Table 1 *FCRL3*−110 polymorphisms in 59 patients with autoimmune pancreatitis, 62 patients with chronic calcifying pancreatitis, and 97 healthy subjects

	Frequency (%)			Autoimmune pancreatitis *v* chronic calcifying pancreatitis (p value)	Autoimmune pancreatitis *v* healthy subjects p value (OR (95% CI))
	Autoimmune pancreatitis (n = 59)	Chronic calcifying pancreatitis (n = 62)	Healthy subjects (n = 97)		
Genotype frequency					
A/A	13.6	6.5	2.1	0.32	0.012 (7.45: 1.53–36.41)
A/G	30.5	32.3	36.1	0.99	0.59
G/G	55.9	61.3	61.9	0.68	0.57
Allele positivity					
A present	44.1	38.7	38.1	0.68	0.57
G present	86.4	93.5	97.9	0.32	0.012 (0.13: 0.027–0.66)
Allele genotype					
A present	28.8	22.6	20.1	0.34	0.10
G present	71.2	77.4	79.9		

OR, odds ratio; CI, confidence interval.

and control subjects ($\chi^2 = 8.12$, $p = 0.017$). Positivity for the −110G allele was significantly decreased in autoimmune pancreatitis patients ($p = 0.012$, odds ratio 0.13; table 1), indicating a significant association of the −110A/A genotype with autoimmune pancreatitis. The frequency of −110A/A alleles was significantly increased in patients with autoimmune pancreatitis compared with controls ($p = 0.012$, odds ratio = 7.45; table 1). There are two possible explanations for these findings: *FCRL3*−110 may be functionally linked with susceptibility to autoimmune pancreatitis, or this allele may be a linkage marker for a neighbouring unidentified susceptibility gene on chromosome 1q 21. No other alleles were found to be significantly associated with autoimmune pancreatitis.

Mean (SEM) serum IgG4 concentrations in patients with *FCRL3*−110A/A, −110A/G, and −110G/G were 1279.4 (404.8) mg/dl, 794.8 (149.4) mg/dl, and 669.2 (78.5) mg/dl, respectively. Serum IgG4 concentrations in patients with autoimmune pancreatitis were found to be significantly positively correlated with the number of susceptible alleles ($r^2 = 0.094$, $p = 0.014$). However, no association between the HLA DRB1*0405-DQB1*0401 haplotype and *FCRL3*−110 alleles was found in this study (data not shown). These results suggest that both the HLA DRB1*0405-DQB1*0401 haplotype and *FCRL3*−110 alleles are related to susceptibility for autoimmune pancreatitis but play different roles in the mechanisms inducing autoimmune pancreatitis.

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References

1 **Yoshida K**, Toki F, Takeuchi T, *et al.* Chronic pancreatitis caused by an autoimmune abnormality. Proposal of the concept of autoimmune pancreatitis. *Dig Dis Sci* 1995;**40**:1561–8.
2 **Okazaki K**, Chiba T. Autoimmune related pancreatitis. *Gut* 2002;**51**:1–4.
3 **Hamano H**, Kawa S, Horiuchi A, *et al.* High serum IgG4 concentrations in patients with sclerosing pancreatitis. *N Engl J Med* 2001;**344**:732–8.
4 **Aparisi L**, Farre A, Gomez-Cambronero L, *et al.* Antibodies to carbonic anhydrase and IgG4 levels in idiopathic chronic pancreatitis: relevance for diagnosis of autoimmune pancreatitis. *Gut* 2005;**54**:703–9.
5 **Kawa S**, Ota M, Yoshizawa K, *et al.* HLA DRB10405-DQB10401 haplotype is associated with autoimmune pancreatitis in the Japanese population. *Gastroenterology* 2002;**122**:1264–9.
6 **Davis RS**, Wang YH, Kubagawa H, *et al.* Identification of a family of Fc receptor homologs with preferential B cell expression. *Proc Natl Acad Sci U S A* 2001;**98**:9772–7.
7 **Hatzivassiliou G**, Miller I, Takizawa J, *et al.* IRTA1 and IRTA2, novel immunoglobulin superfamily receptors expressed in B cells and involved in chromosome 1q21 abnormalities in B cell malignancy. *Immunity* 2001;**14**:277–89.
8 **Kochi Y**, Yamada R, Suzuki A, *et al.* A functional variant in FCRL3, encoding Fc receptor-like 3, is associated with rheumatoid arthritis and several autoimmunities. *Nat Genet* 2005;**37**:478–85.
9 **Ikari K**, Momohara S, Nakamura T, *et al.* Supportive evidence for a genetic association of the FCRL3 promoter polymorphism with rheumatoid arthritis. *Ann Rheum Dis* 2006;**65**:671–3.
10 **Steinberg WM**, Barkin J, Bradley EL 3rd, *et al.* ontroversies in clinical pancreatology: autoimmune pancreatitis: does it exist? *Pancreas* 2003;**27**:1–13.

Extensive intestinal ischaemic necrosis in Wegener's granulomatosis

Wegener's granulomatosis (WG) is a rare form of multisystemic vasculitis. WG most commonly presents as signs and symptoms of upper or lower respiratory tract disease, or both.[1] Although clinical manifestations from the gastrointestinal disease have been described,[2–9] presentation with extensive intestinal ischaemic perforation without renal or pulmonary disease has not been reported. We report a case of WG presenting with extensive small and large bowel ischaemic perforation without renal or pulmonary disease.

A previously healthy 44 year old female was referred for bronchoscopy with an eight week history of lethargy, polyarthralgia, vasculitic skin rash, and distal sensory and motor polyneuropathy. Laboratory analysis showed normal results on full blood count and urinalysis but an elevated erythrocyte sedimentation rate (79 mm/h; normal <15 mm/h) and positive cytoplasmic antineutrophil cytoplasm antibody (c-ANCA; titre 1: 89.10). Chest radiograph was normal. A diagnosis of systemic vasculitis secondary to WG was made and intravenous methyl prednisolone was started.

The following day the patient developed severe abdominal pain with signs of peritonitis. Plain film and computed tomography of the abdomen confirmed pneumoperitoneum. At laparotomy, multiple mid-ileal ischaemic perforations with extensive ischaemic involvement of the left and transverse colon were seen (fig 1A). One metre of small bowel was resected with ileoileal anastomosis and extended left hemicolectomy and a transverse end colostomy. Postoperatively, the patient was continued on intravenous methylprednisolone 1 g for five days followed by dexamethazone 16 mg intravenously daily and cyclophosphamide intravenously 150 mg daily. Histology of the small and large bowel showed extensive vasculitis with fibrinoid necrosis (fig 1B).

On the 32nd day of admission, the patient again developed an acute abdomen and

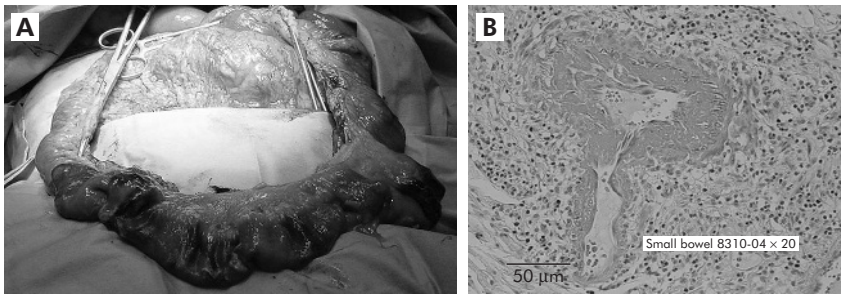

Figure 1 (A) Operative view showing multiple areas of ischaemia, necrosis, and perforations. (B) A section of small bowel showing extensive inflammation and vasculitis with fibrinoid necrosis.

underwent a second laparotomy showing multiple ischaemic perforations at the previous anastomotic site. Further bowel resection, ileostomy, mucous fistula, and refashioning of the colostomy were performed. On day 42 after admission she underwent a third laparotomy due to further ischaemic gangrene of the right colon and ileum; these were excised leaving only 30 cm of jejunum as jejunostomy. Supportive treatment was continued with total parenteral nutrition (TPN). Gradually, cyclophosphamide and steroids were stopped after three and six months, respectively. The vasculitic lesions fully subsided and PR3 ANCA became negative. The patient was discharged on home TPN. Two months later when seen in the outpatients clinic she was well.

WG presents as upper or lower airway symptoms, or both, in 90% of cases.[1] Symptomatic gastrointestinal disease in WG is not reported often. There are a few well documented cases which describe only severe forms of the disease affecting part of the bowel, anywhere in the gastrointestinal tract, in the presence of classic lung and renal involvement (table 1). Interestingly, in our patient, almost the whole of the intestine (small and large) was affected without any sign of clinical disease in the lungs or kidneys. The diagnosis of WG in our patient was based on clinical features of systemic vasculitis, high titre of cANCA, and histological evidence of focal necrotising vasculitis in the resected bowel specimen.

Treatment of bowel disease in WG is for the underlying vasculitis, with cyclophosphamide and glucocorticoids. Bowel perforation in our patient occurred a day after initiation of immunotherapy and thus was unlikely to be the cause of the perforation. Older age, renal disease, and high serum creatinine levels have been advocated as predictors of poor outcome.[10] The younger age of our patient and no sign of renal involvement with creatinine levels remaining normal throughout disease favoured her survival.

This case highlights the fact that extensive gastrointestinal involvement can occur even in the absence of renal or pulmonary disease in WG.

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References

1 **Hoffman GS**, Kerr GS, Leavitt RY, *et al*. Wegener granulomatosis: an analysis of 158 patients. *Ann Intern Med* 1992;**116**:488–98.
2 **McNabb WR**, Lennox MS, Wedzicha JA. Small intestinal perforation in Wegener's granulomatosis. *Postgrad Med J* 1982;**58**:123–5.
3 **Haworth SJ**, Pusey CD. Severe intestinal involvement in Wegener's granulomatosis. *Gut* 1984;**25**:1296–300.
4 **Geraghty J**, Mackay IR, Smith DC. Intestinal perforation in Wegener's granulomatosis. *Gut* 1986;**27**:450–1.
5 **Tokuda M**, Kurata N, Daikuhara H, *et al*. Small intestinal perforation in Wegener's granulomatosis. *J Rheumatol* 1989;**16**:547–9.
6 **Storesund B**, Gran JT, Koldingsnes W. Severe intestinal involvement in Wegener's granulomatosis: report of two cases and review of the literature. *Br J Rheumatol* 1998;**37**:387–90.
7 **Skaife P**, Lee S, Ramadwar M, *et al*. Intestinal perforation as a presentation of Wegener's granulomatosis. *Hosp Med* 2000;**61**:286–7.
8 **Chow FY**, Hooke D, Kerr PG. Severe intestinal involvement in Wegener's granulomatosis. *J Gastroenterol Hepatol* 2003;**18**:749–50.
9 **Pickhardt PJ**, Curran VW. Fulminant enterocolitis in Wegener's granulomatosis: CT findings with pathologic correlation. *AJR Am J Roentgenol* 2001;**177**:1335–7.
10 **Mahr A**, Girard T, Agher R, *et al*. Analysis of factors predictive of survival based on 49 patients with systemic Wegener's granulomatosis and prospective follow-up. *Rheumatology (Oxford)* 2001;**40**:492–8.

Table 1 Gastrointestinal disease in Wegner's granulomatosis

Case reports	Age (y)	Sex	GI location	Respiratory/renal involvement	Perforations	Pathology	Surgery	Outcome
McNabb[2]	50	M	Distal ileum	Both	Multiple	Ulceration	Yes	Survival
Haworth[3]	43	F	Ileum, caecum, rectum,	Both	None	Ulceration	No	Survival
Geraghty[4]	46	M	Small bowel, colon	Both	Three	Necrosis, ulceration	Yes	Death
Tokuda[5]	37	M	Distal ileum	Both	Single	Necrosis, vasculitis	Yes	Survival
Storesund[6] Case 1	26	M	Sigmoid, ascending, transverse colon	Both	Single	Ischaemic vasculitis	Yes	Survival
Storesund[6] Case 2	46	F	Ileum, ascending, transverse, descending, sigmoid colon	Both	None	Inflammation, ischaemic vasculitis	Yes	Survival
Skaife[7]	69	M	Distal jejunum	Both	Multiple	Ischaemic vasculitis	Yes	Death
Chow[8]	46	M	Jejunum	Renal	None	Ulceration, vasculitis	Yes	Survival
Pickhardt[9]	26	M	Ileum, jejunum, colon	Respiratory	None	Necrosis, ischaemic vasculitis	Yes	Survival
Our patient	44	F	Distal jejunum, ileum, caecum, ascending, transverse, descending, sigmoid colon	None	Multiple	Necrosis, gangrenous, ischaemic vasculitis	Yes	Survival