# SYSTEMIC SCLEROSIS (SCLERODERMA) WITH CHRONIC LIVER DISEASE

By H. L. Lim and J. L. Da Costa

**SYNOPSIS**

**The liver is rarely if ever involved in systemic sclerosis. A further case of chronic liver disease associated with scleroderma is therefore documented. The patient had typical skin changes with involvement of the gastrointestinal tract and the heart. Liver function tests were grossly abnormal and a liver biopsy revealed cirrhotic changes, most probably post-necrotic in type. The literature on the association of chronic liver disease with scleroderma is briefly reviewed and its rarity emphasised.**

Scleroderma ("progressive systemic sclerosis", Goetz and Berne, 1945) is a chronic disease of unknown aetiology characterized by diffuse sclerosis of the connective tissue of the integument and other organs. The liver is rarely if ever inolved in scleroderma (Tuffanelli and Winkelmann, 1961) and Bartolomew *et al* (1964) found only 8 cases of chronic liver disease in 727 cases of scleroderma. Another case of scleroderma with liver involvement is reported and the literature on this aspect is briefly reviewed.

## CASE REPORT

A 67-year-old Chinese female was admitted to hospital on 25th February 1971. She was apparently well until two months prior to admission when she developed progressive swelling of her legs and abdomen, anorexia, some weight loss and episodes of diarrhoea in which she passed loose, greenish-brown stools 3 to 4 times/day. At the same time she began to experience breathlessness on exertion. The breathlessness progressively increased until on admission she was breathless at rest.

Physical examination showed her to be afebrile, anaemic, and cachetic. She had a sallow appearance and the skin was thick and taut over the face, hands and feet. There was moderate oedema of the ankles. Her blood pressure was 125/70 mm.Hg. The heart was enlarged but no murmurs were heard. The lungs were clear but her abdomen was distended with ascitic fluid. The liver, spleen and kidneys were not palpable.

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Investigations revealed a haemoglobin of 8·4 g.%; a total leucocyte count of 10,500/c.mm. (polymorphs 89%, lymphocytes 9%, monocytes 2%) and a platelet count of 135,000/c.mm. The erythrocyte sedimentation rate was 17 mm./hour. The peripheral blood film showed moderately hypochromic normocytic erythrocytes. Direct Coomb's Test was negative. Haemoglobin electrophoretic pattern was normal. Marrow (sternal) biopsy showed moderate normoblastic hyperplasia with some megaloblastoid changes. Blood for L.E. cells was negative (3 occasions). Blood for anti-nuclear factor antibodies was negative (3 occasions); Rheumatoid factor negative; Serum iron 151 mcg.%; Blood urea 24 mg.%; Serum electrolytes within normal limits. The bromsulphthalein excretion test showed 18% dye retention; Serum bilirubin 1·2 mg.%; alkaline phosphatase 10·0 K.A. units, serum pyruvate transaminase 170 units (normal in this laboratory, less than 135 units) and serum proteins 6·5 G%: albumin 2·4 G%, globulin 4·1 G% (gamma globulin 3·0 G%). The electrocardiogram showed a prolonged PR interval (0·28 secs.) with ischaemic changes over the left ventricular leads and an intraventricular conduction defect. The chest radiogram showed an enlarged heart with a mild right basal effusion. A barium meal and follow-through examination revealed a dilated and atonic oesophagus. The stomach showed a lack of peristalsis. There was delayed gastric emptying. Skin and liver biopsy findings were reported by Dr. Tan Kheng Khoo.

### LIVER

"Histological examination (Figs. 1, 2 and 3) showed a strip of liver whose architecture was completely destroyed. There were nodules of regenerating liver cells in a fibrous background. Half the bicpsy was composed of isolated areas of regenerating liver cells in the midst of larger areas of necrotic liver cells, inflammatory cells and fibrous tissue. There were numerous polymorpho-

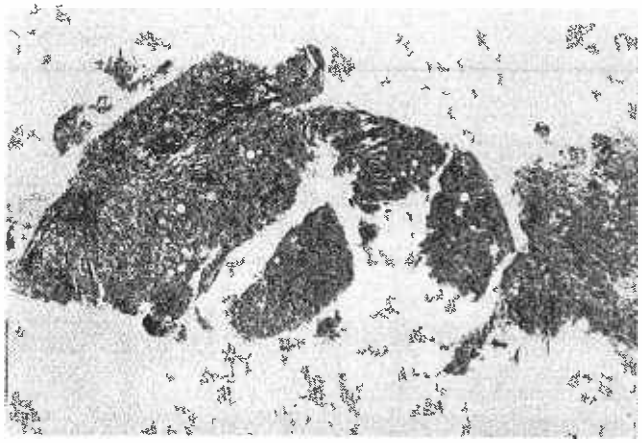

Fig. 1. *Liver:* Section shows fragmented strip of liver biopsy. The enlarged nodule is broken up and it is surrounded by thick fibrosis (H & E × 400).

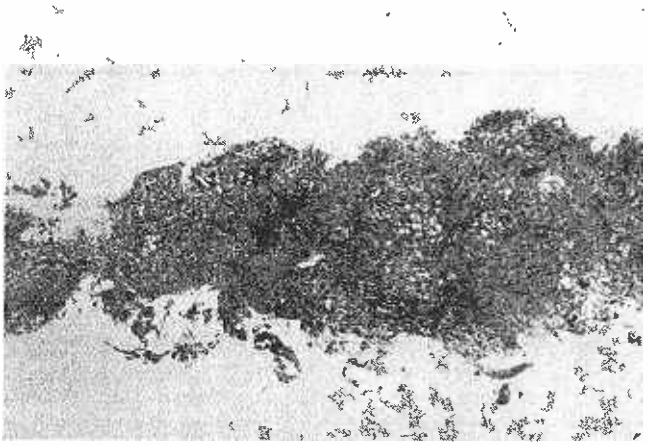

Fig. 3. *Liver:* The remaining portion of the same liver strip showing massive areas of necrosis. Isolated areas of surviving liver cells are discernible (H & E × 40).

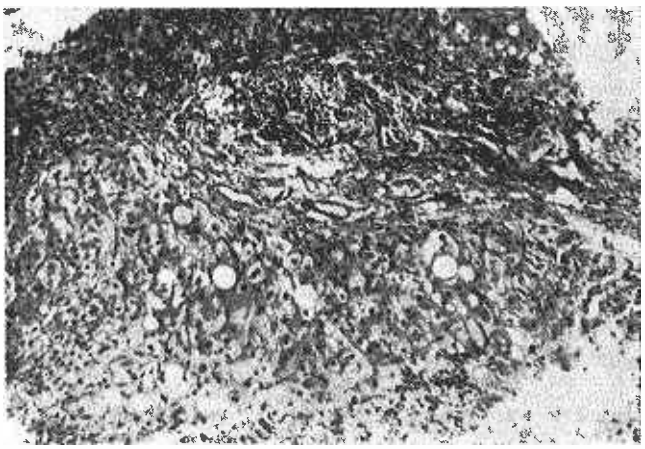

Fig. 2. *Liver:* This is at the edge of the fragmented nodule shown in Fig. 1. The fibrosis and chronic inflammatory cells are well shown (H & E × 100).

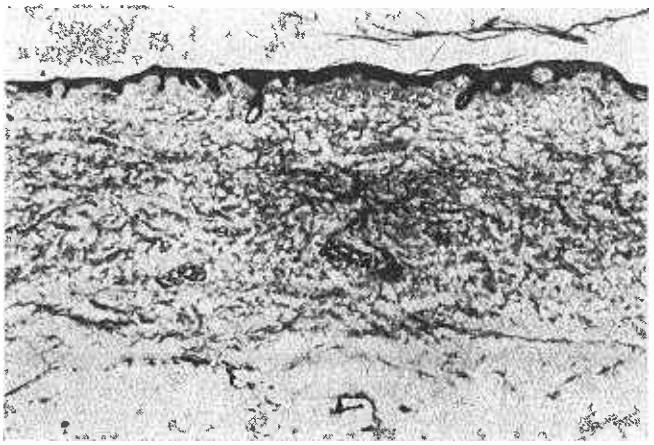

Fig. 4. *Skin:* Note increase in thickness of dermal collagen. Two groups of sweat glands and ducts are higher up than usual in the dermis (H & E × 40).

nuclear leucocytes in this area. However in the older fibrous bands around the larger nodules, lymphocytes were the predominant cells. There was excessive fibrosis surrounding the regenerating nodules.

The picture was that of cirrhosis in an active stage. The type of cirrhosis was difficult to discern from the small strip of liver tissue available. However, it could fit in with a post-necrotic cirrhosis (macro-nodular), though one cannot really exclude the monolobular (Laennec) variety.

SKIN

Histological examination (Fig. 4) showed a strip of skin in which no subcutaneous fat was present. There was no evidence of any erector pili or pilo-sebaceous apparatus. The sweat gland structures were few in number and they were placed higher up in the dermis than normal. Most of them were ducts; very few acini were discernible. The collagen had taken on a more eosinophilic hue and was in larger bundles than normal. The picture was consistent with scleroderma."

Although widespread visceral involvement has been attributed to generalized scleroderma, only a few, vague references to associated liver disease could be found in the literature (Goetz and Berne, 1945; Piper and Helwig, 1955; Beigelman *et al* 1953; Batsakis and Johnson, 1960). These references were based mainly on fragmentary published clinical, histological, radiological and biochemical evidence. Goetz and Berne (1945) in their description of a case of visceral scleroderma mentioned that the liver showed biliary cirrhosis without any detectable abnormality of the biliary tract or pancreas.

Abnormal liver function studies have been reported in some series (Leinwand *et al*, 1954; Stava, 1958). The flocculation tests were abnormal in most of these cases but the more specific tests like the bromsulphathalein test were normal. The abnormalities were thus more likely to be due to protein abnormalities rather than liver disease.

Boyd *et al* (1954) in a radiological review of 63 patients with generalized scleroderma, reported that the liver was enlarged in 13 out of 24 patients who had abdominal X-rays done but they thought that this hepatomegaly might be due to congestive cardiac failure.

Piper and Helwig (1955) in their review of 31 necropsies of patients with systemic sclerosis found that in most instances the liver showed only passive hyperaemia. They found only one case of portal cirrhosis and three cases of focal liver necrosis.

Beigelman *et al* (1953) found hepatic fibrosis in two out of fifteen cases of diffuse scleroderma but both had congestive cardiac failure (confirmed at necropsy) which could account for the fibrosis. However, Calvert *et al* (1958) have described two cases of systemic scleroderma with portal hypertension and varices associated with hepatic fibrosis and another case of systemic scleroderma with hepatic fibrosis was reported by Batsakis and Johnson (1960).

Tuffanelli and Winkelmann (1961) in a clinical study of 727 cases found 7 patients with cirrhosis of the liver: 2 of these had Laennec's cirrhosis, and one had a previous episode of viral hepatitis. In 4 other cases scleroderma was associated with severe cirrhosis of an unknown aetiology. However, Bartholomew *et al* (1964) found 8 cases of chronic liver disease in 727 cases of scleroderma and were not convinced of a relationship between the two diseases. A similar conclusion could be drawn from the study of D'Angelo *et al* (1969) in which there were more instances of liver cirrhosis in 58 controls than in 58 patients with systemic sclerosis.

In the present patient, the bromsulphathalein test was abnormal and liver biopsy showed cirrhosis (most probably of the post-necrotic type). As there was no evidence of previous hepatic or biliary disease, generalized passive venous congestion, or a chronic intestinal lesion, we conclude that the diseased liver was a direct manifestation of the systemic sclerosis.

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