Right Ventricular Cardiomyopathy Accompanied by Protein-Losing Enteropathy and Chylous Effusion

Hideo Matsui, MD; Shinji Negoro, MD; Sumiyuki Nishida, MD; Yoshiyuki Saito, MD; Keita Kunisada, MD; Keiko Yamauchi-Takihara, MD

Severe right-side heart failure developed in a 47-year-old Japanese woman who suffered from hypoalbuminemia and a massive right-side chylous pleural effusion. She had been diagnosed as having protein-losing enteropathy with right ventricular cardiomyopathy. Autopsy showed congenital anomalies of the lymph ducts and abnormal deposition of fibrous and fatty tissue in the right ventricular myocardium. The clinical and pathological findings are consistent with the nonarhythmogenic form of the arrhythmogenic right ventricular dysplasia. (Jpn Circ J 2001; 65: 912–914)

Key Words: Arrhythmogenic right ventricular dysplasia; Cardiomyopathy; Chylous effusion; Fatty replacement; Heart failure; Protein-losing enteropathy

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a cardiac disorder characterized by the fibro-fatty replacement of cardiomyocytes and the main clinical complications are arrhythmia, heart failure, and sudden death. Recently, the genetic locus of Naxos disease, a form of ARVC, has been mapped to chromosome 17q21, in which the gene for plakoglobin is coded. Plakoglobin is a key component of desmosomes and adherens junctions, and is important for the tight adhesion of many cell types, including those in the heart. The finding of a plakoglobin abnormality in ARVC suggests that the proteins involved in cell–cell adhesion play an important role in maintaining myocyte integrity, and when junctions are disrupted, cell death and fibro-fatty replacement occur. The relation between ARVC and fat replacement of the right ventricle (FaRV) has also been discussed recently. ARVC is characterized by fibro-fatty replacement of myocytes with scattered foci of inflammation, but fat infiltration per se is considered a different process and FaRV may be a distinct clinicopathological entity.

The new WHO classification includes the term ‘arrhythmogenic’ in ARVC but some patients do not suffer from ventricular arrhythmias. FaRV is reported to be less arrhythmogenic than typical ARVC and we describe a patient who developed right ventricular dilatation accompanied by chylous pleural effusion and ascites, but without life-threatening ventricular arrhythmias.

Case Report

A female patient had been prescribed diuretics at the age of 37 years for general fatigue accompanied by facial and leg edema. When she was 45 years old, she began to suffer from pleural effusion, watery diarrhea and hypoalbuminemia. Because her symptoms became resistant to medical therapy, she was referred to hospital at age 47. Her past history included left femoral thrombophlebitis at the age of 45, and her family history included dilated cardiomyopathy (DCM) in a younger sister who had died at the age of 40 after an operation for tricuspid regurgitation.

On examination, she was 139 cm tall and weighed 29 kg. There was pretibial and facial edema as well as dilated neck veins. Her blood pressure was 90/44 mmHg with an irregular pulse of 76 beats/min and her ECG showed atrial fibrillation. The chest radiograph showed massive right pleural effusion and transthoracic echocardiography revealed a markedly dilated hypokinetic right ventricle, tricuspid...
Nonarhythmogenic ARVC

regurgitation (grade IV) and a normal left ventricle with an ejection fraction of 52%. Twenty-four-hour Holter monitoring showed a few isolated monofocal premature ventricular contractions (80 beats/day). Neither pulmonary hypertension nor proteinuria was detected, and blood urea nitrogen and serum creatinine values were 29 and 0.6 mg/dl, respectively, with a normal electrolyte and acid–base balance. Blood lactate dehydrogenase was 270 U/L and choline esterase was 1,644 U/L. A complete blood count showed mild leukocytosis (white blood cells; 13,610/mm$^3$) with normal red blood cell and platelet counts. The serum total protein level was 4.1 g/dl and the albumin level was 2.0 g/dl. The pleural effusion was chylous with a high concentration of triglycerides (Fig 1; Table 1). Antinuclear antibodies were negative and there was no evidence of malignant disease. $^{99m}$Tc-labelled human serum albumin scintigraphy identified intestinal albumin loss from the ileocecal portion (Fig 2). An initial diagnosis of protein-losing enteropathy was made, but this did not coincide with chylous pleural effusion. Gastrofiberscopic and colonoscopic examinations revealed only atrophic gastritis with no evidence of amyloidosis. Lymphangiography demonstrated lymphangiectasia in the lower extremities and the abdomen, and an abnormal connection of the thoracic duct to the right venous angle of the subclavian vein (Fig 3).

Severe hypoalbuminemia and pleural effusion persisted in spite of repeated albumin infusions and high doses of diuretics. Six months later, the patient died of renal failure and heart failure and a postmortem examination was performed. The heart weighed 195 g, and the thickness of the right ventricle was found to be 2.0 mm, but that of the left was 12.0 mm. Microscopic examination of the basal portion of the right ventricle demonstrated abnormal deposition of fibrous tissue and massive fatty degeneration (Fig 4A). Generalized submucosal edema and dilatation and extreme thickening of vessel walls were observed, especially in the gastrointestinal system (Fig 4C). There were severe fibrous changes in the liver because of the right ventricular failure. Progressive venous congestion accompanied by congenital anomalies of the lymph ducts may have caused the chylous pleural effusion and ascites.

Discussion

Severe hypoproteinemia, manifested as protein-losing enteropathy, has been reported in association with valvular diseases such as tricuspid regurgitation and mitral regurgitation. In those cases, the serum protein levels became normal after surgical correction. Protein-losing enteropathy is also frequently mentioned as occurring after the Fontan operation and in cases of congenital heart diseases, such as tricuspid hypoplasia. However, only a few cases of protein-losing enteropathy associated with cardiomyopathy have been reported. It is conceivable that severe right-side heart failure induces chronic venous congestion and lymphangiectasia, and, in the present case, abnormal connection of the thoracic duct might have exacerbated lymphangiectasia and induced both protein-losing and poor absorption of fat.
Although the evidence of a direct communication between the lymph duct and pleural cavity clearly explains the chylous effusion, at autopsy it was impossible to detect the passage of the lymph duct.

This is the first report of a nonarrhythmogenic form of ARVC accompanied by protein-losing enteropathy and chylous pleural effusion. Typical ARVC is characterized by right ventricular myocardial thinning, fatty infiltration of the anterobasal and posterolateral right ventricle, subepicardial left ventricular fibro-fatty replacements, myocyte atrophy, and lymphocytic myocarditis, which supports the concept that ARVC represents the end stage of a remote inflammatory process featuring increased cell death, probably apoptosis. Recently, 2 pathological types of ARVC have been proposed: typical ARVC with fat infiltration and scarring (fibro-fatty ARVC) and a form of ARVC characterized solely by fat replacement (FaRV). Compared with fibro-fatty ARVC, patients with FaRV are older (mean 44±13 years vs 31±14 years for fibro-fatty ARVC), more likely to be female, and not to have a history of arrhythmias or a family history of sudden death and reduced frequency of left ventricular involvement. In addition, epicardial fat does not significantly increase in fibro-fatty ARVC, whereas FaRV is characterized by an increase in epicardial fat in all areas of the right ventricle.

Considering these characteristic features of FaRV, the present patient could have been a case of FaRV. Although her ECG showed atrial fibrillation, at no time had she experienced any life-threatening ventricular arrhythmias. ARVC with left ventricular involvement has been reported, but in this case there was no abnormal fibro-fatty degeneration in the left ventricular myocardium nor was there any inflammatory infiltrates. Microscopic examination of the right ventricle showed a mixture of fibrous tissue and fat tissue, which is characteristic of fibro-fatty ARVC. Because of the limited number of case studies, the diagnostic criteria for FaRV have not been clearly defined yet. For the time being, the clinical and pathological findings of the present patient are considered to be consistent with the nonarrhythmogenic form of ARVC.

References