CASE REPORT

If it walks like Crohn's and talks like Crohn's, it must be...

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SUMMARY

A 30-year-old man presented with a 6-month history of nausea, vomiting and diarrhoea. This was associated with 25 kg weight loss and a right-sided abdominal colic. He had been provisionally diagnosed with Crohn's disease 6 months back and treated with budesonide and mesalazine. Investigations including C reactive protein, white cell count, coeliac antibodies, fasting gut hormones and faecal elastase were all normal. Colonoscopy and ileoscopy were normal both macroscopically and microscopically. Small bowel series and labelled white cell scan were both unremarkable. A CT scan suggested the presence of mild right-sided abdominal lymphadenopathy. Laparoscopy of entire small bowel and colon was normal. But had something been missed? An adrenocorticotrophic hormone stimulation test demonstrated inadequate cortisol response and a diagnosis of adrenal insufficiency was confirmed. Addison's disease can present with a variety of gastrointestinal symptoms and should be considered in the diagnostic work-up of these patients.

BACKGROUND

This case demonstrates an unusual presentation of a relatively common clinical entity. It highlights the importance of pursuing investigations where a diagnosis is uncertain, and the benefits of thinking laterally across different specialties. In this case, a patient with a provisional diagnosis of Crohn's disease went on to have multiple normal investigations before being diagnosed with an imminently treatable endocrine condition.

CASE PRESENTATION

A 30-year-old man initially presented with a several-week history of nausea, vomiting and diarrhoea. He had noticed intermittent loose stools which were occasionally blood stained, and a migratory abdominal colic often localising to the right side. Haematological profile and inflammatory markers were within normal limits. Colonoscopy with ileoscopy was performed and was shown to be normal both macroscopically and microscopically. A CT scan of the abdomen was performed and showed mild right-sided lymphadenopathy suggestive of possible inflammatory bowel disease. A provisional diagnosis of Crohn's disease was made and treatment commenced with budesonide and mesalazine. This provided minor relief from his diarrhoea, but had no effect on his abdominal pain.

The man presented to a different centre 4 months later 'feeling worse.' He was lethargic, had anorexia and complained of profuse sweating.

He was vomiting on a daily basis and having ongoing diarrhoea, occasionally with traces of blood. His abdominal pain was unchanged, and he had lost 25 kilograms in weight over the previous 6 months.

There was no other medical history of note. He had no allergies and did not smoke or drink alcohol. His medications included omeprazole, ranitidine, amitriptyline, mebeverine, ondansetron and paracetamol. He was no longer taking budesonide.

On examination, he had no rashes, lymphadenopathy, anaemia or jaundice. He had tenderness in his right lower flank. There were no abdominal masses palpable, no ascites and normal bowel sounds were detected. Blood pressure and pulse were both normal.

INVESTIGATIONS

Haematological and biochemical investigations were all unremarkable including haemoglobin, albumin, electrolytes and inflammatory markers. Coeliac antibodies, fasting gut hormones, human immunodeficiency virus (HIV) test, cytomegalovirus and Epstein-Barr viral serology were all negative. Faecal elastase value was normal. A chest x-ray and ultrasound scan of abdomen were performed and showed no evidence of lymphadenopathy or systemic disease. A barium study of the small bowel showed a normal mucosal pattern with no stricturing.

During the patient's initial presentation, colonoscopy and ileoscopy had been normal but CT scan had demonstrated mild abdominal lymphadenopathy. A repeat CT of the abdomen was performed at an interval of 5 months from the previous scan and showed the persistence of right-sided lymph nodes. These had not increased in size and were small enough to be of doubtful significance.

A labelled white cell scan did not show any abnormality. Laparoscopy showed an entirely normal small bowel and colon. At the time of surgery, appendectomy was performed at the suggestion of mild macroscopic inflammation. It was later found to be microscopically normal.

In the absence of other positive findings, an adrenocorticotrophic hormone (ACTH) stimulation test was performed. This showed an inadequate cortisol response to ACTH (12 nmol/l at baseline, 180 nmol/l after 30 min) which confirmed a diagnosis of adrenal insufficiency.

DIFFERENTIAL DIAGNOSIS

The patient in this case presented primarily with gastrointestinal symptoms of nausea, vomiting, diarrhoea and weight loss. These were associated

To cite: Hall PSJ, Allen PB, Diong KL, et al. *BMJ Case Reports* Published online: [Please include Day Month Year] doi:10.1136/bcr-2012-008051

with generalised systemic features including severe lethargy and fatigue. The only positive finding from the initial battery of investigations was that of mild right-sided abdominal lymphadenopathy, which showed no interval change.

Initial investigations were planned to look for the potential diagnoses of Crohn's disease and gastrointestinal lymphoma. Both these conditions had potentially serious repercussions for the patient, if not detected. They both have potential treatments available, and are notoriously difficult to investigate in certain cases. For these reasons, due attention was given to their investigation and exclusion. With the patient's predominately gastrointestinal symptoms, along with normal blood pressure and serum electrolytes, the diagnosis of adrenal insufficiency was not initially considered.

TREATMENT

Treatment was started with oral hydrocortisone 20 mg in the morning and 10 mg in the evening. Fludrocortisone tablets were commenced at 100 µg daily.

OUTCOME AND FOLLOW-UP

Several weeks after starting glucocorticoid and mineralocorticoid replacement, the patient reported an improvement in symptoms, without complete resolution. His weight had stabilised but had not increased substantially. Subsequent investigations including antiadrenal antibodies, autoimmune screening, urinary 5-hydroxyindoleacetic acid and positron emission tomography—CT (PET-CT) scanning were all unremarkable. An MRI scan of pituitary showed a 4 mm pituitary lesion with prolactin level within the normal range.

DISCUSSION

Adrenal insufficiency can cause a wide variety of non-specific symptoms which can make the condition difficult to diagnose. It commonly mimics other conditions, in this case, Crohn's disease. Considerable time and effort is often expended in searching for these diagnoses before the relatively simple ACTH stimulation test is performed to look for adrenal insufficiency.

There are few documented reports of adrenal insufficiency having presented as Crohn's disease to this extent, although Crohn's disease presenting as Addison's disease has been recognised.¹ It is well known that Addison's disease can present with predominantly gastrointestinal symptoms which can expose a patient to the risks of unnecessary investigation. There is also the substantial risk of the patient suffering the effects of a delay in diagnosis, with adrenal crisis being a recognised complication in these patient groups.²

Patient surveys by the National Adrenal Diseases Foundation (North America) and the Addison's Disease Network (the UK) give an outline of the prevalence of gastrointestinal symptoms at the time of diagnosis of Addison's disease:^{3 4}

Gastrointestinal symptoms of Addison's disease	Prevalence (%)
Weight loss	88–91
Nausea	78–84
Vomiting	61–75
Loss of appetite	78–84
Abdominal discomfort	64–87
Diarrhoea	64
Constipation	61

The more commonly attributed symptoms such as fatigue, hyperpigmentation, salt craving, postural hypotension and muscle weakness may also be present. A successful diagnosis of adrenal sufficiency therefore requires a high index of suspicion throughout the variety of specialties to which these patients may present. The surveys also suggest that the majority of patients require more than 6 months of investigation before a diagnosis of Addison's disease is made. Most have to see three or more medical doctors.^{3 4} The diagnostic dilemma is further explored in figure 1, showing the crossover of symptoms between Addison's disease and Crohn's disease (figure 1).

This patient's case was complicated by the fact that he was treated with oral budesonide for a provisional diagnosis of

Figure 1 The diagnostic dilemma—symptom crossover between Crohn's disease and Addison's disease.

Crohn's disease at his initial presentation. Both Crohn's disease and Addison's disease will respond to some extent to glucocorticoid therapy, demonstrating how presumptive treatment of this nature can 'muddy the water' when trying to make a diagnosis. In this case, the patient's trial of budesonide was short-lived and had ceased some weeks prior to the ACTH stimulation test to look for adrenal insufficiency.

Budesonide is an oral glucocorticoid agent that acts locally with anti-inflammatory effects on ileal and colonic mucosa. It has limited systemic bioavailability owing to extensive hepatic first pass metabolism. This leads to a reduction in steroid-related side effects while still providing a proven benefit in active Crohn's disease, when compared with placebo or 5-aminosalicylic acid compounds.⁵

A pooled safety analysis of budesonide use in Crohn's disease showed that its effect on adrenal function at 1 year was not significant when compared with placebo. It was associated with normal adrenal function in 92% of cases compared with only 75% of patients who had used oral prednisolone. In the short term, budesonide certainly did cause adrenal axis suppression. A study of 58 patients showed that after 8 weeks use, only 42% had a normal ACTH stimulation test. After 8 weeks of prednisolone therapy, 16% of patients had a normal test.⁶ Adrenal crisis associated with budesonide use in Crohn's disease is rare, but it can occur and can be life threatening.⁷

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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Learning points

- ▶ Beware of the patient who comes with a diagnostic 'label'.
- ▶ Treating patients empirically without a firm diagnosis can cause confusion and make further investigations more difficult.
- ▶ Adrenal insufficiency can present with a wide variety of symptoms and requires a high index of suspicion to avoid unnecessary investigations and delays in diagnosis.
- ▶ Oral budesonide is an effective treatment for active Crohn's disease. It causes less systemic side effects but can cause adrenal insufficiency after sudden withdrawal.

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