Case report

Severe intestinal involvement in Wegener's granulomatosis

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SUMMARY A case of Wegener's granulomatosis is described, in which the presentation was blood stained mucus diarrhoea. Severe ileal, caecal, and rectal involvement improved rapidly after treatment with cyclophosphamide, azathioprine, and prednisolone. Although intestinal disease is an uncommon feature of Wegener's granulomatosis, both in our own experience (four of 45 cases) and in the literature, this diagnosis should be considered in view of the response to appropriate therapy.

Wegener's granulomatosis is a systemic vasculitis of unknown aetiology, with distinct clinical and histological features.¹⁻³ The disease is characterised by involvement of the upper airways, lung and kidney, although almost any organ can be affected. The reported incidence of gastrointestinal involvement is low and histological confirmation often lacking, although there is one well documented case with proven ileal pathology.⁴ We would like to report a case in which gastrointestinal symptoms were the principal feature at presentation.

Case report

A 43 year old woman was admitted with blood stained mucus diarrhoea and impaired renal function. She had been well until 11 months previously when she developed right frontal sinusitis and mouth ulcers, which resolved spontaneously. Six months later she noticed deafness, and was found to have bilateral impaired air conduction with secretory otitis media; her symptoms responded to antihistamines and decongestants. Two months before admission she developed pain and swelling of the knees, ankles, elbows, wrists and the small joints of the hands. In the month before admission she became increasingly unwell with anorexia, weight loss of 2.75 kg, and painful red eyes. Two days

before admission she developed profuse diarrhoea, four to five times per day, with blood and mucus. She subsequently noted a widespread blotchy rash, and a decrease in urine output. There was no relevant past medical history.

On examination she was pyrexial at 37.5°C, with mild keratitis, splinter haemorrhages, extensive purpuric lesions over the extremities and buttocks, and numerous oral ulcers (Fig. 1a); there was a large necrotic perianal ulcer surrounded by purpura (Fig. 1b). There was swelling and tenderness of the knees, ankles, wrists, elbows and small joints of the hands. Blood pressure was raised at 160/110 mmHg, but examination of the heart and lungs was otherwise normal. The abdomen was distended, but not tender. Neurological assessment was normal apart from bilateral conduction deafness.

Investigations showed: haemoglobin 10.5 g/dl, white cell count $26.6 \times 10^9/l$ (80% neutrophils), platelet count $315 \times 10^9/l$, plasma creatinine 384 $\mu\text{mol/l}$, serum albumin 37 g/l, alkaline phosphatase 261 IU/l (30-130) and aspartate amino-transferase 106 IU/l.⁷⁻⁴⁰ Immunoglobulins and complement components were normal; rheumatoid factor and antinuclear factor were negative. Circulating immune complexes were detected by rheumatoid factor binding assay. Urine sediment contained numerous red cell casts and free red cells. Renal biopsy showed focal necrotising glomerulonephritis with crescents and mild tubular atrophy (Fig. 2). Stool microscopy and culture for *Shigella*,

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Fig. 1(a) Photograph of mouth at presentation showing labial ulceration. (b) Photograph of buttocks at presentation showing necrotic perianal ulceration with surrounding erythema. Vasculitic skin lesions are also present.

Salmonella, and Campylobacter were negative, as was the amoebic fluorescent antibody test. Sigmoidoscopy revealed ulcerated rectal mucosa, which bled spontaneously, but was normal beyond 10 cm. Rectal biopsy showed essentially normal mucosa and submucosa, with no evidence of vasculitis, granuloma formation of chronic inflammatory bowel disease; there were, however, large

collections of neutrophils on the mucosal surface. Plain abdominal and chest radiographs were normal, but sinus radiographs showed mucosal thickening in both maxillary antra with a fluid concentration on the right. Barium meal and follow through 10 days after admission showed an abnormal and narrowed terminal ileum and caecum (Fig. 3). Barium enema, 19 days after admission showed an ulcerated and ragged caecum; the sigmoid colon did not contract well, but the rectum appeared normal.

Fig. 2 Photomicrograph of renal biopsy showing focal necrotising glomerulonephritis with crescent formation and mild tubular atrophy (H & E $\times 400$ original magnification).

MANAGEMENT AND COURSE

Treatment was started with prednisolone 60 mg/day, cyclophosphamide 3 mg/kg/day and azathioprine 1 mg/kg/day. On this therapy the plasma creatinine fell and the arthritis and skin rash improved, although she continued to have bloody diarrhoea. Ten days after starting treatment cytotoxic agents were stopped, because of leucopenia and thrombocytopenia. At this time discrete pulmonary lesions were detected radiographically, which progressed to cavitation (Fig. 4). Investigations for pulmonary infection, including bronchoscopy, were negative. On day 13 she passed a mucosal cast of her colon, after which she continued to have diarrhoea but without blood. The large perianal ulcer had almost healed by this time, and sigmoidoscopy revealed only minor rectal ulceration and minimal hyper-

Fig. 3 Barium follow through taken 10 days after presentation showing ragged and narrowed terminal ileum and caecum.

aemia. Six weeks after starting treatment barium meal and follow through showed normal ileum but an irregular, contracted caecum; chest radiograph changes were resolving and renal function had returned to normal. Her diarrhoea had resolved after six months, and barium meal and enema were normal. The patient has now been followed for three years and remains in remission.

Discussion

The diagnosis of Wegener's granulomatosis in this patient was based on the combination of upper airways involvement, radiological evidence of lung disease and focal necrotising glomerulonephritis on renal biopsy. Other clinical features were arthritis, oral and anal ulceration, keratitis and a vasculitic skin rash. Fauci's group have recently published their experience of 85 patients with Wegener's granulomatosis,³ and conclude that in order to establish the diagnosis there should be clinical evidence of disease in two of the three principle sites (upper airways, lung, and kidney), with histological confirmation in at least one and preferably two sites. Earlier series (1) described advanced cases studied at necropsy, which accounts for the frequent demonstration of granulomatous vasculitis; this is often impossible in life. As blood stained mucus diarrhoea was the principal presenting feature, inflammatory and infective bowel disease were considered in the differential diagnosis. The distribution of gut involvement, with rectal, caecal, and ileal disease, made ulcerative colitis unlikely. Crohn's disease was a major possibility, but the extra-gastrointestinal manifestations, notably severe respiratory and renal involvement, were against this diagnosis.

Wegener reported gastrointestinal involvement in two of his three patients;⁵ in one of these he described an ulcerating necrotising process in the ileum, colon and rectum with marked oedema and leucocyte infiltration of the submucosa. Goodman and Churg's detailed pathological description of seven patients, six studied at necropsy, does not document bowel involvement,¹ nor did these patients have gastrointestinal symptoms.² Walton, reviewing 56 cases of Wegener's granulomatosis, noted that 24% of the 54 patients studied at necropsy had evidence of bowel disease, but no gastrointestinal symptoms were detailed.⁶ Fauci's reviews in 1973 (18 patients)⁷ and in 1983 (85 patients),³ do not comment on gastrointestinal involvement, and other series also suggest that bowel disease is rare or absent.^{8,9}

Of our 45 patients with Wegener's granulomatosis, four had gut symptoms at presentation;¹⁰ two had abdominal pain, one had abdominal pain and diarrhoea, and one had painless diarrhoea (the subject of this report). In addition, one patient had transient abdominal pain and diarrhoea during a relapse of disease. The pattern of gastrointestinal disease in our patients with various forms of systemic vasculitis, has recently been reviewed.¹¹ Symptoms suggestive of gastrointestinal involvement included abdominal pain, diarrhoea, and blood loss (Table). The incidence of gut involve-

Fig. 4(a) and (b) Chest radiographs taken 16 and 34 days after presentation, showing distinct opacities in both mid zones developing into thin walled cavities.

ment was higher in patients with classical polyarteritis nodosa and microscopic polyarteritis than in those with Wegener's granulomatosis, but no distinct clinical features were observed in the different types of vasculitis.

The treatment of bowel disease in patients with Wegener's granulomatosis is as for the underlying vasculitis. Cyclophosphamide, combined with prednisolone, has had a major impact on the disease.^{3,7} Our treatment regimen also includes

azathioprine,¹⁰ and the effects of plasma exchange are being investigated. The response to treatment is usually dramatic, with rapid improvement in cutaneous, joint and muscle involvement. Recovery of renal function usually occurs within one to four weeks; gastrointestinal features resolve over a similar period, although surgical intervention may be required for the complications of bowel perforation,¹² infarction of the gall bladder,³ and persistent haemorrhage.⁴ Long term remission of the disease can be maintained with cyclophosphamide,^{3,7} or azathioprine combined with low dose prednisolone.¹⁰

Although uncommon, intestinal involvement may be a major feature of Wegener's granulomatosis, and this diagnosis should be considered in patients presenting with bowel symptoms accompanied by evidence of systemic vasculitis. The importance of making the diagnosis is shown in this report, as appropriate treatment can result in rapid resolution of the disease.

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Table Gastrointestinal involvement in patients with systemic vasculitis

Disease group	Patient (no)	With GI involvement (no)	Abdominal pain	Diarrhoea	Bleeding
Polyarteritis nodosa	8	4	3	2	3
Microscopic polyarteritis	17	9	8	4	3
Churg-Strauss syndrome	4	1	0	1	1
Wegener's granulomatosis	45	4	3	2	1

Data from reference 11, but including nine additional patients with Wegener's granulomatosis.

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