

A rare cause of colonic thickening and lymphadenopathy

CASE

A 73-year-old retired analytic chemist presented with 4 weeks of epigastric discomfort, weight loss and loose stools. His medical history revealed pancreatic insufficiency on the background of a pancreatic mass, which had resolved 8 years previously, childhood eczema, and shellfish allergy. Laboratory investigation demonstrated an elevated C-reactive protein of 32 mm/L and IgG of 14.8 g/L with negative endomysial and

auto-antibodies, normal blood count, liver function and amylase.

CT of the abdomen showed concentric thickening of the ascending colon and caecal wall with serosal abnormality and mesenteric lymphadenopathy (figure 1A, B). Ileocolonoscopy revealed an oedematous and inflamed proximal ascending colon, caecal valve and terminal ileum (figure 2A–C). The transverse colon, left colon and rectum were spared. Colonic biopsies showed an infiltrate rich in lymphocytes and plasma cells, with no granuloma or dysplasia (figure 3A).

QUESTION

What further investigations will support the diagnosis? What are the management options?

Figure 1 (A) Coronal portal phase CT of the abdomen showing concentric thickening of the wall of the ascending colon and terminal ileum (arrow). (B) Axial contrast-enhanced CT of the abdomen showing thickening of the wall of the ascending colon (arrow) and a cluster of small mesenteric lymph nodes.

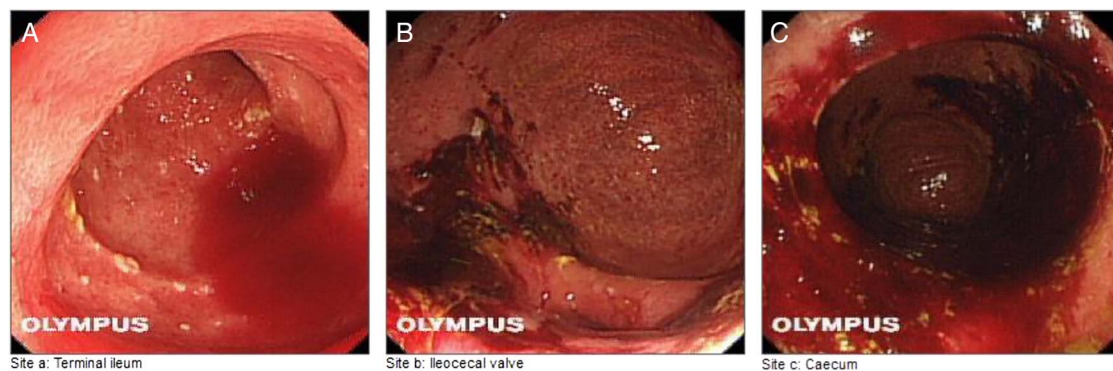
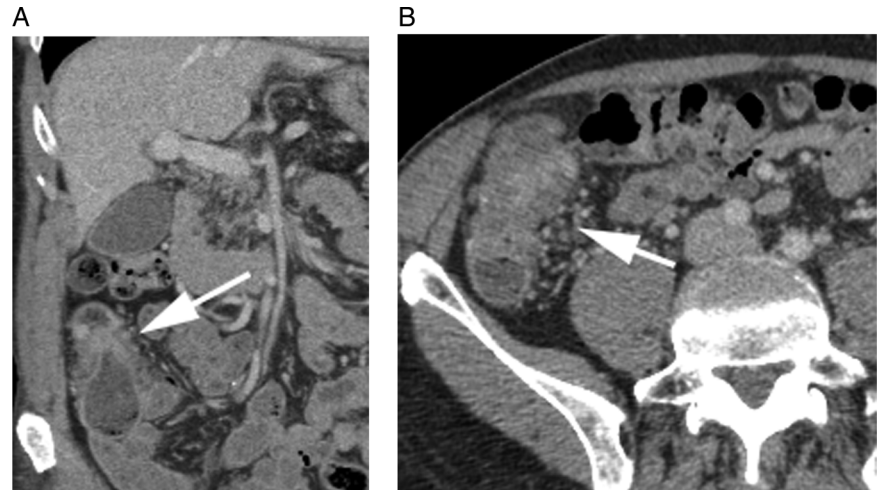


Figure 2 (A–C) Ileocolonoscopy showing mucosal congestion, erythema and multiple small ulcers in the terminal ileum (A, left panel), and erythema, contact bleeding and mucopurulent exudate at the ileocaecal valve (B, right panel) and the caecum (C).

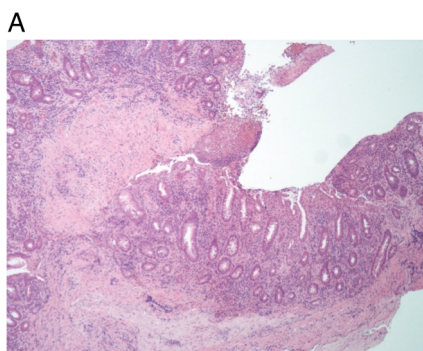


Figure 3 (A) Colonic biopsies (H&E section) showing cryptitis and focal crypt abscesses, and a predominant chronic inflammatory cell infiltrate within the lamina propria and basal lymphoplasmacytosis.

Editor's quiz: GI snapshot

ANSWER

Serology confirmed an elevated serum IgG4 of 6.47 g/L (upper limit of normal (ULN) 1.35 g/L) and IgE of 771 kIU/L (ULN 125 kIU/L), with a polyclonal hypergammaglobulinaemia.

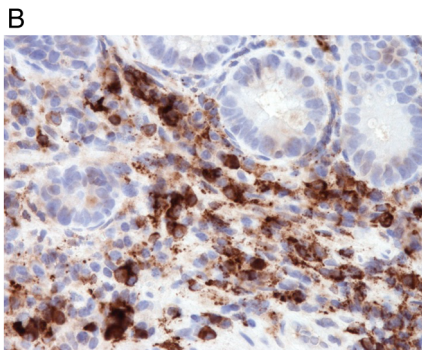


Figure 3 (B) IgG4 immunohistochemical stain ($\times 400$ magnification) showing >50 IgG4-positive plasma cells per high power field. The IgG4 to IgG ratio was 0.45. Obliterative phlebitis and storiform fibrosis were not seen in biopsy specimens, although this is similarly the case in the lymph node, lung, minor salivary and lacrimal glands affected by IgG4-related disease.

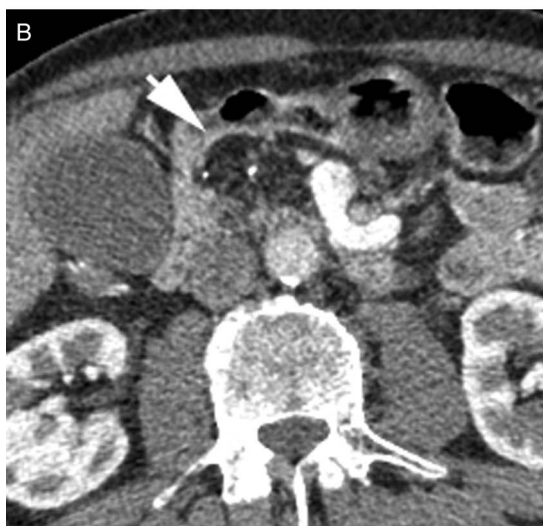


Figure 4 (A) CT contrast-enhanced of the abdomen and pelvis showing a decrease in colonic wall thickening (arrow) with resolution of nodes after corticosteroid therapy. (B) CT contrast-enhanced of the abdomen and pelvis showing complete fatty replacement of the pancreatic parenchyma (arrow) with a few flecks of calcification after corticosteroid therapy.

$\beta 2$ -microglobulin was 3.95 (ULN 3.0) and vasculitic screen was negative. Colonic immunostaining revealed an IgG4 plasma cell count of 80/high power field (HPF) and ratio of IgG4 to IgG of $>40\%$ (figure 3B).

Treatment with prednisolone 40 mg for 2 weeks was commenced, tapering over 3 months. Symptomatic, serological and radiological improvement was observed. Serum IgG4 and IgE levels fell, (4.58 g/L and 380 kIU/L, respectively), but failed to normalise. CT of the abdomen showed a decrease in colonic wall thickening, resolution of nodes and pancreatic atrophy at 6 months (figure 4A, B). Recurrent disease 2 years later prompted a second course of corticosteroids, after discussion at the IgG4 multidisciplinary team meeting.

IgG4-related disease (IgG4-RD) is a systemic fibroinflammatory condition with an older male predominance, which has been linked to chronic occupational exposure,¹ allergic/atopic history and elevated IgE.² In accordance with the comprehensive diagnostic criteria, the presence of a localised colonic mass, elevated serum IgG4, characteristic histology with prominent IgG4-positive plasma cells (>10 /HPF) and IgG4 to IgG ratio ($>40\%$) is sufficient for 'definitive IgG4-RD',³ and suggestive of a novel manifestation; 'IgG4-related colitis' (IgG4-C). Supportive features included burnt-out autoimmune pancreatitis, which satisfied the histology, imaging, serology, organ involvement, response to steroid treatment (HISORT) criteria,⁴ and radiological response to corticosteroid therapy.

IgG4-C has a broad differential, including inflammatory colitis, carcinoma, lymphoma, granulomatous and vasculitic disease, which must be excluded. Cases require multidisciplinary team input. Surgical resection can be avoided by a high index of suspicion. The additional benefit of immunosuppressive agents over corticosteroids alone for relapse has been questioned, although rituximab provides promise in those with refractory disease.⁵

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Contributors ELC was responsible for conception, patient consent, drafting and submitting the final manuscript. LMW performed histological assessment and immunostaining of specimens, and provided histology images. HB performed radiological interpretation and provided radiology images. RWC and JC were responsible for patient investigation and management. All authors were members of the IgG4 multidisciplinary team and critically reviewed and approved the final manuscript.

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REFERENCES

- de Buy Wenniger LJM, Culver EL, Beuers U. Exposure to occupational antigens might predispose to IgG4-related disease. *Hepatology* 2014;60:1453–4.

- 2 Della Torre E, Mattoo H, Mahajan VS, *et al.* Prevalence of atopy, eosinophilia, and IgE elevation in IgG4-related disease. *Allergy* 2014;69:269–72.
- 3 Umehara H, Okazaki K, Masaki Y, *et al.* Comprehensive diagnostic criteria for IgG4-related disease (IgG4-RD), 2011. *Mod Rheumatol* 2012;22:21–30.
- 4 Chari ST. Diagnosis of autoimmune pancreatitis using its five cardinal features: introducing the Mayo Clinic's HISORT criteria. *J Gastroenterol* 2007;42(Suppl 18):39–41.
- 5 Hart PA, Topazian MD, Witzig TE, *et al.* Treatment of relapsing autoimmune pancreatitis with immunomodulators and rituximab: the Mayo Clinic experience. *Gut* 2013;62:1607–15.



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