Gastric antral vascular ectasia in systemic sclerosis: complete resolution with methylprednisolone and cyclophosphamide

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Abstract
A case of severe, transfusion dependent anaemia in a 72 year old woman, which on endoscopy was found to be due to gastric antral vascular ectasia (GAVE), is reported. Repeated endoscopic sclerotherapy was ineffective. She subsequently developed Raynaud’s phenomenon and on further investigation was found to have classical systemic sclerosis with lung involvement. Treatment with pulses of intravenous methylprednisolone and cyclophosphamide resulted in significant improvement in her pulmonary function tests and skin score. Coincidentally, her haemoglobin stabilised and further endoscopic examinations were normal. This is the first report of cyclophosphamide and methylprednisolone leading to complete and sustained resolution of GAVE in association with systemic sclerosis.

Gastrointestinal (GI) complications are well recognised in systemic sclerosis. In general, these complications are sequelae of gut dysmotility, resulting from increased collagen deposition. In a recent series 80% of patients with systemic sclerosis were found to have GI complications: the most common problems were oesophageal dysmotility, lower oesophageal sphincter laxity, bacterial overgrowth, and wide mouth diverticulae with associated malabsorption. GI haemorrhage is also well recognised in diffuse and limited systemic sclerosis and is associated with an increased mortality.

Gastric antral vascular ectasia (GAVE) or “watermelon stomach” has been recognised as a distinct pathological lesion since 1984. GAVE exclusively affects the antrum of the stomach. At endoscopy, parallel, longitudinal folds of gastric mucosa are seen to traverse the antrum, converging at the pylorus. Each contains a column of convoluted dilated capillaries, giving rise to the characteristic appearance. Microscopically there is capillary dilatation with a chronic inflammatory infiltrate. There is pronounced fibromuscular hyperplasia in both the lamina propria and muscularis mucosa, and fibrin thrombi are frequently seen.

GAVE has been recognised in association with scleroderma and, possibly, the antral lesions may represent part of the spectrum of vascular abnormalities seen in systemic sclerosis.

Case report
A 72 year old Caucasian woman was admitted to the care of the gastroenterologists in June 1996 with an eight week history of lethargy and shortness of breath on exertion. A full blood count showed microcytic hypochromic anaemia (haemoglobin 66 g/l). She denied any GI symptoms. She had a previous history of vitiligo and polymyalgia rheumatica, for which she was taking 5 mg of enterically coated prednisolone.

Abdominal examination was unremarkable, though laboratory tests for faecal occult blood were positive. Endoscopic examination and gastric biopsies supported a diagnosis of chemical gastritis. Iron treatment was started after transfusing three units of blood.

Four weeks later the same patient was re-admitted with symptomatic anaemia. Repeat endoscopy confirmed the previous findings. After a further blood transfusion she was discharged. Four weeks later she again presented with anaemia. On this occasion she was noted to be deficient in vitamin B12 with positive gastric-parietal antibodies and was also found to be hypothyroid. Thyroxine and B12 replacement were started after a further blood transfusion. She had a normal colonoscopy and small bowel enteroscopy ruled out angiodysplasia but noted appearances typical of GAVE or “water melon stomach” (fig 1A), and this diagnosis was confirmed on histology.

Over the following six months she had 19 therapeutic endoscopic examinations with sclerotherapy in an attempt to control her chronic blood loss. Over the same period 42 units of blood were transfused (fig 2).

In April 1997 she developed Raynaud’s phenomenon. Her skin was noted to have become taut and the underlying tissue was oedematous. She had lost 20 kg in weight in the preceding six months and had remained persistently anaemic. At this stage she was referred to the rheumatologists.
Examination of the skin showed extensive scleroderma affecting the limbs and chest wall. Pulmonary function tests showed a restrictive deficit with a reduced transfer factor. Thoracic high resolution computed tomography showed changes consistent with pulmonary fibrosis. Antinuclear antibodies were weakly positive (titre 1/40), but extractable nuclear antibodies were negative, including antitopoisomerase (Scl-70). She was admitted to hospital and a course of pulsed, intravenous methylprednisolone (10 mg/kg) with cyclophosphamide (10 mg/kg) was started according to a standard protocol, with mesna as a urothelial protective agent.

Over the next three months her scleroderma improved dramatically. It was noted that co-incident with the start of treatment for her scleroderma she had ceased to require blood transfusions. Repeat endoscopy was normal with no evidence of GAVE. After a further six months of treatment she has not required further blood transfusion and remains well with a stable haemoglobin and normal endoscopic appearance (fig 1B).

Discussion

GAVE was first described in 1984. In 1992 Goustout described a series of 45 patients with recurrent iron deficiency anaemia and GAVE. In that series 72% of the subjects were female and their mean age was 73 years. Sixty two per cent were transfusion dependent, requiring a mean of 10 units of blood over one year. Interestingly, they found a remarkably high incidence (62%) of autoimmune and connective tissue disease in these patients. Scleroderma was reported in eight of the 45 patients (18%). Although GAVE had been previously reported in association with systemic sclerosis, this
series confirmed an association which has subsequently been reported several times in rheumatology publications. The treatment of GAVE is usually endoscopic heater probe cautery or laser coagulation. A significant number of patients proceed to partial gastrectomy. H2 histamine antagonists, tranexamic acid and oestrogen-progesterone preparations have been used as non-surgical treatments for GAVE, with variable success. Cyclophosphamide in conjunction with methylprednisolone has been shown to retard the progression of pulmonary fibrosis associated with systemic sclerosis. Cyclophosphamide and methylprednisolone were given to our patient in view of her lung and skin disease. There had been no other modification in her treatment, and the subsequent complete stabilisation of haemoglobin and resolution of endoscopic abnormalities was unexpected. The patient had undergone 19 sclerotherapeutic interventions in the six months before starting pulsed treatment, and although it is conceivable that this might have played a part in the resolution of her lesion, the temporal relation between the administration of immunosuppressive treatment and the stabilisation of her haemoglobin is impressive (fig 2).

Interestingly, our patient was found to be vitamin B12 deficient. Pernicious anaemia is a common autoimmune disease associated with gastric mucosal atrophy and achlorhydria. It has been shown that treatment with prednisolone can improve gastric mucosal histology and restore gastric acid secretion in some patients with pernicious anaemia. In 1980 Calam and Walker described a patient with achlorhydria and an antral vascular lesion identical to GAVE. Prednisolone treatment resulted in reduction of GI blood loss, though the endoscopic findings remained unchanged. It is unclear whether our patient’s remission was due to cyclophosphamide and methylprednisolone specifically, either separately or in combination, or whether it was a result of immunosuppression. If autoimmune mediated gastric mucosal damage is a significant factor in the development of GAVE, partial resolution may be expected on immunosuppression.

It has previously been suggested that the antral lesions of GAVE, when associated with scleroderma, may represent part of the spectrum of vascular abnormalities seen in systemic sclerosis. It is interesting to speculate that in our patient a combination of autoimmune gastric atrophy and the vascular abnormality peculiar to systemic sclerosis resulted in the florid antral changes of GAVE. There is scope for further study to determine whether scleroderma associated GAVE without pernicious anaemia, or, indeed, non-autoimmune disease associated GAVE, is as sensitive to immunosuppression. Clearly, if our finding could be reproduced in others it might obviate the need for multiple transfusions, repeated endoscopic intervention, and major surgery in this patient group.