Reviewer's report

Title: Ano-rectal stenosis after treatment with Anti-TNF alpha antibodies: a case series

Version: 1 Date: 8 December 2009

Reviewer: Joel E Mawdsley

Which of the following following best describes what type of case report this is?: Unreported or unusual side effects or adverse interactions involving medications

Has the case been reported coherently?: Yes

Is the case report authentic?: Yes

Is the case report ethical?: Yes

Is there any missing information that you think must be added before publication?: Yes

Is this case worth reporting?: Yes

Is the case report persuasive?: Yes

Does the case report have explanatory value?: Yes

Does the case report have diagnostic value?: No

Will the case report make a difference to clinical practice?: No

Is the anonymity of the patient protected?: Yes

Comments to authors:

This case series is a clear description of three cases of patients with rectal and colonic CD developing anorectal stenosis after treatment with infliximab. In 2 of the cases the stenosis developed shortly after treatment, whilst in the third it was several years. The authors explain this delay by stating that stenosis had noted at an endoscopy shortly after treatment but the patient only became symptomatic several years later. The authors postulate that the infliximab treatment was causative in the development of stenosis due to the lack of other obvious factors such as anal surgery or active inflammation at the time of the endoscopy.

Points to Authors
1. Abstract section, subheading Aim - the authors state that they determined any
factors which put these patients at risk of developing stenosis. However, factors were not examined other than it was noted that none of the patients had had anal surgery or active inflammation at the time of the endoscopy. This phrase could be construed as suggesting that comparison was made to a cohort of patients who did not develop stenosis which was not the case. I think the phrase is misleading and should be removed.

2. Introduction - second paragraph. This paragraph describes the common adverse events of infliximab such as opportunistic infections. It is largely irrelevant to the case report. Better would be a mention of concerns of small bowel stenosis due to infliximab (see point 6).

3. Case 1 - It is not stated in this case report if the patient had perianal fistulising disease. This is of relevance. When his disease reactivated in 2007, it is not stated if this was peri-anal disease or if there was rectal inflammation on endoscopy. This is of key relevance as the authors postulate that it is the aberrant healing of rectal disease which lead to the rectal stenosis. Also the dose of infliximab given and adalimumab is not stated.

4. Case 2 - It is stated that the patient had colonic Crohn's but the distribution is not given. Again whether there was active rectal or perianal disease prior to infliximab use is not stated. The dose and number of infliximab doses given is not stated.

5. Case 3 - Again the distribution of rectal disease and the presence of peri-anal disease is not stated. The timing of the colonoscopy when the stenosis was first noted in relation to infliximab being given is not stated or if this was the first endoscopic examination after infliximab use. If the interval were long or this was not the first endoscopy it would detract from the suggestion that the infliximab was a causative agent. Again the dose and number of infusions of infliximab given is not stated.

6. Conclusion. No reference is made to the fact that when infliximab was first used there were major concerns that rapid mucosal healing might lead to stenois, most notably in the small bowel. However, this has largely now been disproven as a concern. Infliximab has been used successfully in small bowel stenosing disease without problem (Pelletier AL et al. 2009, Pallotta N et al 2008.) and I would think this to be of relevance to this case series as the putative mechanism of aberrant mucosal healing is the same. Large trials of infliximab in fistulising CD (including peri-anal CD) have not reported stenosis as a complication which also might be mentioned. I am not sure of the relevance of the sentence and reference to TNF levels in wound fluid and topical infliximab for wound healing.

7. All three cases are written with initials and given in the present tense. This could be removed to further protect patient anonymity depending on the journals preferred style.

Quality of written English: Acceptable

Declaration of competing interests:
'I declare that I have no competing interests'