Author’s response to reviews

Title: Spontaneous remission of Crohn's disease following a febrile infection: case report and literature review

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Author’s response to reviews: see over
Dear Rachel Neilan,

Our reply to the referee comments is listed below:

**Referee 1**
1. The comments from referee 1 is that we should shorten the paper, and reduce the speculative comments. We have shortened the paper and reduced speculative comments.

**Referee 2**
1. The comments from reviewer 2 are that we should consider adding information on chronic granulomatous disease and chronic variable immune deficiency. As these are more recent clinical entities, they post-date the era when fever therapy was tried in inflammatory bowel disease. However, as per the reviewer suggestion, we examined the literature for cases of spontaneous remission of these diseases in association with fever, but could not locate any such reports.

2. The reviewer asked about the surgical and pathology report. Unfortunately, this report was very cursory with no mention of whether there was a change in the fistula/abscess at surgery relative to the endoscopy that was carried out a month previously.

3. We have had a physician review the case report with respect to terminology as requested and made necessary changes.

4. The patient’s URI-related symptoms have been added as suggested.

5. The reviewer asked for clarity on antibiotic usage preceding the surgery. This treatment was instituted for the fistula-associated abscess. This has been corrected in the text.

6. The reviewer asked for a description of the patient’s respiratory symptoms during her upper respiratory infection. This has been added.

7. The other comment was that including information on ulcerative colitis was confusing. Crohn’s disease was first described by Burrill Crohn in 1932, where he stated that the disease simulates the clinical characteristics of ulcerative colitis.\(^1\) Epidemiologic studies have shown a continual increase in the incidence of IBD over the last five decades.\(^2\) The rising incidence of IBD is largely due to the increase in Crohn’s disease.\(^2\) Thus during the era in the 1920s and 1930s when ulcerative colitis was treated with fever therapy, we do not know if this included cases of Crohn’s disease as well because this latter condition was both not well recognized nor as prevalent as it is today. We did include the case series by Lobel et al which included cases of both conditions going into remission following fever. Moreover, medications currently used in the divergent categories of aminosalicylates, immunosuppressives, corticosteroids, and biologics are similarly used to treat both conditions. Thus, if fever were therapeutic for one condition then one would expect a similar response for the other. Therefore, we believe that
including information on ulcerative colitis is highly relevant with respect to this case report.


Let us know if there are any further questions.

All the best,

J. P. van Netten
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