Instructive Case: An adolescent with urinary frequency, fevers and lower abdominal pain.

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A 16-year-old girl presented to her general practitioner (GP) with a 7 to 10 day history of: urinary frequency, lower abdominal pain (suprapubic area and labiae), and fever. She reported bilious vomiting at night, and 3-weeks of alternating constipation and diarrhoea. She was unsure if there was blood or mucus in the stool. She did not complain of menorrhagia, dysmenorrhea or menstrual irregularity, and was in week 3 of her cycle. She denied sexual activity, drug use or smoking. She had no history of recent travel or any sick contacts. There was a family history of ulcerative colitis (an aunt and grandfather). Her GP requested a full blood examination (FBE), identifying haemoglobin (Hb) of 70g/L, and referred the patient to the emergency department (ED).

On examination, in the ED, she was alert, tachycardic (130 beats per minute [bpm]), febrile (38.2°Celsius), normotensive (120/70 mmHg) and had no orthostatic hypotension. She had a soft, mildly distended abdomen with tenderness in both iliac fossae and the suprapubic area. There was voluntary guarding, normal bowel sounds and no palpable masses. No lymphadenopathy was identified and she had no rash.

Initial investigations demonstrated the following: Hb 67g/L [115-165g/L], packed cell volume 21.8 [37-47%], mean cell volume 64 [80-96fL], mean cell Hb 19.5 [27-32pg], mean cell Hb concentration 30.7 [32-36g/dL], red cell distribution width 17.3 [11-16%]; leukocytes 17.3 [4.0-11.0 x 10⁹/L], neutrophils 14.4 [2-8 x 10⁹/L]; platelets 681 [150-450 x 10⁹/L]; and c-reactive protein 269mg/L [0-10mg/L]. Iron studies showed a raised ferritin (320ug/L) and low iron (1micromol/L). Biochemistry was normal apart from a low albumin (23g/L). Urine microscopy demonstrated polymorphs, erythrocytes and protein. Abdominal x-ray was normal. Faecal enzyme immunoassay for *Giardia* and *Cryptosporidium* were negative. Faecal concentrate microscopy did not reveal ova, cysts or parasites. Faecal culture did not isolate *Salmonella*, *Shigella* or *Campylobacter*.

The patient was diagnosed with microcytic anaemia, without identification of a specific cause. As the patient was asymptomatic, no blood transfusion was undertaken. She was given analgesia, fluids and antibiotics for a presumed urinary tract infection. She was

discharged home with two-stage follow up: at the hospital's registrar-led paediatric rapid-review clinic and, later, at a tertiary centre gastroenterology clinic.

Five days later the patient returned to the ED for clinical review. She reported worsening abdominal pain, fatigue and dizziness. On examination, her HR, while lying supine, was 120bpm, rising to 132bpm on standing. Orthostatic hypotension was identified with supine blood pressure of 110/60mmHg, falling to 85/50mmHg on standing. Urine full ward test showed haemoglobinuria and proteinuria. On this occasion the FBE demonstrated platelets of 824 [$150-450 \times 10^9/L$], with no significant change in other parameters. Her liver function tests had changed, revealing: alanine transaminase 43 [0-30U/L], aspartate aminotransferase 101 [0-30U/L], alkaline phosphatase 146 [45-140U/L] and gamma-glutamyl transferase 43 [0-30g/L]. Albumin was unchanged at 23g/L.

An abdominal ultrasound (Fig. 1) demonstrated a lesion superior to the bladder with surrounding hyperaemia, and subsequent MRI confirmed an abscess with enterovesical fistulae (Figs. 2 and 3). A provisional diagnosis of Crohn's disease was made. Following blood transfusion, she was transferred to a tertiary centre for further management.

Discussion

This patient had an intramural bladder abscess secondary to ileovesical and multiple enteroenteric fistulae secondary to Crohn's disease. An Australian study established the crude annual incidence rate of IBD at 29.3 cases per 100,000.¹ The incidence of CD and UC were 17.4 cases per 100,000 and 11.2 cases per 100,000 respectively.¹ Patients typically present between 15 to 25 years of age, with 25 to 30% of all CD patients presenting before 20 years of age.² Common clinical features of CD at the time of diagnosis include: abdominal pain (95%), weight loss (80%) and diarrhoea (77%).³

The incidence of all types of fistulae in CD increases over time from 5.5% (95% Confidence Interval [CI] 4.2-7.1) one year after diagnosis; to 18.7% (95% CI 14.5-23.9) ten years after diagnosis.⁴ However, rectovesical fistulae were rare (0.2% [95% CI 0.1-0.9] one year after diagnosis to 1% [95% CI 0.3-3.1] 10 years after diagnosis). There were no fistulae between bladder, ileum and multiple segments of small bowel within the study by Gupta et al.⁴ This highlights the unusual presentation of the patient detailed above. Early detection of fistulae is important as they cause significant reduction in the patients' quality of life. The mainstay of treatment for fistulae is surgery, aiming to maintain sphincteric function, where relevant, and subsequent prevention of further fistulae.⁵

Initial investigations in IBD commonly reveal anaemia, leukocytosis, thrombocytosis and a raised c-reactive protein as was seen in this patient. Infection may also cause such changes. The most common cause of microcytic anaemia in children is iron deficiency, which is usually due to dietary inadequacy and may be associated with low B12 and folate levels.^{6,7} Iron deficiency in adolescent girls can result from menstrual blood loss. Haemolytic anaemias may be due to a hereditary condition such as thalassaemia, spherocytosis or sickle cell disease. In this particular case, the anaemia is likely a result of iron deficiency related to malabsorption and enteric blood loss. Note that if multiple cell lines are affected, bone marrow suppression or malignancy may be responsible. If the patient is from a high-risk population, or has recently travelled, infections such as malaria, tuberculosis, hepatitis and intestinal parasites should be considered.⁶

The presented case demonstrates the diversity of presentations in Crohn's disease. Distant inflammatory sequelae and local fistula formation can lead to protean clinical features.^{3,8} In the presence of anaemia, inflammatory bowel disease needs to be considered, especially where a history of altered bowel habits has been elicited.

Learning Points

- Fistulae associated with Crohn's disease can lead to a variety of clinical presentations depending on the anatomical structures are affected.
- Fistulae increase in incidence over time following the diagnosis of Crohn's disease. Enterovesical fistulae are rare.
- If the cause of anaemia cannot be clearly identified consider a broad differential diagnosis that includes inflammatory, infectious and malignant processes. History and examination will guide further investigation.

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Multiple choice questions

The cumulative incidence of all types of fistula in children with Crohn's disease, 1 year and 10 years after diagnosis, respectively is closest to:

- a) 6% at 1 year and 19% at 10 years
- b) 1% at 1 year and 35% at 10 years
- c) 1% at 1 year and 19% at 10 years
- d) 6% at 1 year and 72% at 10 years
- e) 1% at 1 year and 28% at 10 years

Correct answer is a.

Retrospective data from tertiary centres managing children with IBD inform this response. The cumulative incidence of any fistula, more than triples, from 1 year to 10 years post diagnosis. Aside from fistulae, patients should be screened for the extra intestinal manifestations of IBD. These include: musculoskeletal (arthritis, osteomalacia), skin (erythema nodosum, pyoderma gangrenosum), mouth (aphthous ulcers), hepatobiliary (primary sclerosing cholangitis, cholelithiasis) ocular (uveitis) and metabolic dysfunction (growth retardation).

In a patient with anaemia, leukocytosis, thrombocytosis and fever, which is of the following is NOT important to exclude

- a) infection
- b) inflammatory bowel disease
- c) malignancy
- d) Kawasaki's disease
- e) trauma

Correct answer is e.

Inflammation, infection and malignancy can be responsible for fever and the haematological abnormalities described. The diagnostic work up will relate to clinical features such as changes in bowel motions in IBD, or recent travel. In the absence of localising symptoms and/or signs, a broad approach to diagnosis must be undertaken.

The most common cause of microcytic anaemia in children is

- a) Anaemia of chronic disease
- b) Thalassemia
- c) Iron deficiency
- d) Sickle cell anaemia
- e) Lead poisoning

Correct answer is c.

While it is important to consider microcytic anaemia as a trigger to investigate for chronic disease, the most common cause of microcytic anaemia is iron deficiency. Children, especially those under 2 and adolescents have additional iron requirements during growth, and the intake of both iron and vitamin C must be considered. Factors that may be important include: a lack of vitamin C consumption, consumption of non-heme sources of iron, breast fed infants older than 6 months without iron supplementation, and older infants who consume more than 500ml of cow's milk, who may be at risk of nutritional iron deficiency. A thorough history will aid in ruling out blood loss as a cause of iron deficiency and should include a menstrual history in older females. Finally, malabsorptive syndromes must be considered in a patient without obvious cause of iron deficiency.

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