CASE REPORT

Crohn's disease unmasked following etanercept treatment for ankylosing spondylitis

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SUMMARY

We describe the case of a 45-year-old man with ankylosing spondylitis being treated with etanercept who presented with a 1 month history of abdominal pain. CT abdomen revealed an ileocaecal mass associated with an abscess, resulting in a laparotomy and right hemi-colectomy. Histology of the resected specimen showed the classical features of Crohn's disease. Etanercept was stopped and he was started on adalimumab. He is currently in clinical remission from both ankylosing spondylitis and Crohn's disease.

BACKGROUND

This case highlights an important adverse clinical effect of the use of etanercept in ankylosing spondylitis. It brings together rheumatology and gastroenterology, and is relevant to all general physicians. There are only 12 similar cases described in the literature of patients with ankylosing spondylitis on etanercept who developed new gastrointestinal symptoms due to Crohn's disease soon after the initiation of treatment.[1–6]

There are several inflammatory conditions where the pathology involves tumour necrosis factor-α (TNF-α), including rheumatoid arthritis, ankylosing spondylitis, psoriasis and inflammatory bowel disease. This case report and literature review demonstrates that the actions of the different anti-TNF-α agents may be different and that etanercept has a risk of inducing or unmasking Crohn's disease.

CASE PRESENTATION

A 45-year-old man presented to the rheumatology clinic in 2009 with a 10 year history of back pain, which worsened over the 12 months prior to his appointment. During those 12 months he suffered from four episodes of iritis, and noticed gradual neck involvement. He was otherwise well with no other medical or gastrointestinal history, and had no personal or family history of significance. Prior to his appointment he used over-the-counter anti-inflammatory drugs with no significant relief.

On examination he was tall and slim, with a kyphotic posture. He had a chest expansion of only 2.5 cm, a 'tragus-wall' distance of 19 cm, and his Schober's test was only 0.5 cm. Additionally, he had only 45° of cervical spine rotation in either direction. On general examination, his chest was clear, heart sounds were normal and there was no evidence of peripheral arthritis or skin changes.

Spinal X-rays from August 2009 showed significant sacroiliitis, which was not evident on images from May of that year. There was very little evidence of spondylitis elsewhere.

A diagnosis of ankylosing spondylitis was made based on clinical and radiological findings along with raised inflammatory markers.

In line with National Institute for Health and Clinical Excellence guidelines, the patient qualified for anti-TNF therapy based on the lack of significant response to anti-inflammatory medications and the high disease activity. Etanercept was therefore started in January 2011 as weekly 25 mg injections with good effect.

In June 2011 he presented to the emergency department with a 1 month history of lower abdominal pain, which peaked on the day of admission. His bowels had not opened for 2 days prior to admission, but he denied other gastrointestinal symptoms.

On examination his abdomen was soft and non-distended, with moderate tenderness across his lower abdomen associated with guarding. Cardiovascular, respiratory and systemic examinations were within normal limits.

INVESTIGATIONS

Blood results demonstrated a marked inflammatory response (admission bloods: C reactive protein 212, white cell count 18.9, neutrophil count 13.7).

A CT abdomen was requested which showed prominent fluid-filled loops of small bowel with thickening and increased enhancement of the bowel wall.

DIFFERENTIAL DIAGNOSIS

The most likely explanation for these radiological findings was a new diagnosis of active small bowel Crohn's disease.

TREATMENT

The patient was admitted as an emergency, and underwent a laparotomy with ileocaecal resection and right hemi-colectomy.

Histology of the resected ileum showed inflammatory changes consistent with the diagnosis of Crohn's disease.

OUTCOME AND FOLLOW-UP

The patient recovered well from his surgery, and was referred to the gastroenterology clinic for follow-up. It was thought that the trigger to the onset of his symptoms was etanercept, which was then discontinued. adalimumab was then started as an alternative anti-TNF agent, which would benefit both his ankylosing spondylitis and his Crohn's

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disease. In December 2011 he had closure of his ileostomy and restoration of continuity.

He is currently doing very well from both the ankylosing spondylitis and Crohn's disease point of view, and continues to have regular follow-up from both specialties.

DISCUSSION

Ankylosing spondylitis is characterised by inflammation of the axial skeleton typically associated with back pain, morning stiffness and the presence of HLA-B27. Although TNF-α blockade has therapeutic benefit in a number of inflammatory disorders, Etanercept has failed to show any efficacy in the management of inflammatory bowel disease.[7]

Twelve similar cases have been documented of patients treated for ankylosing spondylitis with etanercept developing gastrointestinal symptoms soon after starting treatment and subsequently been diagnosed with Crohn's disease.[1–6] This is particularly noteworthy as abdominal pain is a common symptom in primary care and therefore may be easily overlooked by general physicians, leading to a prolonged, untreated duration of active bowel inflammation. It is therefore necessary to have a high index of suspicion in such patients.

The mechanisms behind this effect have yet to be elucidated, although numerous theories have been postulated. Ankylosing spondylitis can be associated with inflammatory bowel disease with subclinical lesions resembling Crohn's disease seen in up to 50% of patients.[8] It could therefore be considered a chance association that the development of Crohn's disease occurred shortly after starting etanercept. Nevertheless, similar cases of the emergence of Crohn's disease shortly after the starting of other anti-TNF agents in ankylosing spondylitits, such as infliximab and adalimumab, have not been reported.

Also, there are a few case reports of new onset Crohn's disease after etanercept use in other conditions, such as psoriasis[9] and juvenile idiopathic arthritis.[10] This would indicate that the development of Crohn's disease is indeed an effect of etanercept rather than the simple association of two linked conditions. Perhaps there is a case for all patients who are being considered for etanercept to have ileocolonoscopy as part of their evaluation to document whether or not there are any mucosal lesions that may be a harbinger of full-blown Crohn's disease.

Learning points

- Consider new onset Crohn's disease in patients with ankylosing spondylitits treated with etanercept presenting with new gastrointestinal symptoms.
- Ankylosing spondylitis and other inflammatory conditions such as psoriasis and juvenile idiopathic arthritis respond to any of the antitumour necrosis factor-α agents (including etanercept), unlike Crohn's disease which only has proven benefit from infliximab and adalimumab.
- It may be appropriate to check if there are intestinal lesions in patients with ankylosing spondylitis prior to starting treatment with etanercept.

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