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Letter to the Editor (Case report)

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ANCA-associated vasculitis of the appendix

Key message

- ANCA-associated vasculitis can manifest as an isolated appendicitis, and careful histopathological examination is paramount.

SIR, A 27-year-old female was referred to hospital with a 4-day history of right upper quadrant and flank pain, associated with high-grade pyrexia. This was preceded by a 6-month history of upper respiratory tract symptoms, including coughing and sneezing, lethargy, malaise and weight loss. Two months before presentation, she experienced a similar episode of abdominal pain lasting a day. Her past medical history was unremarkable aside from seasonal allergic sinusitis since age 11 years. She was on no medications. There was a maternal history of Hashimoto's thyroiditis.

The patient was initially treated for right pyelonephritis owing to leucocyturia and haematuria, but no organism was isolated on culture. Despite treatment her abdominal pain worsened, and abdominal CT scan showed poor parenchymal enhancement on the superior pole of the right kidney, suggested to be either pyelonephritis or renal infarction. She proceeded to surgical evaluation and management. Laparoscopy revealed an ischaemic right kidney. An appendicectomy was performed to exclude appendicitis as a cause of her abdominal pain, because the appendix was discoloured in appearance without accompanying evidence of a change in transmural thickness or perforation. Initial histological assessment revealed a normal appendix.

Autoimmune serological studies performed for further evaluation of her haematuria and renal infarct demonstrated the simultaneous presence of cANCA (titre 1 in 80) and anti-PR3 antibodies (44 IU/ml, normal <6 IU/ml) on two separate occasions. This was associated with raised inflammatory markers and C4-hypocomplementaemia in the absence of a rheumatoid factor or ANA. Lupus anticoagulant was detected. Although initial urinalysis performed before laparoscopy demonstrated haematuria (red cells $>100 \times 10^6$/l), subsequent samples were absent for dysmorphic red cells, protein and casts. Her renal indices were within normal limits. CT renal angiogram demonstrated a superior right renal infarct and a right renal artery thrombosis. CT of the sinuses showed mild inflammatory changes. Septal and post-nasal space biopsies showed reactive lymphoid hyperplasia. CT chest was normal. A renal biopsy was not performed owing to the absence of urinary abnormalities and normal renal function. Given the infarction, thrombosis and positive lupus anticoagulant, the patient was commenced on therapeutic enoxaparin. A progress CT renal angiogram 1 month later showed maturation of her renal infarct and resolution of renal artery thrombosis.

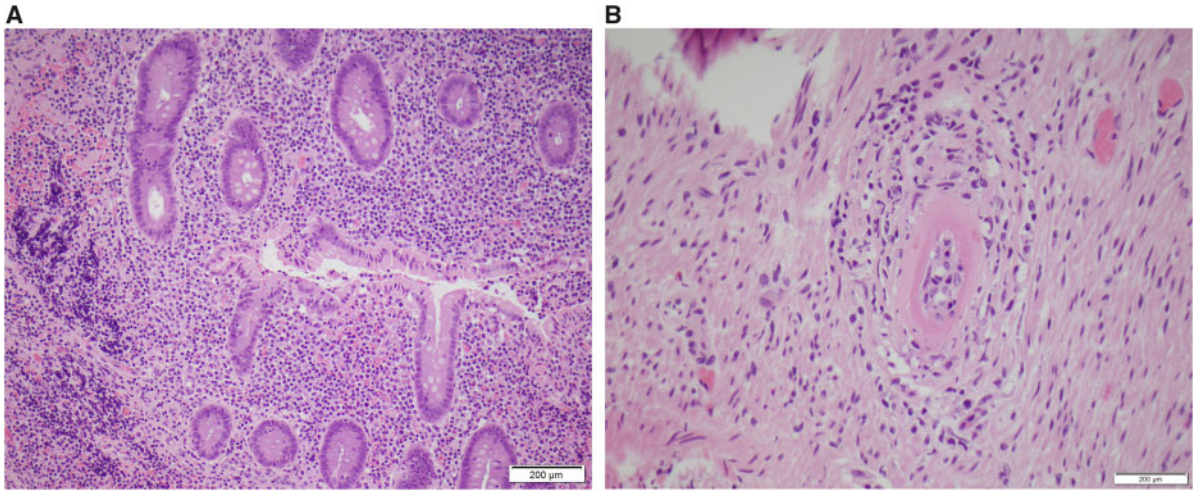
The patient's histopathology of the appendix was re-examined to assess for a possible site of ANCA-associated vasculitis (AAV) in the absence of an overt vasculitic process in other organs. Targeted examination revealed vessels in both the submucosa and the muscularis propria showing a lymphohistiocytic infiltrate associated with fibrinoid necrosis of the vessel walls, intramural inflammatory cells and endothelial hyperplasia (Fig. 1). There was no eosinophilia or granulomas, and the mucosa appeared normal. Small-vessel vasculitis of the appendix was diagnosed.

The patient was followed up for 4 months post-appendectomy, at which point her inflammatory markers had normalized without any immunosuppression. She had persistent anti-PR3 antibodies at 35 IU/ml. A progress CT renal angiogram showed maturation of her renal infarct and resolution of renal artery thrombosis. At this time, there were no disease manifestations of concern to warrant immunosuppression. The patient will be followed up for evidence of an exacerbation of vasculitis in other organs, especially sinopulmonary and renal involvement.

Gastrointestinal involvement in systemic vasculitis has been well documented. Common symptoms include abdominal pain, nausea, vomiting, melaena and haematemesis. Gastroduodenal ulceration has been demonstrated endoscopically. Involvement can include the small and large bowel, pancreas, gall bladder and appendix. Manifestations typically relate to ischaemia, with perforation and peritonitis responsible for the majority of mortality. Mortality has been estimated at $\leq 25\%$ [1].

Vasculitis involving the gastrointestinal tract is most commonly associated with medium-vessel vasculitis, such as polyarteritis nodosa, and usually occurs as part of the systemic vasculitic process. Pagnoux *et al.* [1] reported that in six of 62 patients with vasculitis affecting the gastrointestinal tract, the appendix involved, but all of these patients had other manifestations of their disease. Systemic vasculitis involving the appendix has been described in SLE [2], Henoch–Schönlein purpura [3], eosophilic granulomatosis with polyangiitis [4] and RA [5]. A larger case series, comprising 608 patients with vasculitis affecting the abdominal vasculature or viscera, found 18 cases of localized involvement, only one of which involved the appendix [6]. ANCA was not detected in any of the localized cases. There have been case series on single-organ vasculitis affecting the appendix, but these cases are attributable to polyarteritis affecting medium-sized vessels [7]. There have been reports of isolated small-vessel vasculitis of the appendix, but the ANCA was not reported, and an evaluation for occult sinopulmonary and renal

Fig. 1 Histopathology of the appendix



(**A**) Normal mucosa (Haematoxylin and Eosin, ×400). (**B**) Vessels in the muscularis propria and submucosa with a perivascular lymphohistiocytic infiltrate, associated with fibrinoid necrosis of the vessel wall, intramural inflammatory cells and endothelial hyperplasia (Haematoxylin and Eosin, ×400).

disease was not performed in all cases [8]. To our knowledge, our case is the only published case of AAV with isolated involvement of the appendix.

Anti-PR3 and anti-MPO antibodies have been demonstrated in relationship to chronic bacterial (tuberculosis, staphylococcal and streptococcal), viral (HCV and parvovirus B19) and fungal infections [9]. This has not been observed with acute appendicitis. Furthermore, there was no evidence of neutrophilic inflammation or abscess formation on histology of our patient's appendix.

IBD is rarely associated with AAV but was excluded in our case on the basis of normal mucosal histopathology [10]. The patient's renal infarct is most likely to be associated with the presence of a thrombosis associated with lupus anticoagulant from her AAV [11]. Vasculitis of the renal artery was considered unlikely given the resolution of changes in the vessels after 1 month.

This unique case enforces the importance of close histopathological examination, given the diverse nature in which pathologies such as vasculitis can manifest. Interestingly, Plaut [12] examined 6576 appendices and found that necrotizing arteritis had been overlooked in 1.34% of cases, which raises the possibility that many cases of vasculitis of this organ might be undetected. Moreover, our case demonstrates, for the first time, that AAV can cause appendicitis in the absence of systemic manifestations. These patients need to be followed closely to monitor serological positivity and for the development of systemic features requiring immunosuppression.

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