A Case Report of Cholesterol Pericarditis

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CHOLESTEROL pericarditis is a very rare disease, in whose pericardial fluid are demonstrated cholesterol crystals. Since Alexander's first description in 1919, more than 30 cases have been reported in the world literature. The case presented here, is characterized by complete loss of complaints in spite of the large cardiac silhouette of 10 year's duration.

CASE REPORT

A 24-year-old man, an official, was admitted to our Clinic in April, 1962, for evaluation of huge cardiac shadow. In 1952, he was fortuitously found to have an enlargement of the cardiac shadow, when tuberculin reaction turned positive. He was then suspected of pericarditis in a certain clinic, but, having no serious complaints, he had left it untreated since. Though he had been said to have "enlarged heart" on yearly X-ray examinations in his school days thereafter, he could do mountain-climbing, skiing, or the like, as any of his friends did. In recent years the cardiac shadow had extremely enlarged and he was admitted to our Clinic.

The patient did not remember having had any trauma or febrile disease. His family history was non-contributory.

The physical examination on admission revealed a well-developed, well-nourished man in apparent good health. Temperature was 36.4°C and pulse was 70 per min., regular and normal-sized without a paradoxical pulse present. The blood pressure was 130/86 in both arms. The respirations were of cost-abdominal type with a rate of 18. Neck veins were slightly distended. There were 2 slight bulges of the anterior chest wall, one at the left costal margin, the other at the right 3rd rib on the parasternal line. The apex beat was not palpable. Cardiac dullness was greatly increased from the right anterior axillary
Heart sounds were faint, but no murmurs were heard. The breath sounds and vocal fremitus were diminished in both bases, particularly on the left side. The liver was palpable 4 finger-breadths below the costal margin and slightly firm with no tenderness. No other organs were palpable and no signs of ascites present. No edema was found in any part of the body surface. Neurological examinations indicated no abnormalities. The ocular fundi were normal.

Laboratory examinations were as follows: blood study showed an erythrocyte count of 4,660,000, hemoglobin of 100% Sahli and a leucocyte count of 5,000 with normal differentials. Urinalysis showed increased urobilinogen and a trace of albumin. The blood sedimentation rate was 9 mm. per hour. Total serum protein was 8.0 Gm./100 ml., non-protein nitrogen 26.0 mg./100 ml., and total cholesterol 180 mg./100 ml. Serum electrolytes were within normal limits. Liver function was slightly impaired; thymol turbidity test was 3.7 units, zinc sulphate test 13.6 units, bromsulphthalein test 20 % after 45 min., serum alkaline phosphatase 2.7 Bessy units and total bilirubin 1.2 mg./100 ml., with 0.5 mg./100 ml. direct. Electrophoretic study of serum protein showed 59.5 % albumin, 14.7 % α-globulin, 13.6 % β-globulin and 12.6 % γ-globulin, with 20 % α- and 80 % β-lipoprotein. The serologic test for syphilis, C-reactive protein, Rose reaction and LE cell study were all negative. ASLO was 250 units. The tuberculin test was positive. Basal metabolic rate was -15 % and -8 % on 2 occasions, and protein-bound iodide was 8 μ/100 ml. I131 study revealed normal uptake by the thyroid. The venous pressure was equivalent to 180 mm H2O at the cubital vein, with the increase on deep inspiration. Circulation time was delayed, showing 22 sec. with Decholin and 15 sec. with ether. Vital capacity was 2,010 ml.

Posteroanterior and anterior oblique X-ray films of the chest are shown in Fig. 2, 3 and 4, which showed lowered diaphragmatic domes on both sides, and gigantic globular cardiac silhouette occupying almost two thirds of the thoracic cavity.
cavity. Comparison with the X-ray film taken 3 years prior to admission (Fig. 1) indicates the development of the disease during this period.

Transversal planigraph (Siemens) of the chest disclosed the homogenous cardiac shadow with anterior and bilateral extension (Fig. 5).

On roentgenocardiographic examination, pulsation was minimal on the entire cardiac borders.

An electrocardiogram revealed normal sinus rhythm with marked low voltage in all leads. P waves were slightly broad and notched in Lead I and aVL, inverted in Lead III and aVR, and there was no significant change in ST segment and T wave (Fig. 6).
Phonocardiograph showed no abnormal findings except for decreased intensity.

Peritoneoscopic examination revealed slightly swelled liver, on whose smooth surface were recognized reticular structures due to proliferating fibrous tissue. This and histological examination of the biopsied liver tissue gave evidence of liver fibrosis or the initial stage of liver cirrhosis.

To rule out other diseases showing such gigantic cardiac silhouette, right heart catheterization was performed, which disclosed that the pressure of the right ventricle was slightly elevated in systole and noticeably elevated in diastole with early diastolic dip and end-diastolic plateau, and that of the right atrium showed slight elevation (Fig. 7).

Angiocardiography revealed right-upward displacement of the whole heart within the cardiac shadow without gross anatomical abnormalities of atria, ventricles and great vessels.
From the above-mentioned data, it became evident that the huge cardiac shadow was due to abundant accumulation of fluid in the pericardial cavity.

On April 30, 1962, pericardial aspiration was performed at the 5th intercostal space on the left medioclavicular line, with the removal of 400 ml. of deep straw-colored, turbid fluid, in which were seen fine silky-shimmering flecks, giving it a "gold paint appearance". Examination of the fluid revealed a specific gravity of 1.026, positive Rivalta reaction, many histiocytes with occasional white cells, total protein 6.0 Gm./100 ml. with A/G ratio 1.33, Na 139 mEq./L., K 4.0 mEq./L., and Cl 114 mEq./L. The cholesterol content of the whole fluid and the supernatant fluid were 82 and 32 mg./100 ml. respectively. As seen in Table I, every fraction of the lipids of the fluid was less than that of the serum. Microscopic examination of the centrifuged fluid showed numerous cholesterol crystals (Fig. 8). Bacteriological studies were all negative.

### Table I. Lipid Content of the Pericardial Fluid and the Serum

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<th>Whole fluid</th>
<th>Supernatant fluid</th>
<th>Serum</th>
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<tr>
<td>Cholesterol</td>
<td></td>
<td></td>
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<tr>
<td>total</td>
<td>82 mg./100 ml.</td>
<td>36 mg./100 ml.</td>
<td>188 mg./100 ml.</td>
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<tr>
<td>ester</td>
<td>18</td>
<td>11</td>
<td>117</td>
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<tr>
<td>Total phospholipids</td>
<td>—</td>
<td>—</td>
<td>166</td>
</tr>
<tr>
<td>Total fatty acids</td>
<td>63</td>
<td>50</td>
<td>416</td>
</tr>
<tr>
<td>Neutral fats</td>
<td>53</td>
<td>44</td>
<td>231</td>
</tr>
<tr>
<td>Total lipids</td>
<td>145</td>
<td>86</td>
<td>659</td>
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On June 11, 1,600 ml. of the same fluid was aspirated, and 1,000 ml. of air was injected into the pericardial cavity. X-ray film of the chest demonstrated the whole contour of the small-sized heart with the fluid level in the thickened pericardium (Fig. 9).

After having 400 ml. of similar fluid tapped on the other 2 occasions, with the result of decreased venous pressure and increased vital capacity, the patient
was discharged from the hospital on June 23 without complete removal of the fluid.

The patient was followed up thereafter, and on June 9, Aug. 13 and Sept. 8, pericardial aspirations were repeated, each time yielding 800 to 1,200 ml. of serosanguineous fluid with a cholesterol content of 80 to 105 mg./100 ml. with no more crystals. After each aspiration, cardiac silhouette regained its previous size in a month, suggesting that repeated aspirations would not induce spontaneous improvement. From Sept. 22 to Oct. 29, prednisolone (25 to 40 mg.) was administered into pericardial cavity once a week, which seemed to have suppressed the additional accumulation of the fluid, but couldn’t effect its complete disappearance.

On Dec. 7, the patient was operated upon at the Second Department of Surgery of Tokyo University Hospital.

Thoracotomy was done through mid-sternal incision. The pericardium, 3 to 5 mm. in thickness, closely adhered to the anterior chest wall, forming a gigantic sac in the thoracic cavity. When it was opened, the small heart covered with yellowish white epicardium was just floatingly beating in the amber fluid of approximately 1,000 ml. of serosanguineous character. The pericardial and epicardial surface was almost smooth except for several calcified portions around the outflow tracts of great vessels. The pericardium was closely adherent to the mediastinal pleura on both sides, which required both pleural cavities to be opened. After laying aside both phrenic nerves, pericardiectomy was performed for the most part of the pericardium, leaving diaphragmatic region and a posterior part of the heart. With removal of the constricting epicardium, the heart became enlarged and its action increased.

The patient’s postoperative course was unfavorable, and due to respiratory insufficiency, he died on Dec. 9.

Pathologic findings: The diagnosis was chronic fibrous pericarditis.

1. Surgical materials: Microscopic examination of the pericardium showed
marked thickening of fibrous tissues with occasional focal perivascular infiltration of lymphocytes and with some areas of hyaline degeneration. The fibrous tissues were relatively rich in capillaries. There was no deposition of cholesterol crystals. No macrophages, foam cells or giant cells were recognized (Fig. 10).

2. Autopsy materials: The heart weighed 400 Gm. with no particular changes except for mild interstitial edema in the myocardium and endocardium. The liver, weighing 1,270 Gm., was reddish-brown in color and the surface was slightly nodular with irregularly developing connective tissues. Microscopically, marked chronic congestion with centrolobular bleeding and necrosis was noted. Kidneys and spleen showed moderate degree of congestion and the same was mildly noticed in both lungs.

**Discussion**

As for the etiology of cholesterol pericarditis, no definite explanations have been made so far. Although a few of the cases previously reported were attributed to myxoedema, tuberculosis, rheumatism or malignant tumors, most of the remaining cases were of unknown origin. In a survey of literature, it would be generally acceptable that cholesterol pericarditis is not a primary disorder in itself, but a special form of chronic serosanguineous pericarditis of non-specific origin. In the case presented, the cause is likewise quite unknown.

Concerning the origin of cholesterol crystals, 2 plausible hypotheses appeared in the literature; the most likely one of these, as mentioned by Daniel and Puder, is based on the disruption of soluble lipoprotein macromolecules originating from the blood cells in the pericardial fluid. It
was also demonstrated by Stewart et al.\textsuperscript{24} that absorption of large molecule substance from the pericardial wall is very slow in the patient of chronic pericardial effusion. This status of mal-absorption would prepare deposition of crystalline cholesterol over a long space of time. The other hypothesis was proposed by Claisse et al.\textsuperscript{7} that the necrotic degradation of superficial layers of pericardial cavity results in lysis of cellular element and liberation of cholesterol fixed within the tissues. They proposed this idea on the histological ground that there were recognized in the pericardial wall, nodules and striations of cholesterol, and clefts corresponding to soluble fatty acids. These findings were also thought to be concerned with atheromatous state of their cases.

Regardless of the whereabouts of the origin of cholesterol, however, the cause determining crystallization of cholesterol seems to have the least relation with etiology of the disease, and it will be more reasonable to think it as a matter of pure local condition rather than that of systemic disturbances of lipid metabolism.

In our case, pericardial aspirates after discharge were of serosanguineous character free of crystals, which may suggest that cholesterol concentration was due to lipoprotein of blood cell origin.

Experimental observations by Ehrenhaft and Taber\textsuperscript{15} indicated that intrapericardial injection of autogenous dog's blood, lipid fraction of the blood, and crystalline cholesterol suspension produced pericardial reaction, which consisted in pericardial thickening, formation of granulation tissue, and adhesions. This result, however, is not directly applicable to cholesterol pericarditis, and besides, analogical considerations are often dangerous, but it would suggest the prognosis of this disease in a way.

Various attempts have been made of the treatment of this disease. Merrill\textsuperscript{19} reported a case which was well treated by thyroid extract, and in Arnold's cases\textsuperscript{3} noticeable effects were not obtained by intrapericardial administration of heparin and antibiotics. In 2 cases reported by Claisse et al.,\textsuperscript{7} pericardial fluid disappeared as the result of intrapericardial application of corticosteroid. Pericardial aspiration can surely induce symptomatic improvement for a short period of time, but complete disappearance of the fluid does not seem to be brought about by this procedure alone. The most important problem is the indication of pericardiectomy, which would be the only radical and definite way of treatment, although the result was unfavorable in our foregoing case.

\textbf{Summary}

A case was presented of cholesterol pericarditis of unknown origin. The patient had been free of complaints for the past 10 years with huge
cardiac silhouette. Intrapericardial administration of prednisolone was found to have a little effect on fluid accumulation. The postoperative course of pericardiectomy was unfavorable in this case.

References