Acute Congestive Heart Failure Associated with a Limited Form of Systemic Sclerosis and Primary Biliary Cirrhosis

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Abstract
This is the first case of a limited form of systemic sclerosis (ISSc) associated with acute congestive heart failure (CHF) and primary biliary cirrhosis (PBC). A 58-year-old woman with ISSc was admitted because of a sudden onset of CHF. The intravenous administration of nitroglycerine and furosemide ameliorated the symptoms of CHF within 24 hours. She had both anticentromere antibodies and anti-p25 doublet/triplet antibodies to intrahepatic microsomes. Thallium scintigraphy at rest demonstrated significant perfusion defects in both the anteroseptal and inferior myocardium. A coronary angiogram revealed normal coronary arteries and no vasospasm was provoked by the intracoronary administration of acetylcholine. The present case indicates that minute care should thus be taken for the prevention of acute CHF even in patients with a limited form of SSc when thallium perfusion defects are identified.

Key words: scleroderma heart disease, thallium perfusion defects, anticentromere antibody (ACA), anti-p25 doublet/triplet antibodies

Case Report
A 58-year-old woman was admitted to our hospital, because of sudden dyspnea of two hours duration in June 1996. Two years earlier, this patient first noted Raynaud's phenomenon in her toes. She thereafter visited our outpatient clinic, and was given a diagnosis of ISSc based on the clinicopathological findings of the third and fourth digits on her left foot, and the presence of ACA. She had no calcinosis nor telangiectasia, but upper gastrointestinal tract roentgenogram revealed lower esophageal hypomotility. She had been followed up without medication.

On admission, her height was 152.0 cm; weight, 47.0 kg. Her temperature was 36.6°C; pulse, 104/min with irregular rhythm; blood pressure, 150/90 mmHg; respiratory rate, 34/min. Jugular venous dilatations were noted. A third heart sound was audible in the apex, and coarse crackles were heard in the bilateral lung fields. Her bilateral fingers were slightly sclerotic and pigmented. She had no other clinical manifestations, such as xerophthalmia and xerostomia.

An arterial blood gas analysis under conditions of 5 l/min oxygen administration via a face mask showed the following: pH, 7.403; PaCO₂, 35.5 Torr; and PaO₂, 50.6 Torr. A chest radiograph showed cardiomegaly (cardiothoracic ratio: 67.0%) with severe pulmonary congestion (Fig. 1). An electrocardio-
A

B

Figure 1. Chest radiograph findings on admission (A) showing cardiomegaly with diffuse reticulonodular shadows in the whole fields of both lungs, but one month later (B) both cardiac failure and pulmonary congestion had markedly improved.

Figure 2. Electrocardiogram findings on admission showing varying wide QRS configuration and frequent ventricular premature beats.

gram revealed a wide variability in QRS configuration and frequent ventricular premature beats (Fig. 2). Echocardiography revealed interventricular septal paradoxical movement, mild tricuspid and mitral regurgitation, left atrial dilatation (diameter: 42.0 mm), and reduction of left ventricular wall motion (ejection fraction: 49%). A Swan-Ganz catheter was intravenously inserted and showed the following: mean right atrial pressure, 9 mmHg; pulmonary atrial pressure, 27/14 mmHg; and pulmonary wedge pressure, 12 mmHg.

A laboratory analysis revealed the following: white blood cell count, 12.9×10^3/μl (neutrophils, 55.3%); hemoglobin level, 12.5 g/dl; platelet count, 15.5×10^4/μl; erythrocyte sedimentation rate, 54 mm/h; C-reactive protein, 1.5 mg/dl; AST, 91 IU/l; ALT, 67; lactate dehydrogenase, 396 (normal range: 100–225); alkaline phosphatase (ALP), 1,428 (normal: 100–340); the myocardial band fraction of creatine kinase, 4% (normal: 0–3); myosin light chain, 1.4 ng/ml (normal: 0–2.5); troponin T, 0.14 ng/ml (normal: 0–2.5); γ-glutamyltranspeptidase (γ-GTP), 398 IU/l; cholinesterase (CHE), 1,661 IU/l; total cholesterol, 230 mg/dl; HDL-cholesterol, 60.1; and triglyceride, 165. The remaining blood chemistry findings were within the normal limits. HBs antigen and HCV antibody were both negative. Immunoglobulin (Ig) G was 1,931 mg/dl; IgA, 288; IgM, 522; C3, 115 mg/dl; C4, 52; CH50, 64.6 U/ml. Antinuclear antibody was positive at a titer of 1:1,280 with a centromere staining pattern. The titer of ACA was 130 U/ml as measured by enzyme-linked immunosorbant assay (ELISA) (normal: 0–10).

Tests for antibodies to RNP, Scl-70, Jo-1, SS-A, SS-B, and dsDNA yielded negative results. Rheumatoid factor was 97 IU/ml. A urinalysis revealed no abnormalities.

She was therefore given a diagnosis of acute CHF. The intravenous administration of nitroglycerine and furosemide improved the symptoms of CHF within 24 hours. Thereafter, thallium scintigraphy at rest demonstrated significant perfusion defects on an early image in both the anteroseptal and inferior myocardium of the left ventricle (Fig. 3). A coronary angiogram revealed no organic stenoses. No vasospasm was provoked by the intracoronary administration of acetylcholine. A left ventriculogram revealed a reduced motion of segments 3 and 4 with an ejection fraction of 54%.

Despite the improvement of hepatic congestion due to CHF, the titers of AST, ALT, ALP, CHE, and γ-GTP all increased. A further laboratory analysis revealed the following: AST, 64 IU/l; ALT, 78; ALP, 1,490; CHE, 1,672; γ-GTP, 473; serum Cu,
Acute CHF in ISSc

Figure 3. Thallium scintigraphy at rest on Bull's eye mapping. The early image (A) revealed significant perfusion defects in anteroseptal and inferior myocardium, which had an incomplete redistribution on the delayed image (B).

167 mg/dl (normal: 14–63); serum ceruloplasmin, 44.1 mg/dl (normal: 21–33). Percutaneous liver biopsy specimens showed infiltration of mononuclear cells and moderate fibrosis in the enlarged portal area (Fig. 4). Anti-p95 (originally designated as anti-Is) (7), anti-LKM (7), and antimitochondrial M2 antigen (8) and antismooth muscle cell antibodies were all negative, but anti-p25 doublet/triplet (originally designated as anti-MM) (9) was positive at a titer of 1:1.

After being discharged from the hospital, no recurrence of CHF has been noted for three years while the patient has been treated with a regimen consisting of long-acting isosorbide dinitrate 40 mg/day, nilvadipine 8 mg/day, and methylprednisolone 6 mg/day. Repeated echocardiography revealed no significant change in right and left ventricular dimensions, functions, or estimated pulmonary artery pressure (20/13 mmHg). Liver aminotransferases was persistently slightly elevated (AST, 34 IU/l, ALT, 28).

Discussion

Follansbee et al (6) reported that, in patients with dSSc, ventricular conduction disturbances, such as either CLBBB or bifascicular block (right bundle branch block with left anterior fascicular block), might be closely associated with a reduction of the left ventricular ejection fraction and advanced fibrosis of the myocardium. In the present case with ISSc, asymptomatic CLBBB preceded the sudden onset of CHF. However, the patient’s myocardial fibrosis was mild, if present, because the ejection fraction did not severely decrease.

Pathological examinations in scleroderma heart disease demonstrated structural abnormalities in both the myocardium and such conduction systems as the sinus node, AV node, His bundle, or its branches, associated with widespread narrowing lesions of the small coronary arteries (but not the epicardial coronary arteries) in the myocardium and the nutrient arteries of impulse formation and conduction (10). Bulkley et al (11) hypothesized that “myocardial Raynaud’s phenomenon” may be responsible for the occurrence of contraction band necrosis and myocardial fibrosis as a result of sustained or repeated episodes of interrupted microcirculation, that are randomly distributed throughout the myocardium. The patient’s perfusion defects on the early image of thallium scintigraphy (Fig. 3) and normal coronary angiograms might indicate the extent and severity of impaired microcirculation. The pathogenetic mechanism of acute CHF, in the present case, may be due to the impaired microcirculation associated with transient but severe vasospasms of small coronary arteries, thus provoking conduction and rhythm disturbances as well as cardiac dysfunction. Other causes for acute CHF, such as myocarditis and/or pericarditis, were considered to be less likely based on the clinical course and findings of laboratory, radiological, and echocardiographical examinations.

Patients with SSc who have significant myocardial perfusion defects may therefore be at an increased risk of developing subsequent serious cardiac disease or sudden death (12). The present case indicates that minute care should thus also be taken for the prevention of acute CHF even in the limited forms of SSc when thallium perfusion defects are identified in such patients. A high-risk group of patients with scleroderma heart disease should be controlled by the administration of vasodilator drugs (13) to improve the microcirculation. These treatments may also help prevent fibrosis of the myocardium.

Antimitochondrial antibodies (AMA) are detected in the sera of 95% of patients with PBC, while ACA are found in 9–29% of patients with PBC (14). The present patient also had anti-p25 doublet/triplet (originally designated as anti-MM) antibodies to intrahepatic microsomes. Takano et al (9) described that: 1) these antibodies were found in 30% of patients with PBC
and in 87.5% of those with autoimmune hepatitis, and 2) corticosteroid therapy was mostly effective in the treatment of PBC patients with these antibodies.

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References