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Immunoglobulin A vasculitis presenting as terminal ileitis in late adulthood

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Abstract

Adult-onset immunoglobulin (IgA) vasculitis presenting as terminal ileitis is a rare clinical encounter which can mimic inflammatory bowel disease or infectious gastroenteritis. A high index of clinical suspicion is required to reach the correct diagnosis and to implement the appropriate management plans. Herein, we report a case of an elderly female presenting with a short history of abdominal pain, vomiting, bloody diarrhoea, fatigue and reduced appetite. Based on the blood tests and imaging, she was initially managed as having an infective or inflammatory bowel condition. Subsequently, she developed a vasculitic rash in her lower limbs with accompanying renal involvement including haematuria and sub-nephrotic range proteinuria. She underwent a renal biopsy which confirmed the diagnosis of IgA vasculitis. She was started on a course of corticosteroid therapy which induced clinical remission.

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Case presentation

A 72-year-old female presented with a two-day history of bloody diarrhoea, lower abdominal pain, vomiting, reduced appetite and fatigue. Her past medical history included hypertension, transitional cell carcinoma of the bladder and perianal fissure. On examination, she was apyrexial with a pulse rate of 105 beats per minute and blood pressure 140/95mmHg. There was generalised abdominal tenderness and soft stool in the rectum with fresh blood on per-rectal examination. Initial laboratory investigations revealed the following: white cell count 13.5×109/l (4–10×109/l), haemoglobin 158 g/l (120–150 g/l), platelets 263×109/l (150–410×109/l), C-reactive protein (CRP) 103 mg/l (0–10mg/l), serum creatinine 83µmol/l (45-84), alanine aminotransferase (ALT) 12 IU/l (5-65), alkaline phosphatase 80 IU/l (30–130) and total bilirubin 10µmol/l (<20). The initial clinical impression was that of diverticulitis and she was managed with intravenous antibiotics, analgesia and antiemetics. A computed tomography (CT) scan of the abdomen and pelvis was performed which showed no evidence of acute diverticulitis. However, wall thickening was noted in the distal ileum with perienteric fat stranding and perienteric fluid collections (Figure 1). Furthermore, there was associated congestion of the small bowel mesentery with sub-centimetre mesenteric lymphadenopathy. The radiologist concluded that overall, the appearance was suggestive of acute inflammation in the ileum with differentials of Crohn's disease or infectious ileitis. The patient made good clinical progress with conservative management. A few days after discharge, she developed a purpuric rash on her lower limbs. She was investigated further by her general practitioner (GP) with a series of urine dipstick and urine protein-creatinine

Figure 1 CT scan showing wall thickening of the distal ileum (white arrows) with evidence of perienteric fat stranding and fluid collection (red arrows).

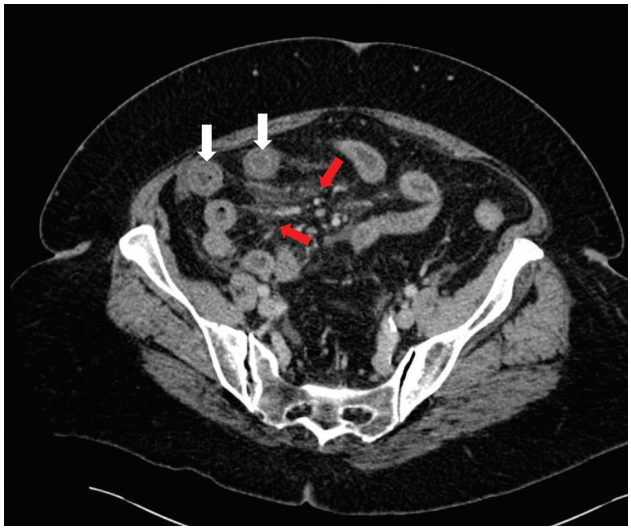

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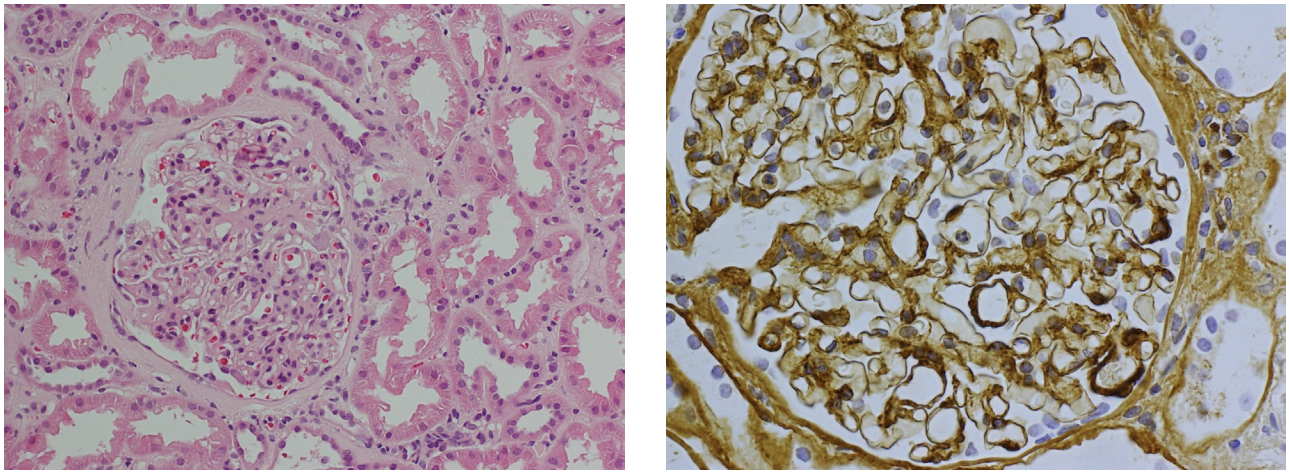
Figure 2 Renal biopsy showing mesangial and cellular proliferation (left) and strong granular mesangial IgA staining on immunohistochemistry (right)



Ratio (PCR) tests. This revealed consistent haematuria and sub-nephrotic range proteinuria with a urine PCR of 201mg/mmol (<15 mg/mmol). Additional immunology screening showed normal antinuclear antibodies (ANA), antineutrophil cytoplasmic antibodies (ANCA) and myeloma screen. She was reviewed by the nephrologist who started her on 2mg perindopril once daily. She also underwent an elective renal biopsy which revealed mesangial proliferation with strong mesangial IgA deposition, in keeping with IgA vasculitis (Figure 2). She was treated with a tapering course of oral prednisolone over six months, which induced remission with a decrease in her urine protein/creatinine ratio (PCR) to 75mg/mmol and complete resolution of her symptoms.

Discussion

IgA vasculitis (IgAV), previously known as Henoch-Schönlein purpura (HSP), is a systemic small-vessel vasculitis predominantly affecting the skin, kidneys, joints and the gastrointestinal (GI) tract. Although approximately 90% of IgAV cases occur in the paediatric population, it can arise rarely in adulthood, as in our case.[1] The incidence of IgAV in adults is estimated to be 1.3 per 100,000, with a mean age at presentation of 50 years.[2]

In 2010 the European League Against Rheumatism (EULAR), Paediatric Rheumatology International Trials Organisation (PRINTO) and Paediatric Rheumatology European Society (PRES), proposed revised criteria for classifying IgAV.[3] They defined IgAV as the presence of purpura (a mandatory criterion), with at least one of four features including (1) diffuse abdominal pain, (2) histopathological evidence of leucocytoclastic vasculitis with predominant IgA deposition or proliferative glomerulonephritis with predominant IgA deposition, (3) acute arthralgia or arthritis and/or (4) renal involvement either in the form of proteinuria or haematuria. These criteria were found to achieve a sensitivity of 100% and specificity of 87% for defining IgAV. The important caveats are that they were derived for a predominantly paediatric population and were not intended to be used as a diagnostic tool. Furthermore, they do not reflect the wide repertoire of GI manifestations that can occur with IgAV. Some experts have proposed replacing diffuse abdominal pain with 'gastrointestinal involvement', as IgAV frequently results in other GI symptoms including nausea, vomiting, haematemesis, melaena and haematochezia. Importantly, GI symptoms have been identified as a key factor for predicting the risk of renal injury in IgAV.[4] GI manifestations of IgAV that have been previously reported include intussusception, acute appendicitis, mesenteric ischaemia, intestinal perforation, pancreatitis, acute cholecystitis, pancreatitis, biliary cirrhosis and terminal ileitis.[5]

The patient reported here had terminal ileitis presenting with vomiting, abdominal pain and haematochezia. Terminal ileitis is commonly associated with Crohn's disease (CD).[6] However, it is important to recognise alternative causes, particularly in patients who do not reflect the typical patient demographic for CD, or in those where atypical systemic signs or symptoms are present. The differential aetiology for terminal ileitis is extensive including infectious (especially *Yersinia enterocolitica* and *Mycobacterium tuberculosis),* malignant (small-bowel adenocarcinoma, lymphoma or carcinoid), ischaemic (typically with caecal involvement due to the distribution of the ileocolic branches of the superior mesenteric artery), drug-induced (especially NSAIDS, oral contraceptives and digoxin), vasculitic (IgAV, polyarteritis nodosa, Churg-Strauss Syndrome) and infiltrative (eosinophilic gastroenteritis, amyloidosis and ileitis associated with spondyloarthropathy).[7]

IgAV manifesting as terminal ileitis is rare and has been reported 14 times in the literature thus far, including our case.[8] Patients have ranged in age from four years to our patient, who, at 72 years, is the oldest reported case of IgAV presenting as terminal ileitis. The most frequent presenting symptoms in these patients were abdominal pain along with arthralgia and purpura. Although these patients typically presents with a purpuric rash, in some cases skin lesions only ensued after the initial GI symptoms.

We suggest that IgAV should be included in the differential for any patient presenting with abdominal pain and

haematochezia. Furthermore, performing a simple urine dip can be critical in unmasking the diagnosis of an underlying systemic vasculitis. In patients with terminal ileitis and evidence of haematuria and/or proteinuria, it is important to perform a full autoimmune screen to look for causes of systemic vasculitis, as well as imaging of the kidneys to screen for underlying nephrolithiasis. Although the diagnosis of IgAV is usually made based on clinical manifestations, histological confirmation of the organ involved may be required in cases of diagnostic uncertainty. The presence of a leucocytoclastic vasculitis with predominant IgA deposition on the skin biopsy is considered pathognomonic of IgAV. In patients with significant renal involvement, renal biopsy may be advocated to establish the diagnosis.

In particularly rare cases of IgAV, patients can present with terminal ileitis without extra-intestinal manifestations. In such cases, it can be difficult to differentiate between IgAV, CD or the other aforementioned causes of terminal ileitis. Stool culture and enteric PCR can identify common infectious causes. However, faecal calprotectin is unlikely to be clinically useful in this setting, as any cause of intestinal inflammation can result in a rise in calprotectin levels.[9] Clinically, in the absence of infection or ischaemia, patients with terminal ileitis will most likely be treated with systemic steroids on the presumption that the diagnosis is CD and these patients may end up being placed on unnecessary longterm immunomodulator therapy. Hence, a tissue diagnosis through ileocolonoscopy ideally should be sought for all patients with terminal ileitis to confirm CD, although it may not always be endoscopically feasible to intubate the terminal ileum. In general, the majority of patients with IgAV manage to reach spontaneous resolution with supportive treatment alone. Although there are no high-quality randomised controlled trials (RCTs) which support the use of corticosteroids or immunosuppression for IgAV, in selected cases, such as those with severe GI involvement or intractable arthritis, a course of corticosteroid therapy may prove beneficial.

Conclusion

This case highlights that IgAV can present in late adulthood as a terminal ileitis, mimicking the usual suspects of inflammatory bowel disease or infectious gastroenteritis. The presence of extra-intestinal manifestations in a patient with terminal ileitis such as purpura, arthralgia or proteinuria/haematuria on the urine dip, should raise the clinical suspicion of an underlying diagnosis of IgAV. However, it is important to remember that GI manifestations can rarely be the sole presenting feature of IgAV. Seeking a histological diagnosis can be useful in clinching the diagnosis of IgAV in such cases.

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