Dear Sir,

We present the case of a 42 year old woman admitted with a flare of ileo-colonic Crohn’s disease (CD). The patient had been diagnosed with CD in 2011, was commenced on adalimumab 40 mg every other week in 2012 and had been well for over a year. The patient was on no other medications. Corticosteroids were commenced and symptoms resolved. The patient was discharged on a decreasing dose of steroids and adalimumab was increased to 40 mg weekly.

Four weeks later, the patient presented with an itchy, papular rash and bloody diarrhoea. The adalimumab was stopped and intravenous steroids were commenced. Skin biopsy showed the presence of moderate peri-vascular lymphohistiocytic infiltrate and suggested a diagnosis of erythema multiforme. Both rash and bowel symptoms improved with steroid therapy and the patient was commenced on infliximab (5 mg/kg) and azathioprine prior to discharge.

Following third infliximab infusion the patient presented with a blistering rash (Fig. 1). A further skin biopsy was performed with direct immunofluorescence which showed linear deposition of complement at the dermo-epidermal junction. Raised serum bullous pemphigoid (BP) antibody levels were also noted and a diagnosis of BP was confirmed.

Titres of antidrug antibodies were performed; the patient was anti-adalimumab antibody negative and anti-infliximab antibody positive. Infliximab and azathioprine were discontinued and steroid therapy was recommenced. There has been no recurrence of BP but the patient remains extremely symptomatic from a CD perspective and ustekinumab has been commenced. How our patient reacts clinically to the introduction of a third monoclonal antibody is difficult to predict.

Numerous cases of anti-TNF induced auto-immune diseases have been reported in the literature, ranging from localised to systemic disease. The authors would argue that this is a case of anti-TNF induced BP given the age profile of the patient, the observed clinical presentation and the temporal relationship between the appearance of the skin lesions and introduction of anti-TNF medications.

To our knowledge, this is the first reported case of infliximab-induced BP. While the mechanisms driving this phenomenon are not well understood, we feel that a possible explanation can be found in the concept of immunogenicity2 and the formation of human anti-human antibodies3 (HAHA) to monoclonal antibodies. The immunogenicity to infliximab would support this postulate. A recently published systematic review4 suggests that HAHA positivity is associated with decreased efficacy of both infliximab and adalimumab. This apparent immunogenicity is also capable of leading to severe cytokine reactions.5 While their overall role in anti-TNF efficacy has yet to be fully elucidated they certainly appear to be important. Furthermore, their potential role in anti-TNF induced auto-immune diseases requires further study but may represent a possible mechanism for these paradoxical phenomena.

Conflict of interest

None declared.
References


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