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Golimumab may induce exacerbation of inflammatory bowel disease when it is used for the treatment of ankylosing spondylitis: A case report with a review of literature.

--Manuscript Draft--

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Abstract:	Golimumab is a human IgG monoclonal antibody specific for human tumor necrosis factor alpha (TNF- α). Golimumab has been approved for use in rheumatological conditions; however, its use in inflammatory bowel disease (IBD) is still in clinical trials. We report a case of an exacerbation of ulcerative proctitis after starting on golimumab for ankylosing spondylitis (AS).

John C. Somberg, MD,
Editor-in-chief,
The American Journal of Therapeutics.

May 4, 2012.

Dear Dr. Somberg,

We would like to submit a case report titled “Golimumab may induce exacerbation of inflammatory bowel disease when it is used for the treatment of ankylosing spondylitis: A case report with a review of literature.” to be considered for publication in The American Journal of Therapeutics.

According to the literature search this is the fourth case reported suggesting exacerbation of inflammatory bowel disease while being on golimumab.

This manuscript is not under consideration elsewhere and has never been published in the past. This case has not been funded by any organization.

We look forward to your review.

Sincerely,

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4 **Title:** Golimumab may induce exacerbation of inflammatory bowel
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6 disease when it is used for the treatment of ankylosing spondylitis: A case
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8 report with a review of literature.
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Abstract

Golimumab is a human IgG monoclonal antibody specific for human tumor necrosis factor alpha (TNF- α). Golimumab has been approved for use in rheumatological conditions; however, its use in inflammatory bowel disease (IBD) is still in clinical trials. We report a case of an exacerbation of ulcerative proctitis after starting on golimumab for ankylosing spondylitis (AS).

Key word:

Golimumab; Inflammatory Bowel Disease

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4 **Introduction:**
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9 Golimumab is a human IgG monoclonal antibody specific for human
10 tumor necrosis factor alpha (TNF- α). Golimumab has been approved for
11 use in rheumatological conditions; however, its use in inflammatory
12 bowel disease (IBD) is still in clinical trials. We report a case of an
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14 exacerbation of ulcerative proctitis after starting on golimumab for
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16 ankylosing spondylitis (AS).
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26 **Case:**
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31 A 25-year-old male with ulcerative proctitis was treated with topical
32 mesalamine with symptoms resolution for 14 months. In January 2011, the
33
34 patient started complaining of right hip and lower back pain. An X-ray
35
36 revealed joint space narrowing and right sacroiliitis. Blood test for HLA
37
38 B27 was positive. The patient was referred to rheumatologist for further
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40 management. He was started on golimumab for the treatment of AS in
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46 March 2011.
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50 One month later his joint and back pain improved markedly with
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52 golimumab treatment. Three months after being on golimumab, he
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54 presented with hematochezia associated with watery diarrhea and weight
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58 loss. Physical examination was unremarkable except for left lower
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4 quadrant tenderness. Colonoscopy revealed active ulcerative proctitis
5 confirmed by biopsy. The dose of topical meselamine was increased to
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7 twice a day. The patient's symptoms partially improved after one month,
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9 however, some symptoms persisted. Golimumab therapy was stopped and
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11 adalimumab was started as treatment for intestinal and extra-intestinal
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13 manifestations of IBD. His symptoms improved markedly within a few
14
15 weeks of golimumab cessation and initiation of adalimumab. Follow up
16
17 flexible sigmoidoscopy revealed resolution of proctitis. His proctitis is
18
19 currently in remission, however he still has minimal joint discomfort.
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29 **Discussion:**
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33 TNF- α , originally known as cachexin, was described in 1975 and
34
35 recognized for its ability to lyse tumors in a variety of in vitro models
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37 (hence the name "tumor necrosis factor"). [1] Golimumab, human
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39 monoclonal antibody that binds to human tumor necrosis factor alpha
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41 (TNF- α). Although TNF- α inhibitors share same mode of action, they
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43 show some therapeutic differences in their effects on extra-articular organ
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45 manifestation. [2-4]
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53 We present a case of golimumab-induced flare up of ulcerative proctitis
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55 with a review of literature. Our patient had been in remission for almost
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57 14 months and had acute flare up of ulcerative proctitis (confirmed with
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4 colonoscopy and biopsy) after being introduced on Golimumab therapy
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6 and his symptoms remarkably improved within few weeks of switching the
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8 therapy to adalimumab. In the English literature search there have been
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10 total of 4 cases (including our patient) [Table 1] who had paradoxical
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12 acute flare up of Inflammatory bowel disease after been started on
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14 golimumab. This type of paradoxical effect of TNF- α inhibitor has been
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16 reported for extraarticular manifestations, [5,6] however, the mechanism
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18 of action is still unclear, although an imbalance of cytokines and
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20 interferon α in genetically predisposed individuals has been suggested.
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26 [7,8]
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31 **Conclusion:**
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36 To our knowledge this is the fourth reported case in the English literature
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38 suggesting worsening of inflammatory bowel disease on golimumab. In
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40 conclusion, the use of golimumab for treating ankylosing spondylitis in
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42 patients with inflammatory bowel disease may exacerbate their intestinal
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44 disease.
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Case	Age	Sex	Type of		Rheumatological		**Duration
			IBD	Site of Dz	Dz		
1	47	Female	CD	TI	AS	4	
2	43	Female	CD	TI	AS	2	
			non-				
3	72	Male	specific	Pancolonic	AS	5	
			UP (CD vs				
*4	25	Male	UC)	Rectum	AS	3	

Key: **IBD**: Inflammatory bowel disease, CD: Chrons disease, UC: Ulcerative coliti,

UP: Ulcerative proctitis, Dz: disease, TI: Terminal Ileum, AS: Ankylosing spondylitis

* is the patient seen in our clinic

** Time span in months from starting the Golimumab and exacerbation of IBD

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