Rare disease

A difficult case of Crohn's disease?

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Summary

A young lady with a long history of recurrent infections was referred to the gastroenterology department by an infectious disease consultant because of a long history of profuse diarrhoea. A nitroblue tetrazolium (NBT) test performed in her mid-teens had shown zero reduction of the dye. The clinical, biochemical, radiological and endoscopic findings were suggestive of possible underlying Crohn's disease. However, the NBT test was more suggestive of a granulomatous colitis which frequently mimics Crohn's disease in patients with Chronic granulomatous disease. Management with immunosuppressants is proving to be very difficult in this patient in view of recurrent sepsis on introducing these drugs.

BACKGROUND

Chronic granulomatous disease (CGD) is a rare genetically heterogenous primary immunodeficiency disorder. About 20% of patients are affected by granulomatous colitis mimicking Crohn's disease. Although the inflammatory process in the gut in CGD may be different from that in

Crohn's, the clinical, endoscopic, radiological and histological features may be indistinguishable. Management of this granulomatous colitis can be a challenge in view of the high risk of sepsis on introducing immunosuppressant drugs.

Figure 1 MRI scan showing complex, bilateral perianal fistulae with no evidence of ischiorectal or pelvic abscesses.

Figure 2 Colon biopsy: H&E high power $\times 200$: epithelioid granulomata with giant cells in a background of non-specific inflammation.

Figure 3 Colon biopsy: H&E high power $\times 200$: cryptitis and crypt abscess on the left, with an increased lamina propria cellularity on the right composed of an acute and chronic inflammatory cell infiltrate.

CASE PRESENTATION

A 23-year-old lady presented with a long history of profuse diarrhoea, frequently nocturnal and associated with abdominal pain. She had been investigated with a colonoscopy at the age of 7 which had revealed a non-specific

colitis. She also had a history of recurrent infections since childhood, ranging from perianal abscesses (requiring surgical drainage and seton insertion), to perivaginal abscesses and maxillary sinusitis. The nitroblue tetrazolium (NBT) test performed in her mid-teens had shown

Figure 4 Capsule endoscopy – small bowel inflammation with ulceration and stricturing visible.

zero reduction of the dye. There was no family or social history of note.

INVESTIGATIONS

Laboratory investigations showed: haemoglobin 9.8 (11.5–16.5) g/dl, haematocrit 31.8 (36–45)%, mean corpuscular volume 66.7 (76–95) fl, platelets 565 (140–400) $\times 10^9/l$, erythrocyte sedimentation rate 74 (10–14) mm/h and C reactive protein 109 IU/l (<10). An MRI scan (figure 1) was done to exclude perianal abscesses. A colonoscopy showed active inflammation with skip lesions throughout the colon (figures 2 and 3). Capsule endoscopy was also performed. (figure 4). A CT of the abdomen did not demonstrate any further significant pathology. Genetic testing revealed an autosomal recessive form of CGD.

DIFFERENTIAL DIAGNOSIS

Inflammatory bowel disease (Crohn's).

TREATMENT

In view of the severity of the disease she was initially prescribed ciprofloxacin, metronidazole and fluconazole. Management with -interferon was ineffective. She was started on infliximab in 2009 which had to be stopped after

a single dose in view of the development of perianal and perivaginal abscesses. Her symptoms persisted and a few months later, a second attempt to manage the patient with infliximab was made, but the patient once again developed a perivaginal abscess prompting us to stop the treatment.

OUTCOME AND FOLLOW-UP

This patient's bowel symptoms have remained unremitting and are proving to be a major challenge in her management. Allogenic bone marrow transplant might be a therapeutic option if her symptoms persist and the patient accepts the risks associated with this procedure.

DISCUSSION

The diagnosis is CGD. CGD has an incidence of 1/250 000 live births and is a rare genetically heterogenous primary immunodeficiency disorder which results from the absence or malfunction of NADPH oxidase in phagocytic cells rendering the patient susceptible to recurrent life threatening infections by a spectrum of bacteria and fungi. Microorganisms are phagocytosed normally but persist within cells, thus stimulating granuloma formation. The diagnosis is based on demonstration of a defective respiratory burst by the quantitative dihydrorhodamine 123

flow cytometry assay or the qualitative NBT dye test (zero reduction).^{1 2}

About 20% of the patients are affected by granulomatous colitis mimicking Crohn's disease. Its optimal treatment is yet to be determined. Topical treatments such as 5-aminosalicylates and budesonide can be used for mild-to-moderate disease or proctitis while systemic treatment with prednisolone, azathioprine and infliximab can be used for severe and fistulating disease. Metronidazole and/or ciprofloxacin can be added in the latter pathology. In case of treatment failure (such as in our patient), stem cell transplantation from an identical human leucocyte antigen donor should be considered.^{1 3} Although the inflammatory process in the gut in CGD may be different from that in Crohn's, the clinical, endoscopic, radiological and histological features may be indistinguishable. Histological differences between the two entities are the presence of pigment-laden macrophages within the lamina propria in CGD and the granulomata may be more well defined as opposed to the poorly formed granulomas typical of Crohn's disease.^{1 3 4}

Similar case reports offer conflicting advice with Al-Mobaireek⁵ suggesting a good response to steroids while Arimura *et al*⁶ suggest that steroids should be avoided in CGD colitis following a fatal case of unclassified colitis in CGD treated with steroids. Rosh *et al*⁷ describe an interesting report of a patient who was unresponsive to conventional therapy but who achieved a rapid clinical response to cyclosporine.

Learning points

- CGD is a rare genetically heterogeneous primary immunodeficiency disorder.
- Twenty per cent of patients with CGD are affected by granulomatous colitis mimicking Crohn's disease.
- The optimal treatment of this type of colitis is yet to be determined.

Competing interests None.

Patient consent Obtained.

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