Reviewer's report

Title: Two patients with intestinal failure requiring home parenteral nutrition, a NOD2 mutation and tuberculous lymphadenitis

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Reviewer: Shahin Shafiani

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In this manuscript, Schaffler et al. report two patients with intestinal failure who developed fever and weight loss during HPN. Catheter related infections were ruled out and FDG uptake in mediastinal lymph node suggested tuberculous lymphadenitis. Presence of Mtb was confirmed in one case and indirect evidence was used in the other case to initiate anti-tuberculosis chemotherapy, which resolved the infection in both cases. This study is novel and important in that it highlights the need to detect other infections than those caused by catheter use, particularly in patients that also harbor NOD2 mutations.

I recommend publication in BMC Gastreoenterology after addressing the following points:

The recommendation by the authors to “include tuberculous lymphadenopathy as a specific differential diagnosis of suspected catheter related infection in patients with intestinal failure who carry mutations in their NOD2 gene” is too broad a recommendation based on these two cases, because:

The link between the three NOD2 mutations (R702W, G908R, and 1007fs) and mycobacterial infections is not as strongly established as they are with Crohn’s disease, particularly in Caucasian people. While R702W causes susceptibility to tuberculosis in African Americans, R702W, G908R and 1007fs mutations are not associated with tuberculosis in S. Africa and R702W is not associated with tuberculosis in India. In the absence of robust epidemiological data linking certain NOD2 mutations in Caucasians with susceptibility to tuberculosis, it might be a stretch to conclude that these two mutations alone (though a risk factor for intestinal failure) could have been responsible for tuberculoid lymphadenitis when the patients have been under prolonged treatment and HPN, and as a result may have a weakened immune system predisposing them to other infections. In particular, it seems likely that the second patient could be infected with non-tuberculoid mycobacteria, which are ubiquitous but cause opportunistic infections.

In addition, there are no strong data linking NOD2 specifically to “extrapulmonary” tuberculosis.

Rewriting parts of discussion to highlight the possibility of infections, particularly tuberculosis, in patients with NOD2 mutations other than those caused by catheter reflects these findings more precisely. The authors can suggest further
investigation of NOD2 mutations in patients with intestinal failure as a possible future prognosis for predisposition to tuberculosis.

The Materials and Methods should expand to include other procedures performed such as PCR for Mycobacterium, bacterial detection etc.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

"No" to all of the above.