNA of T. whipplei in gingival plaque (9). Whipple’s disease is thought to be caused by a not-yet-characterized immune defect rendering the host prone to the bacterium T. whipplei. The hallmark of Whipple’s disease is the histopathological finding of macrophages containing diastase-resistant p-aminosalicylic acid (PAS)-positive material, which are T. whipplei bacteria or partly digested remnants thereof. In patients with Whipple’s disease, tissue macrophages are unable to kill and clear T. whipplei. This deficiency in killing then causes Whipple’s disease (5). The postulated immune defect can be simulated in vitro by the deactivation of human macrophages by interleukin-4; the human macrophages are then unable to kill T. whipplei (6). Therefore, histopathological examination and staining of tissue biopsies (PAS/diastase-PAS staining) are essential for the diagnosis of Whipple’s disease. The mere presence of DNA of T. whipplei, as demonstrated by PCR, without a demonstration of the macrophages harboring it, is not Whipple’s disease. It remains doubtful whether clinical syndromes which are non-specific (such as polyarthritis) plus demonstration of DNA of T. whipplei alone, without demonstration of PAS-positive macrophages (i.e., immunodeficient macrophages unable to digest T. whipplei), qualify as some kind of forme fruste of Whipple’s disease (1).

REFERENCES


Authors’ Reply

We agree with Schneemann and colleagues that a positive PCR result for T. whipplei in human specimens should be interpreted in the context of clinical signs and symptoms of the patient and corroborating laboratory data, including the results for PAS staining of specimens.

As the title of our article summarizes, the intent of our study was to compare a new PCR method, real-time PCR, to conventional PCR for detecting T. whipplei in human specimens. As we state in the Discussion, the real-time PCR method was comparable in accuracy to the conventional PCR method, but the real-time PCR method was much faster and much easier to perform. Our intent was not to prove the clinical significance of a positive PCR result for T. whipplei in human specimens.

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