

Primary biliary cirrhosis and scleroderma complicated by Barrett's oesophagus

A case report

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Summary

Oesophageal problems are common in patients with scleroderma, but the association of primary biliary cirrhosis and scleroderma is uncommon. A Barrett's oesophagus identified in a patient with primary biliary cirrhosis and scleroderma is described. The Barrett's oesophagus was probably a complication of scleroderma and resulted from low lower-oesophageal sphincter pressure and severe gastro-oesophageal reflux.

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An association between primary biliary cirrhosis (PBC) and scleroderma was first emphasised by Reynolds *et al.*¹ in 1971. Later, Cameron and Payne² reported Barrett's oesophagus in a patient with scleroderma in 1978. However, no report has been published in the English language of PBC and scleroderma complicated by Barrett's oesophagus. We report such a case.

Case report

A 48-year-old emaciated woman was hospitalised in October 1986 because of persistent pruritus, Raynaud's phenomenon, heartburn, and abnormal results of liver biochemical tests. On physical examination she was pale and jaundiced. The skin over the face, hands, forearms, abdomen and legs was shiny, tight and thickened, and a smooth, non-tender liver was palpable two finger-breadths below the right costal margin. Results of laboratory investigations were: serum bilirubin value 2.9 mg/dl (normal 0.2 - 1.6 mg/dl); alkaline phosphatase 830 U/l (normal 10 - 95 U/l); aspartate transaminase 129 U/l (normal 5 - 45 U/l); alanine transaminase 121 U/l (normal 0 - 40 U/l); and γ -glutamyltranspeptidase 408 U/l (normal 3 - 60 U/l). The blood urea nitrogen level was 9 mg/dl (7 - 20 mg/dl), and serum creatinine 0.6 mg/dl (0.6 - 1.4 mg/dl). The stool was positive for occult blood. The patient was anti-mitochondrial antibody-positive and antinuclear anti-body-positive (speckled pattern) with a titre of 1:640. Serum C3 and C4 values were within normal limits. Immunoglobulins G, A, and M were elevated — 1 800 mg/dl (normal range 980 - 1 460 mg/dl), 659 mg/dl (normal range 190 - 350 mg/dl) and 384 mg/dl (normal range 83 - 205 mg/dl), respectively. Tests for

serum hepatitis B surface antigen were negative. No calcinosis, telangiectasias or xanthomas were present.

Chest radiography was normal. Pulmonary function studies were within normal limits. Upper gastro-intestinal tract endoscopy revealed the squamocolumnar junction to be 28 cm from the incisors (Fig. 1) and a biopsy specimen showed specialised columnar epithelium and gastric fundic-type epithelium. Oesophageal manometry disclosed no pressure gradient between the lower oesophageal sphincter and intragastric areas. Peristalsis was normal in the upper-third of the oesophagus but absent in the lower two-thirds. Twenty-four-hour oesophageal pH-monitoring confirmed the presence of severe gastro-oesophageal reflux (during the total 24-hour monitored period, a pH < 4 was noted during 23% of the monitoring time, and there were 10 reflux episodes that were \geq 5 minutes in duration. The longest reflux episode was 80 minutes). Endoscopic retrograde cholangiography showed that the bile ducts were normal.

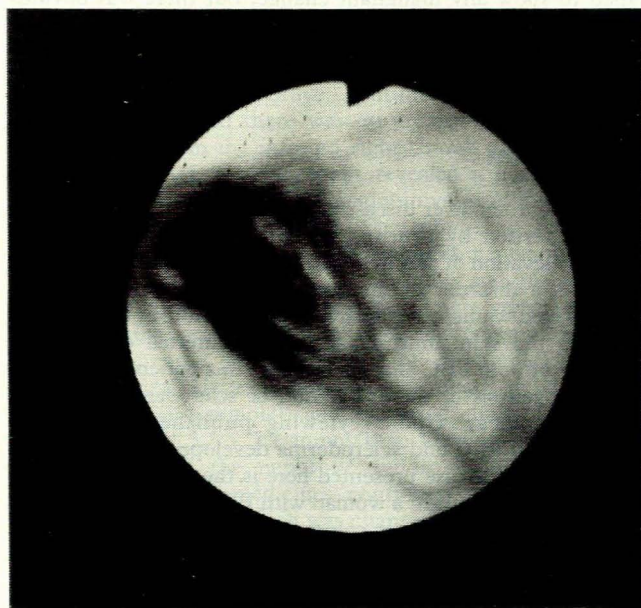


Fig. 1. The squamocolumnar junction is distinct but irregular, with islands of columnar epithelium.

Because of the recurrent oesophagitis, in December 1986 the patient was subjected to an antireflux operation utilising the Belsey Mark IV method. A wedge biopsy of left lobe of liver at that time revealed plasma cells and lymphocytes infiltrating the medium and small bile ducts. Focal extension of the inflammatory cells into the bile duct epithelium with disruption of the basement membrane was also seen (Fig. 2). Some of the bile ducts were totally replaced by aggregates of lymphoid cells. Limiting plates were also focally destroyed. Ill-defined granulomas were seen both in the portal tracts and

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the lobular parenchyma. The postoperative course was unremarkable, except for minor symptoms of heartburn.

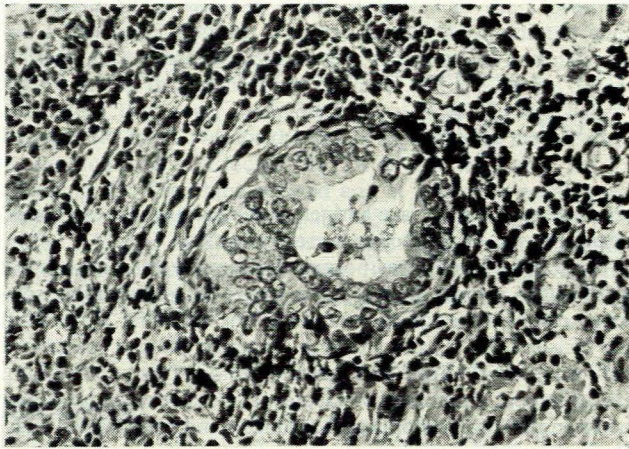


Fig. 2. A damaged bile duct surrounded by dense infiltrate of mononuclear cells (H and E \times 400).

Based on clinical findings and biochemical, histological, radiological and endoscopic examinations, simultaneous occurrence of primary biliary cirrhosis and scleroderma complicated by Barrett's oesophagus was diagnosed.

In July 1989 follow-up biopsy of the distal oesophagus failed to show any malignant change, but there was obvious oesophageal stricture. The serum creatinine level was 0,5 mg/dl, but the serum bilirubin value had increased to 10,4 mg/dl.

Discussion

PBC is a chronic liver disease affecting middle-aged women; it is characterised by pruritus, jaundice, hyperlipidaemia, and marked elevation of serum alkaline phosphatase levels. Scleroderma is a disorder of the connective tissue often affecting middle-aged women; it is characterised by fibrous tissue deposition in the skin, muscle and various internal organs. The presence of both PBC and scleroderma in a patient is rare, and the pathogenesis of the association of scleroderma and PBC remains unclear. Upon reviewing published reports, no patients with PBC and scleroderma developed Barrett's oesophagus.^{1,3-10} The case presented here is the first occurrence of Barrett's oesophagus in a woman with PBC and scleroderma.

Barrett's oesophagus is columnar epithelium lining of the distal oesophagus. It has clinical importance primarily because it predisposes to the development of oesophageal adenocarcinoma. Studies on the incidence of cancer in Barrett's oesophagus suggest that patients with this condition develop oesophageal cancer at a rate some 30-fold to 350-fold higher than that of the general population.¹¹ Endoscopic evaluation of patients with reflux oesophagitis has revealed that 8 - 20% had Barrett's oesophagus.¹² However, the incidence of Barrett's oesophagus in the general population is unknown, but its real

frequency is probably much higher than has previously been estimated.¹³

The incidence of oesophageal involvement in scleroderma is 54 - 86%. It is now widely accepted that patients with scleroderma can have oesophageal motor disorders leading to chronic reflux oesophagitis and gradually to the development of Barrett's oesophagus.

Iacone *et al.*¹⁴ found that patients with Barrett's oesophagus had less lower oesophageal sphincter pressure and more oesophageal acid exposure than patients with oesophagitis and normal volunteers. Furthermore, the extent of Barrett's involvement was linearly related to the level of lower oesophageal sphincter pressure and the number of reflux episodes that were \geq 5 minutes in duration. They¹⁴ concluded that Barrett's oesophagus is related to profound mechanical incompetence of the lower oesophageal sphincter, resulting in a severe form of gastro-oesophageal reflux. Katzka *et al.*¹⁵ also noted that lower oesophageal sphincter pressures in scleroderma patients with Barrett's oesophagus were generally lower than in scleroderma patients without Barrett's oesophagus, although these differences were not significant.

The patient presented here had a very low lower oesophageal sphincter pressure (0 mmHg) and severe gastro-oesophageal reflux, which could predispose to the development of Barrett's oesophagus.

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