CASE REPORT

Twenty years of biological therapy in an patient with IBD

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SUMMARY

This interesting case is the first to our knowledge to report outcomes of a patient with Crohn's disease (CD) treated with the biological drug, infliximab, for around 20 years. The case highlights the positive effect of long-term use of infliximab in achieving and maintaining remission in a patient with CD.

In this case, loss of response to infliximab was not dependent on length of exposure to the drug. It also appeared that infliximab was still efficacious after drug holidays, which can be especially important around times of pregnancy. Of interest, 'loss of response' to infliximab occurred at one particular time point. The drug was then reintroduced at a later date, which gave the patient clinical benefit. This case suggests that in some situations infliximab can be reintroduced in patients with previous 'loss of response'. Importantly, in this case, Infliximab had no major adverse effects during the 20 years follow-up.

BACKGROUND

Crohn's disease (CD) is a chronic, relapsing–remitting disease which can affect any part of the gastrointestinal tract. Around one-third of patients with CD would develop perianal fistulas over their lifetime.¹ The presence of perianal CD is associated with a poor disease course. Infliximab has been approved by Food and Drug Administration (FDA) since 2002 for treatment of moderate–severe CD. Long-term treatment with infliximab and combined medical and surgical treatment lead to remission in around 36–58% of perianal CD cases.² However, its use can also be associated with various side effects and loss of response eventually. Here, we report a case of a patient with perianal CD who was on infliximab for almost 20 years. This case highlighted the important issues associated with the use of infliximab.

CASE PRESENTATION

A young woman first presented with abdominal pain for 2 years at the age of 19 in 1980. She had an appendectomy in 1983 in Manchester. Histology showed an inflamed appendix. However, she still had persistent abdominal pain postoperatively. There was also marked weight loss. A small bowel barium study showed abnormalities at the ileocaecal valve. She was then diagnosed to have CD involving ileocaecal region (Montreal Classification A2L3B1) in 1985 and eventually underwent a ileocaecal resection in 1985 due to perforation of the

terminal ileum with peritonitis. She was diagnosed with perianal involvement with multiple perianal fistulae at the age of 21. She had multiple operations, including multiple fistulotomies and seton insertions, during this stage. Medically, she was treated initially with azathioprine which induced pancreatitis and methotrexate which she did not respond to. The decision was taken to start an experimental drug at the time called infliximab. She was the 33rd patient to ever receive this new drug in 1997. She has remained on infliximab monotherapy on and off for over 20 years only having a drug holiday around the time she was pregnant in 2003. In 2005, she was restarted on infliximab and was on this for 3 years until she lost response to this drug, presenting with development of a new perianal fistula. No drug level/antibody levels were checked at that time. She was then switched to adalimumab in May 2008, which was increased to weekly injection in August 2008. This was discontinued in January 2009 due to worsening of perianal pain. In September 2010, she was recommenced on infliximab, as she had a good response prior to pregnancy and would like to try it again. She stopped the infliximab in August 2011 due to worsening of perianal sepsis and underwent proctectomy in 2011. She restarted infliximab again in February 2013 following worsening of her perianal CD and increased abdominal pain and diarrhoea.

Since this date, she has been maintained on infliximab and her CD was well controlled. MRI pelvis in 2014 showed healed perianal fistulas. She has not had adverse side effects from infliximab.

Past medical history includes appendicectomy in 1985, caesarean section and right oophorectomy for a benign ovarian mass in 2003 and depression.

She is currently on infliximab 5 mg/kg every 8 weeks and folic acid supplements.

She is a married accountant with one child and has never been a smoker and is fully functional.

She has a family history of malignancy. Her father died of non-Hodgkin's lymphoma at the age of 61 and her mother died of oesophageal cancer at the age of 81.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis of perianal fistula includes:

1. CD
2. Hidradenitis suppurativa
3. Diverticulitis
4. Tuberculosis
5. Intravenous infection

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TREATMENT

She remains on infliximab currently.

OUTCOME AND FOLLOW-UP

She was last followed up in April 2017. On follow-up, she reported feeling well, opening her bowels 6 times per day with no blood or mucus. Her weight and appetite were stable and her joint pains had improved. She also reported that her perianal region was much more improved.

We visited her during her infliximab infusion in April 2017 where she reported still feeling well. She was not bothered by her perianal symptoms.

DISCUSSION

Infliximab has been approved for treatment of moderate-severe CD by FDA since 2002. The pivotal study by Targan *et al* in 1998 showed that 65% of patients with active CD responded at 4 weeks to doses of 5, 10 or 20 mg/kg of infliximab versus 17%

for placebo and 33% of patients achieved remission versus 4% for placebo.³

So far, there has been no case report on 20-year use of infliximab. Previous studies in 2008 and 2011 confirmed the overall long-term safety use of infliximab for 5 years and 10 years, respectively.^{4,5} Most common systemic side effect was skin eruptions in 20% of patients.⁴ Around 2% of patients developed malignancies in the 10-year follow-up period.⁵ Study by Baert *et al* revealed that reinitiating infliximab therapy could be safe and effective in inflammatory bowel disease (IBD) after a median discontinuation of 15 months.⁶

In this case, this woman developed some transient arthralgia after 20 years use of infliximab. Arthralgia is a relatively common symptom in patients with IBD.⁷ A 20-year follow-up study of patients with IBD revealed 30% of them had musculo-skeletal symptoms. Another study in Greece showed that 30% of patients with CD had arthritis/arthralgia.⁸

Contributors WYM is responsible for interviewing the patient, literature search and writing up the case. JS is responsible for interviewing the patient and writing up the case. He also helped with the planning of the manuscript, including conception and design. AH helped with the refinement of the manuscript.

Competing interests None declared.

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Patient's perspective

I am proud to have been the 33rd ever patient to receive this 'experimental drug'. At the time my disease was so bad, they said this was the 'last throw of the dice'. I was desperate to try anything and I was so grateful that I was given this drug. I believe this drug has kept me well and avoided further operations. I am reluctant to ever stop it as without it I feel my Crohn's disease progresses.

Learning points

- Despite known complications of long-term infliximab, infliximab appears to be well tolerated and efficacious over long duration of time in certain patients, in this case up to around 20 years.
- Infliximab can still be safe and efficacious after a drug holiday.
- Previous loss of response to infliximab does not necessarily preclude patients from rechallenge with it.

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