LETTER TO THE EDITOR

Mycobacterium avium paratuberculosis and Crohn’s Disease: An association requiring more research

Dear Sir,

I wish to respond to Dr. Van Kruiningen’s recent viewpoint article entitled, “Where are the weapons of mass destruction— the Mycobacterium paratuberculosis in Crohn’s disease?” 1 By emphasizing the studies which do not find an association of Crohn’s disease (CD) and Mycobacterium avium paratuberculosis (Map) and dismissing the positive studies he implies that this association is still controversial. At this point, two meta analyses have concluded that this association is established.2,3 The debate has shifted to whether Map is causative of CD or inconsequential in the disease.

Van Kruiningen suggests that only two possibilities exist for the discrepancies between negative and positive studies—false positives and sample contamination. He does not include the possibility of false negative studies. A single example illustrates the pitfalls of this oversight. Van Kruiningen states that “Freeman and Noble, in 2005, repeated the methods of Naser et al. on 22 patients and were unable to culture MPTB.” In fact, Naser and Collins pointed out that Freeman and Noble did not repeat their methods since they used culture medium which does not support the growth of Map and they did not describe using controls.4

Van Kruiningen invokes a common fallacy of this debate. He quotes the conclusion of Selby in the Australian trial that the failure of antimycobacterial drugs to provide a sustained benefit does not support a significant role for Map in the pathogenesis of CD. The failure to cure the disease does not disprove mycobacterial causation. Buruli ulcer is a well recognized mycobacterial infection for which there are no currently effective antimycobacterial drugs. It would be a fallacy to conclude that mycobacteria are not involved in the pathogenesis of Buruli ulcer because our known antimycobacterial drugs do not cure it.

In his discussion, the author does not mention recent genetic studies from the human and veterinary literature which lend further support to the mycobacterial hypothesis. Recent work has shown that the same genetic mutation (CARD 15/NOD2) is found in leprosy patients, cattle with Johne’s disease which is caused by Map and in CD patients.5,6 It is improbable that a bacterium which causes disease in so many animal species including primates,7 is a harmless commensal in the genetically susceptible human host. Fortunately, other scientists are ignoring Van Kruiningen’s concluding advice to move on and find the real agent responsible for this disease. Commencing in early 2012, Redhill Biopharma will conduct United States and European multicenter, controlled clinical trials of combination rifabutin, clarithromycin and clofazimine. In contrast to the Australian trial, the study will include Map testing and the drug dosages will be higher. These important studies should provide greater understanding of the role of Map in CD and focus necessary attention on this elusive and enigmatic zoonotic bacterium.

Conflict of interest statement

I am a shareholder of RedHill Biopharma which will be conducting an upcoming clinical trial of antimycobacterial therapy in Crohn’s disease. The trial will begin in 2012. Otherwise, I have no other conflict of interest.

References


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