Author’s response to reviews

Title: Nontuberculous Mycobacterium Infection Complicated with Haemophagocytic Syndrome: A Case Report and Literature Review

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Dear editor,

Thanks for your comments and suggestions. For your questions:

1. Why would this patient have disseminated NTM infection? Did she receive comprehensive immune check? What were the results?

We tried to find out if the patient had any underlying immunosuppressive conditions. But she had no history of taking immunosuppressive drugs, no history of recurrent infection or relevant family history, and no symptoms suggesting possible autoimmune diseases (eg. lupus, vasculitis, Still’s disease). Image studies like thoracic abdominal and pelvic CT scan showed no signs of malignancy. After admission, we also evaluated the patient’s immune state. The counts of B cells, T cells and NK cells were all decreased (B cell 7/ul↓, CD4+T cell 101/ul↓, CD8+T cell 94/ul↓, NK cell 6/ul↓, CD28+CD8+T cell 49/ul↓) while the level of immunoglobulins (IgG, IgA and IgM) were within normal range. Her anti-HIV Ab test was negative. We doubt the decrease of the patient’s lymphocytes and NK cells might be the result, rather than the cause, of her NTM infection since her B cell, T cell and NK cell counts gradually rose to near-normal levels after treatment. Auto-antibodies like ANA and ANCA were also negative.

But we still can not rule out the possibility that our patient might have undiscovered immunosuppressive conditions. One of the cases we reviewed in the article was found to have advanced femoral sarcoma 5 months after being diagnosed with disseminated NTM infection. Since our patient, unfortunately, lost follow-up 6 months later, we didn’t have the opportunity to perform a more thoroughly investigation of underlying immunosuppressive conditions like malignancy.
2. Where was the port of entry for the mycobacteremia? Was there any other focus of NTM involvement?

M. intracellulare was grown from both the blood culture and the cervical lymph node biopsy tissue culture of the patient. Her chest CT scan also revealed bilateral nodules and right pleural effusion indicating possible pulmonary involvement, even though no pathogens were successfully grown from the patient’s sputum. No other focus of NTM involvement was found. M. intracellulare is reported to exist wildly in the environment and the lung is the most common organ involved in M. intracellulare infection. Thus, we suspect that the port of entry of the mycobacteremia might be from the respiratory tract, as is usually seen in patients with disseminated M. intracellulare infection.

3. Was the patient seropositive for interferon-gamma autoantibody? I think this is an important and obligatory test for such a patient.

As a matter of fact, adult-onset immunodeficiency was suspected. But, unfortunately, serum test for interferon-gamma autoantibody hasn't been available in most areas in China until recently. So we were not able to verify our suspect before the patient was discharged and then lost follow-up.

We sincerely thank you for your comments and we have made some adjustment and clarification in our article, especially more discussion about the possible port of entry of M. intracellulare and the suspect and limitation on the exploration of possible underlying immunosuppressive conditions, hoping to discuss more deeply and provide more information about our case.

Last but not least, although our work is far from perfect, yet to our knowledge, this is the first time NTM cases complicated with HPS have been summarized and reviewed. We do hope our work might call attention to clinicians with this particular condition and inspire further investigation and study in this area.

As mentioned in your letter, the language of the manuscript has been revised by American Journal Experts and we will upload the editorial certificate.
Yours sincerely,

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