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PRACTICE

EASILY MISSED

Inflammatory bowel disease

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This is one of a series of occasional articles highlighting conditions that may be more common than many doctors realise or may be missed at first presentation. The series advisers are Anthony Harnden, professor of primary care, Department of Primary Care Health Sciences, University of Oxford, and Richard Lehman, general practitioner, Banbury. To suggest a topic for this series, please email us at practice@bmj.com.

A 21 year old woman presented to her general practitioner with tiredness and abdominal discomfort for the past year. She is treated for iron deficiency anaemia (attributed to menorrhagia) and for presumed irritable bowel syndrome. After hospital admission a few months later with suspected appendicitis, tests reveal vitamin B_{12} deficiency and raised inflammatory markers, prompting gastroenterology referral. Colonoscopy with terminal ileal biopsy confirms a diagnosis of Crohn's disease.

What is inflammatory bowel disease?

Inflammatory bowel disease encompasses ulcerative colitis and Crohn's disease, both idiopathic chronic diseases of the gastrointestinal tract. Ulcerative colitis is characterised by diffuse inflammation affecting the mucosa of the colon only. Crohn's disease involves patchy transmural ulceration that can affect any part of the gastrointestinal tract. Around 5% of patients have features of both subtypes and are labelled inflammatory bowel disease "unclassified."[1]

Why is it missed?

Recent data on the incidence of delayed diagnosis are limited. A recent Swiss cohort study found the median diagnostic delay among patients with Crohn's disease was 9 months and was 4 months among patients with ulcerative colitis. Age <40 years and ileal disease were independently associated with a long diagnostic delay in Crohn's disease.[4]

Lower gastrointestinal symptoms are common in general practice, and symptoms typical of irritable bowel syndrome are often described in patients with inflammatory bowel disease.[5] A large UK based case-control study found that patients with inflammatory bowel disease were three times more likely to have a prior diagnosis of irritable bowel syndrome.[6] A prospective cohort study found patients with probable and possible pre-existing irritable bowel syndrome were likely to experience longer symptom duration before diagnosis of inflammatory bowel disease.[7] Onset of both diseases is often insidious, and there are no pathognomonic signs or symptoms of either. Many patients have vague, non-specific symptoms for some time, consistent with chronic low level inflammation which can mimic irritable bowel syndrome. In addition the relapsing and remitting nature of inflammatory bowel disease compounds the diagnostic difficulty.

Why does this matter?

Delay in the diagnosis of inflammatory bowel disease has been suggested to reduce patient quality of life but also to reduce response to medical therapy.[8] A retrospective cohort study showed that longer diagnostic delay in Crohn's disease was associated with greater risk of bowel stenosis and of intestinal surgery for Crohn's disease.[8]

Current statistics suggest up to 50% of patients with Crohn's disease will require surgery within 10 years of diagnosis,[3] but evidence suggests a reduction in surgery over the past decade owing to treatment advances.[8] Improved remission rates and short term treatment efficacy have been observed in those treated aggressively at an early stage.[9] In addition, early biological therapy with mucosal healing may modify the course of the disease.[9]

Gastrointestinal malignancy is more common in patients with inflammatory bowel disease, and surveillance colonoscopy is recommended for patients with colitis from 10 years after the onset of symptoms. Therefore, timing of diagnosis is crucial.

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The bottom line

- Inflammatory bowel disease can present with symptoms similar to irritable bowel syndrome
- Diarrhoea of >6 weeks' duration, especially with weight loss and where cancer is not suspected, warrants testing (such as full blood count, C reactive protein or erythrocyte sedimentation rate, coeliac antibodies, and thyroid function)
- NICE guidelines recommend measuring faecal calprotectin in all patients with suspected inflammatory bowel disease, as it is useful in excluding the disease
- Delayed diagnosis of inflammatory bowel disease is associated with reduced response to medical therapy and higher incidence of surgical intervention

How common is inflammatory bowel disease?

- A large systematic review showed the incidence and prevalence of inflammatory bowel disease are increasing with time,[2] in particular among second generation Asian migrants in the UK
- The incidence of ulcerative colitis is about 10-20/100 000/year, with a reported prevalence of 100-200/100 000 people[3]
- The incidence of Crohn's disease is around 5-10/100 000/year, with a prevalence of 50-100/100 000 people[3]
- There is little gender difference in the prevalence of inflammatory bowel disease, but it is more common in white people

How is inflammatory bowel disease diagnosed?

Clinical features

Both Crohn's disease and ulcerative colitis most commonly present in late adolescence and early adulthood, with a small second peak in the fifth decade in the case of ulcerative colitis.[10] Non-bloody diarrhoea lasting more than six weeks makes infective causes less likely and warrants further investigation.[10] Fever and anorexia are not seen in irritable bowel syndrome and nocturnal symptoms are unusual, whereas they are not uncommon in inflammatory bowel disease.[1]

Some 90% of patients with ulcerative colitis report bloody diarrhoea,[10] usually triggering prompt investigations; in addition, abdominal pain and urgency of defecation are commonly seen. Crohn's disease tends to have a more varied presentation—chronic diarrhoea is the most common symptom, but abdominal pain and weight loss are seen in 70% and 60% of patients, respectively.[11] Other patients can present more acutely with intestinal obstruction due to stricturing disease or perianal complications including abscesses and fistulas.

Between 25% and 40% of patients with inflammatory bowel disease have extraintestinal manifestations, more often affecting those with Crohn's disease. The musculoskeletal system (arthritis, ankylosing spondylitis) and skin (erythema nodosum, psoriasis, pyoderma gangrenosum) are most commonly affected and may be the presenting feature.[12]

Investigations

There is no single diagnostic test for inflammatory bowel disease: a combination of clinical, radiological, endoscopic, and histological investigations are used in secondary care. In primary care, check full blood count for anaemia or microcytosis (suggesting iron deficiency or anaemia of chronic disease) and for thrombocytosis (indicating inflammation). Check C reactive protein or erythrocyte sedimentation rate: these inflammatory markers can indicate disease activity but lack sensitivity and specificity. Exclude coeliac disease (with antibody testing), thyroid dysfunction (with serum thyroid stimulating hormone level), and infective diarrhoea (stool microscopy). As malabsorption may occur in inflammatory bowel disease, check serum B_{12}, folate and ferritin levels, and transferrin saturation.

Faecal calprotectin is released into the colon in excess in the presence of inflammation. The National Institute for Health and Care Excellence (NICE) recommends testing for this to help distinguish inflammatory bowel disease from other non-inflammatory bowel conditions such as irritable bowel syndrome in those with lower gastrointestinal symptoms of recent onset and where cancer is not suspected[3]—that is, those without referral criteria for malignancy.[13]

A recent systematic review has shown a cut-off of 50 μg/g of faecal calprotectin to be sensitive and specific for inflammatory bowel disease,[14] but more data are needed to determine optimal threshold values in primary care. Values >50 μg/g are not diagnostic but warrant specialist assessment within four weeks. The test's utility lies in its high negative predictive value.[14] Thus, a normal result means inflammatory bowel disease is unlikely.

Lower gastrointestinal endoscopy with histological confirmation on biopsy is considered the first line diagnostic test after referral. Plain abdominal x ray is essential if acute colonic inflammation or bowel obstruction is suspected, but is not diagnostic and not recommended for routine use.[10 11]

How is inflammatory bowel disease managed?

Refer patients who have bloody diarrhoea, diarrhoea of >6 weeks' duration, abdominal pain with weight loss, raised faecal calprotectin, or unexplained vitamin B_{12} or folate deficiency in an adult <40 years old. Management is based in secondary care and made on an individual basis, dependent on disease extent, location, and behaviour with the aim to induce and maintain remission via a multidisciplinary approach. Diet and lifestyle advice (such as eating a balanced diet and staying well hydrated, exercising, and avoiding stress) is important, with smoking cessation crucial in Crohn's disease. Medical management is individualised and includes glucocorticosteroids, immunomodulators, biological therapy, and mesalazine (5-aminosalicylic acid) in ulcerative colitis. Nutritional deficiencies should be corrected. The need for surgery is declining, but currently 10% of ulcerative colitis patients will need a colectomy and up to 50% of patients with Crohn's disease will require surgical management in the first 10 years after diagnosis owing to stricturing or fistulating disease.[3]

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