Comment on: Possible miliary tuberculosis during adalimumab therapy with negative γ-IFN release assays: reply

Sir, We would like to thank Mangat et al. [1] for their interest in our article [2] and would like to make the following comments.

We did not isolate any organisms including non-tuberculous mycobacterium (NTM) from sputum or bronchoalveolar lavage fluid. NTM infection is rare in the immunocompromised patient with otherwise structurally normal lungs, more frequently affecting those with chronic lung disease such as chronic obstructive pulmonary disease or bronchiectasis (which was not present in this patient). NTM are also ubiquitous throughout the environment [3] and identification of these organisms, particularly if confined to a positive mycobacterium PCR, would not necessarily confirm these as the causative organism even in the absence of tuberculous mycobacterium. We agree, however, that a positive PCR result for Mycobacterium tuberculosis (MT) would have been of interest, but it was not locally available. Because of rapid deterioration in an immunocompromised patient, the decision to treat empirically for tuberculosis was essentially made on clinical grounds. The patient did not develop significant evidence of side effects (e.g. liver toxicity) and, hence, in the absence of microbiological confirmation, risks of inadequate treatment outweighed the risks of continuing treatment.

If this case does in fact represent NTM infection then these opportunistic organisms may potentially cause significant disease in patients treated with anti-TNF. Duration of treatment in NTM is often longer than for MT, however; in this case, the cause of immunosuppression was withdrawn. The patient was followed up during and after the completion of treatment and has not suffered relapse.

We would agree with Mangat et al. that an ELISPOT test is potentially more informative in immunocompromised patients. Our patient did have this test prior to commencing anti-TNF therapy as part of the RHAPSODY trial protocol, but it was not available locally when she became unwell. From the limited head-to-head comparison data available, the pooled sensitivity of TBSPOT-TB, while greater than QuantiFERON Gold, is still not complete. Recent national guidelines for tuberculosis diagnosis [4] and an NHS Health Technology Assessment [5] have reviewed the use of γ-IFN assays in latent tuberculosis and briefly considered the use of γ-IFN release assays to rule out active infection. Caution should be exercised for both MT and NTM infection in the immunocompromised patient. The current national guidelines for assessing risk and managing MT infection in patients who are due to start anti-TNF therapy do not yet consider these issues [6].

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