Author's response to reviews

Title: Reversible hypothyroidism and Whipple disease

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THE BIOMED CENTRAL EDITORIAL TEAM

To Whom It May Concern:

RE: MS - 1162385350809512 (REVERSIBLE HYPOTHYROIDISM AND WHIPPLE DISEASE)

Thank you for the email dated November 14th, 2005 regarding the above. My responses the reviewers’ comments are as follow:

REVIEWER 1 (PROFESSOR DIDIER RAOULT):

1. The negative controls included DNA isolate from E. Coli and normal duodenal tissues from two patients. None sustained amplification. The size of the amplicon was 160 base pairs. The PCR products were analysed by agarose gel electrophoresis, stained with ethidium bromide, and visualised under UV light. Both strands of the PCR product were sequenced and the results compared to 16S rRNA gene sequences deposited in GenBank and EBML databases by mean of University Wisconsin Genetic Computer Group (GCG) software package (Madison, Wisconsin).

2. Immunohistochemistry is not available routinely and thus was not performed. Agreeably, PAS positivity, commonly seen in Whipple disease is non-specific.

3. The link between the putative Whipple’s disease and hypothyroidism has been further discussed.

4. The majuscule in T. whippleii has been uniformly removed.

REVIEWER 2 (PROFESSOR THOMAS MARTH)

Major Compulsory Revisions:

1. Gratefully and as directed, the reference by Rodarte JR (Arch Intern Med, 1972; 129: 479) has been reviewed and included in the discussion.

2. Agreeably, there is no direct evidence of thyroid involvement by T. whippleii other than the temporal relationship between the response to antibiotic therapy and the incomplete recovery of thyroid reserve.

3. The role of low circulating protein level associated with malabsorption in the presence of hypothyroidism has been discussed as requested.
Minor Essential Revisions:

1. The normal thyroid volume quoted in the original manuscript was thought to be correct and the author respectfully asks the reviewer to refer to the following references for confirmation: Barrere X et al., Clin Endocrinol, 2000; 52: 273-278 and Wesche MFT et al., Clin Endocrinol (Oxford), 1998; 48: 701-706.

2. Levo-thyroxine was indeed the formulation used. Lio-thyronine was not considered and in retrospect would have added more evidence to the malabsorptive state.

3. More clinical details have been included in the clinical note section. The neurology of TW is very interesting although in the absence of clear-cut neurological symptoms and an excellent clinical response, no consideration was given to the further investigation of the central nervous system, including MR imaging and CSF examination.

4. With apologies, as part of a negative control, it was Mycobacterium Tuberculosis that was cultured for, not TW. The PCR was performed at our reference laboratory and more details are included in the revised manuscript, including the PCR amplicon and sequence analysis.

5. It is much appreciated that using peripheral blood mononuclear cells to monitor WD is unreliable. Ideally, a repeat endoscopy would add further information to the resolution of WD but this was not done, again based on the clinical response.

6. The fact that WD affects the all portions of the small bowel and rarely the colon has been emphasized in the revised manuscript.

I am grateful for the reviewers’ direction and guidance.

With kind regards and it is hoped that the revised manuscript is to the reviewers’ excellent standard.

Yours Sincerely,

Huy A Tran

HUY A. TRAN