A challenging case of chronic diarrhoea

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Case

A man, aged 69 years, presented with a 2-year history of diarrhoea, including nocturnal symptoms, faecal incontinence, abdominal pain and weight loss of 22 kg. He had no per-rectal bleeding. His past medical history included chronic obstructive pulmonary disease (COPD), gout, paroxysmal atrial fibrillation, biventricular failure, aneurysmal dilatation of the ascending aorta, chronic renal failure, hypertension, previous excess alcohol intake and previous endoscopic retrograde cholangiopancreatography (ERCP) for choledocholithiasis. His current medications reflected these conditions. He was an ex-smoker and denied current alcohol use.

Abnormal findings on examination were cachexia, hypotension, reduced air entry in both lung bases and moderate bilateral peripheral oedema. The abdominal examination was unremarkable.

Question 1

What are the differential diagnoses?

Question 2

What non-radiological investigations should be considered?

Answer 1

A history of chronic diarrhoea with weight loss and nocturnal symptoms is suggestive of an organic cause. The main differential diagnoses to consider are:

- malignancy (eg lymphoma, colorectal cancer, pancreatic carcinoma)
- coeliac disease
- inflammatory bowel disease
- thyrotoxicosis
- pancreatic exocrine insufficiency
- mesenteric ischaemia
- drug-induced effects
- acute infectious causes (these are unlikely)
- chronic infectious causes (eg tuberculosis and human immunodeficiency virus infection).

Answer 2

Non-radiological investigations to be considered include:

- full blood evaluation
- stool examination
- oesophagogastroduodenoscopy
- colonoscopy.

Results for this patient are shown in *Table 1*.

Case continued

The patient underwent suboptimal colonoscopy, which was reported as normal with the caveat that the bowel preparation was inadequate. A plan was put in place to repeat the colonoscopy and take biopsies, but the patient continued to deteriorate and was unable to tolerate the bowel preparation. Radiological investigations were used to assist in developing a working diagnosis. The results were highly suggestive of Crohn's disease.

Table 1. Suggested investigations with the results for this case

Blood examination							
Investigation	**Result**	**Units**	**Reference range**	**Investigation**	**Result**	**Units**	**Reference range**
Hb	118	g/L	135–180	Na^+	135	mmol/l	135–145
WCC	9.4	$x10^9$/L	4.0–11.0	K^+	4.4	mmol/l	3.5–4.1
Platelets	501	$x10^9$/L	140–400	Urea	8.4	mmol/l	2.9–8.2
MCV	87	fL	80–100	Creatinine	112	µmol/l	64–108
CRP	121	mg/L	<5.0	Ca^{2+}	2.21	mmol/l	2.15–2.55
INR	1.2			Mg^{2+}	0.65	mmol/l	0.70–1.10
Albumin	20	g/L	35–50	PO_4^{3-}	0.80	mmol/l	0.81–1.45
Bili (total)	20	µmol/L	<20	Free T4	22	pmol/l	10–23
Bili (conj)	8	µmol/L	<4	TSH	4.1	mIU/L	0.4–4.0
ALP	133	U/L	56–119				
GGT	18	U/L	<55	Coeliac antibodies	Negative		
ALT	28	U/L	<45	Vasculitis screen	Negative		
AST	44	U/L	<35	Quantiferon assay	Negative		
Vit D	46	nmol/L	50–150	Anti-*S. cerevesiae*	Negative		
Iron	8	µmol/L	12–31	C-ANCA	Negative		
Transferrin	0.7	g/l	1.6–3.4	P-ANCA	Negative		
Ferritin	199	µg/L	30–300				
Folate	32.4	nmol/L	>7.0				
Stool examination							
Investigation	**Result**	**Units**	**Reference range**				
Calprotectin	750	µg/g	<112				
Clostridium difficile	Negative						
MC&S	Negative						
Oesophagogastroduodenoscopy							
Macroscopic findings consistent with possible coeliac disease and oesophagitis							
Helicobacter pylori CLO test:	Negative						
Stomach biopsy:	Mild chronic gastritis						
Duodenum biopsy:	Mild active duodenitis						
Colonoscopy							
Reported as normal, but given suboptimal bowel preparation, recommendation to repeat colonoscopy when possible.							

ALP, alkaline phosphatase; ALT, alanine aminotransaminase; ANCA, anti-neutrophil cytoplasmic antibodies; ASCA, anti-*Saccharomyces cerevisiae* antibodies; AST, aspartate aminotransferase; Bili (conj), conjugated bilirubin; Bili (total), total bilirubin; CLO, *Campylobacter*-like organism; CRP, c-reactive protein; GGT, gamma-glutamyltransferase; Hb, haemoglobin; INR, international normalised ratio; MC&S, microscopy culture and sensitivity; MCV, mean corpuscular volume; TSH, thyroid stimulating hormone; WCC, white cell count

Question 3

What radiological investigations would aid in the diagnosis? What features might be seen?

Answer 3

Computed tomography (CT) and magnetic resonance (MR) enterography and enteroclysis are the main imaging modalities that would aid in the diagnosis of Crohn's disease. CT and MR have equal accuracy, but MR enterography is preferred as radiation exposure is minimised and it is less invasive than enteroclysis.[1] The use of plain film imaging is largely unsupported.

There are three diagnostic features of Crohn's disease identifiable on CT:

- mural stratification
- mural hyperenhancement
- small bowel wall thickening >3mm.

These features are considered good indicators of clinically active disease.[2] In addition, MR imaging (MRI) can also identify ulcerations, increased mesenteric vascularity (comb sign), mesenteric inflammation and reactive adenopathy. CT and MRI can also detect extraintestinal manifestations and complications of Crohn's disease (eg sacroiliitis, fistulae and abscesses).

It should be noted that normal imaging results alone do not sufficiently exclude a diagnosis of Crohn's disease.

Case continued

The patient's MR enterography showed numerous thickened hyperenhancing segments of small bowel (*Figures 1, 2*). The terminal ileum had several mildly narrowed segments with minimally increased enhancement without wall thickening, and mesenteric lymphadenopathy was present. Although these findings were consistent with a working diagnosis of Crohn's disease, repeat colonoscopy was still planned, when the patient was more stable, to obtain histological evidence to support a definitive diagnosis.

Question 4

What are the features of this condition?

Question 5

What management would you follow for this patient?

Answer 4

Crohn's disease is a chronic inflammatory bowel disorder that may affect any segment of the intestinal tract with a predisposition for the terminal ileum and colon. The hypothesised aetiology of Crohn's disease is thought to be a consequence of an inappropriate immunological reaction to intestinal bacteria in a genetically susceptible individual.[3] The clinical and pathological features of Crohn's disease are classically compared to ulcerative colitis (*Table 2*). The clinical course of the disease is relapsing and remitting.

Answer 5

The main aim of treatment for Crohn's disease is to achieve the best possible clinical, biochemical and histological control with the least adverse effects from medication. The development of biological anti-tumour necrosis factor (anti-TNF) agents (eg infliximab and adalimumab) has significantly advanced the treatment of Crohn's disease and improved the induction and maintenance of clinical remission in patients with moderate-to-severe disease, especially in those who are corticosteroid-dependent.[4]

Until recently, the step-care approach has been used, but recent evidence has suggested benefits of more aggressive initial treatment:[5] an immunomodulator should be introduced early to maintain remission and avoid the need for multiple courses of steroids. Many patients with an exacerbation of Crohn's disease can be treated on an outpatient basis with oral steroids (to induce remission) and 6-mercaptopurine (6-MP) or azathioprine (to maintain remission).[6] If outpatient treatment fails, intravenous hydrocortisone may be required and hospitalisation is warranted.

Note that 5-aminosalicylic acids have no role in the treatment of Crohn's disease and are no longer recommended.

If medical therapy for active Crohn's disease fails, surgical resection of the inflamed bowel with restoration of continuity is indicated. Urgent surgery may be required in rare cases of sustained or recurrent haemorrhage, perforation, abscess and toxic megacolon. Partial small bowel obstruction or intra-abdominal abscess may sometimes be treated conservatively if there is no evidence of ischemia.[7,8]

Nutritional therapy is an important consideration for the treatment of the disease and for any associated malnutrition.[9] Issues such as employment difficulties, psychological health, sexual dysfunction, child development and smoking cessation should not be overlooked.[10]

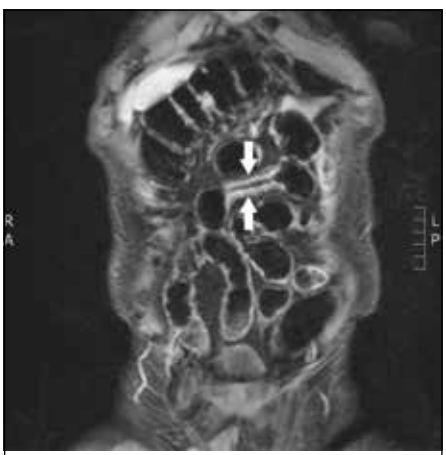

Figure 1. MR enterography T1 weighted vibe post-contrast coronal image 1 demonstrating a significantly thickened, hyperenhancing segment of small bowel (arrows)

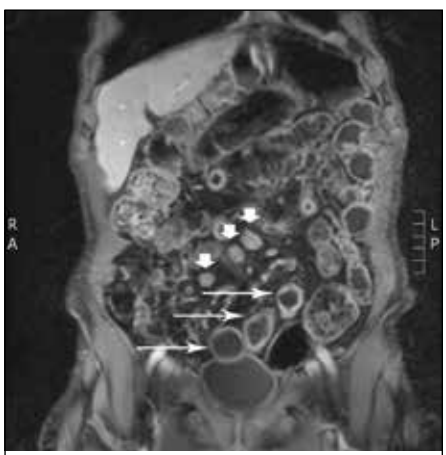

Figure 2. MR enterography T1 weighted vibe post-contrast coronal image 2 demonstrating significant lymphadenopathy (block arrows) with multiple thickened, hyperenhancing segments of bowel (thin arrows)

Table 2. Microscopic and macroscopic features of Crohn's disease and ulcerative colitis

	Crohn's disease	Ulcerative colitis
Clinical features		
Frank per-rectal blood	+	++
Mucus in stool	+	++
Abdominal pain	++	+
Abdominal mass	+	–
Perianal manifestations	+	–
Fistulae	+	–
Small bowel obstruction	+	–
Recurrence post surgery	++	–
ANCA	–	+
ASCA	+	–
Pathological features		
Location	Terminal ileum 35% Caecum 30%	Colonic +/– backwash ileitis
Distribution	Skip lesions	Continuous; distal to proximal
Granulomata	Yes	No
Crypt abscesses	Rare	Common
Cobblestone appearance	Yes	No
Transmural inflammation	Yes	No

ANCA, anti-neutrophil cytoplasmic antibodies; ASCA, anti-*Saccharomyces cerevisiae* antibodies

Key points

- Chronic diarrhoea with weight loss and nocturnal symptoms should prompt a search for an organic cause.
- CT and MR enterography and enteroclysis can aid in the diagnosis of Crohn's disease.
- Normal imaging results alone do not exclude a diagnosis of Crohn's disease; conversely, imaging cannot definitively confirm a diagnosis of Crohn's disease (this requires histological evidence).
- More aggressive initial treatment may be better than a step-care approach.

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