Massive Pericardial Effusion in a Patient with Hashimoto's Thyroiditis: Histological Examination of Underlying Cardiomyopathy

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An unusual case of a hypothyroid patient with huge pericardial effusion due to Hashimoto's thyroiditis is reported. Cardiac tamponade occurred during admission. Eight hundred milliliters of pericardial effusion was withdrawn by pericardiocentesis. Even after successful replacement of thyroid hormone, she had recurrent effusion two years later. Refractory pericardial effusion is a rare complication in treated hypothyroid patients. Underlying cardiomyopathy was presented with hemodynamic and histological examinations.
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Key words: hypothyroidism, myxedema, cardiac tamponade

Introduction

Cardiovascular manifestations in hypothyroidism include pericardial effusion (1, 2), cardiomyopathy (1, 3-5), accelerated atherosclerosis (1, 6, 7) and hypertension (1). Pericardial effusion caused by hypothyroidism is demonstrated by echocardiogram in as many as 30% of patients (8), however, a large amount of effusion is rare and associated cardiac tamponade is extremely rare; to our knowledge, only 22 reports of this disorder appear in the English literature (7, 9-14). Among them, precise hemodynamic data were described in two papers (11, 14), and histological observation was made in two reports (7, 13).

Case Report

A 61-year-old woman, who had a history of systemic hypertension, was admitted to a hospital on May 30, 1989, with complaints of fatigue, dyspnea, palpitation, alopecia, dry skin, systemic edema and weakness of muscle strength.

On physical examination, blood pressure was 150/70 mmHg without paradox; pulse, 62 beats/min; temperature, 37.3°C. Thyroid gland was not palpable. Her heart sounds were faint without murmurs. There was nonpitting edema on face and legs. Muscle strength of extremities was weak associated with Gowers' sign. Muscle atrophy was absent. Deep tendon reflexes were generally diminished.

Laboratory data were as follows: Hb, 12.4 g/dl; hematocrit,

36.4%; red cell count, $4.1 \times 10^6/\text{mm}^3$; white count, $18,800/\text{mm}^3$; erythrocyte sedimentation rate, 12 mm/1h; the test for C-reactive protein, negative; serum sodium, 148 mEq/l; potassium, 2.1 mEq/l; chloride, 101 mEq/l; serum aspartate aminotransferase, 537 IU/l, alanine aminotransferase, 138 IU/l; lactate dehydrogenase, 5,179 IU/l; creatinine phosphokinase, 637 IU/l (MM = 99%, MB = 1%); and total cholesterol, 373 mg/dl. Cortisol level at A.M. was 33.5 $\mu\text{g/dl}$ (normal, 2.7-15.5 $\mu\text{g/dl}$). 17-ketosteroid in urine was 1.51 mg/day. The values of adrenocorticotrophic hormone and growth hormone were normal.

Function tests of the thyroid showed a severe hypothyroidism with 0.8 $\mu\text{g/dl}$ of serum L-thyroxine (T_4) (normal, 4.5-12.3 $\mu\text{g/dl}$), unmeasurable triiodo-L-thyronine (T_3) (normal, 0.7-2.1 ng/ml) and 38.99 $\mu\text{IU/ml}$ of thyroid-stimulating hormone (TSH) level (normal, 0.24-3.70 $\mu\text{IU/ml}$). High titers of antimicrosomal antibodies ($\times 204,800$, normal: $< \times 100$) were noted. The test for antithyroglobulin antibodies was negative.

Electrocardiogram showed low voltage in the limb leads and generalized flattening of the ST-T segment; ST depression was found in II, III, aVf and V5 (Fig. 1a). Electrocardiogram on the second admission (Fig. 1b) showed no displacement of ST segments characteristic for ischemic heart disease. The voltage of QRS complexes was increased after treatment of L-triiodothyronine (Fig. 1b). A chest X-ray film revealed a globular-shaped cardiopericardial silhouette, moderate left pleural effusion, and marked vascular congestion with Kerley B lines on the right (Fig. 2). Massive pericardial effusion associated

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Fig. 1. Electrocardiograms of first admission (a) and second admission (b). Note an increase of voltage of QRS complexes.

Fig. 2. Chest radiograph showing gross cardiomegaly.

with mild pleural effusion and ascites was demonstrated by echocardiographic and computed tomographic technique (Fig. 3). Liver congestion was not evident. Right-heart catheteriza-

tion revealed impaired hemodynamics (Table 1).

Eight hundred milliliters of pericardial effusion was withdrawn by pericardiocentesis, and the removed fluid was examined for cytological, chemical and bacterial analysis. Mesothelial cells were the only cellular element; there were neither inflammatory cells nor malignant cells. Culture for bacteria including acid-fast bacilli was negative. Total protein was 5.2 g/dl. Evaluation of cholesterol was not performed. Two days after the pericardiocentesis, cardiac function was improved and the PCW was down to 0 mmHg (mean) (Table 1).

Under the diagnosis of hypothyroidism due to Hashimoto's thyroiditis and associated heart failure, the patient was started on a prescription of L-triiodothyronine 50 µg/day per os (P.O.) and digoxin 0.25 mg/day P.O. The L-triiodothyronine was finally increased to 75 µg/day. Two months later, her physical conditions improved and became symptomless. Serum T₄ and T₃ were 7.8 µg/dl and 0.98 ng/ml, respectively. However, TSH still remained at the high level of 36.88 µIU/ml. Other laboratory data were within normal limit. Two years later, she had recurrent pericardial effusion and dilatation of right and left ventricles. Data of right-heart catheterization is shown in Table 2. Coronary arteriogram demonstrated no stenotic lesions (Fig. 4). The left ventricle was mildly dilated (Fig. 5). Myocardial biopsy was carried out from the right ventricle and the tissue fragments were fixed in 10% formalin for light microscopic observation. The endocardium was thickened by accumulation

Fig. 3. Echocardiogram of the heart lying in a large pericardial effusion (PE). Note pendicular motion of septal and posterior walls. Free wall of left ventricle: 20 mm, septum: 18mm.

Table 1. Hemodynamic Values of before and after Pericardiocentesis

	Before pericardiocentesis		After pericardiocentesis	
	Systole/Diastole	Mean (EDP)	Systole/Diastole	Mean (EDP)
RA	13/8	9	4/-1	3
RV	29/0	(15)	20/0	(8)
MPA	31/18	24	18/7	12
PAW	20/17	18	1/0	(0)
CO (CI)	2.19 (1.50)		4.22 (2.89)	
EDVI	41.78		47.95	
ESVI	20.55		17.12	
EF	0.50		0.64	

RA: right atrium (mmHg), RV: right ventricle (mmHg), MPA: main pulmonary artery (mmHg), PAW: pulmonary artery wedge (mmHg), CO: cardiac output (L/min), CI: cardiac index (L/min/m²), EDVI: end diastolic volume index (ml/m²), ESVI: end systolic volume index (ml/m²), EF: ejection fraction (%), EDP: end diastolic pressure.

of mucinous ground substance with sparsely textured spindle cells (Fig. 6). Myofibers showed attenuation and focal vacuolation. Basophilic mucoid degeneration of the myofibers was not evident. The interstitium was in part wide due to the collection of mucoid material and fat infiltration. Mild infiltration of lymphoid cells was seen.

Table 2. Right-Heart Catheterization in Second Admission

	Systole/Diastole	Mean (EDP)
RA	8/0	2
RV	24/0	(9)
MPA	21/6	12
PAW	5/0	2
CO (CI)	6.39 (4.38)	

RA: right atrium (mmHg), RV: right ventricle (mmHg), MPA: main pulmonary artery (mmHg), PAW: pulmonary artery wedge (mmHg), CO: cardiac output (L/min), CI: cardiac index (L/min/m²), EDP: end diastolic pressure (mmHg).

Discussion

In the majority of hypothyroid patients with pericardial effusion, the pericardium is histologically normal. However, in patients with a large quantity of effusion, cholesterol pericarditis is a well-known phenomenon. It is not always specific for hypothyroidism (15, 16), histologically characterized by the infiltration of mononuclear cells, crystallization of cholesterol, giant cell formation and fibrous thickening (1, 7, 13), which may reduce a distensibility of the pericardium leading to cardiac tamponade. The cholesterol crystals incite a vigorous cellular reaction following fluid overexudation and pericardial thickening. Chronic accumulation of the fluid and diminished

Fig. 4. Left (a) and right (b) coronary arteriograms showing no stenosis.

reabsorption of cholesterol might increase its concentration, and allow precipitation and crystallization of cholesterol. However, the pathogenesis has not been fully understood.

In hypothyroid patients, cardiac output was markedly reduced, and the mean decrease from normal individuals was reported at 47% (17), however, associated cardiogenic shock was rare (18). Echocardiographic evaluation and follow-up examination of untreated hypothyroid patients demonstrates reversible cardiomyopathy including asymmetric septal hypertrophy, reduced amplitude of systolic septal excursion, reduced percent of systolic septal thickening, reduced dimension of the left ventricular outflow tract and systolic anterior motion of the mitral valve (5). Although microscopic changes in the myocardium warranting a diagnosis of "myxedema heart" are not found, the histologic pictures most frequently recognized are swelling of myocardial cells, vacuolation, degeneration of fibers, fatty infiltration and interstitial edema (1, 4). Since, most hypothyroid patients with cardiac tamponade were not fatal and recovered with pericardiocentesis and administration of thyroid hormone (9–12, 14), only a few reports included a histopathological investigation (7, 14). The epicardium and the coronary arteries were more vulnerable sites than the myocardium and endocardium. The coronary arteries showed luminal

Fig. 5. Left ventriculogram in diastole. Right anterior oblique view. Note mild dilatation of the ventricle.

Fig. 6. Light micrograph of the endocardium and myocardium showing thickening of the endocardium due to accumulation of mucinous ground substance (HE stain, $\times 170$).

stenosis by accelerated atherosclerosis. The development of coronary atherosclerosis was highly associated with hypertension and hypercholesterolemia which were frequently encountered in hypothyroidism.

In the present case, clinical manifestations suggesting cardiac tamponade involved dyspnea, faint heart sound, diminished cardiac output and systemic venous congestion associated with liver dysfunction. The fluid accumulation was considered to be caused by hypothyroidism; tuberculous and carcinomatous pericarditis could be ruled out based on the cytology and culture of the fluid. Cardiac infarction-associated pericarditis was also excluded by coronary angiography. In addition, histological examination of the myocardium supports in part the cardiomyopathy observed in myxedema. Cardiac function was remarkably improved after pericardiocentesis. However, persistent dilatation of the right and left ventricles was demonstrated with echocardiogram and angiogram over the four-year

follow-up period. Underlying cardiomyopathy should be strongly suspected in hypothyroid patients with persistent dilated ventricles and low ejection fraction. The chronic cardiac failure could accelerate fluid accumulation and diminish reabsorption as a result of venous congestion.

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