Cholesterol Pericarditis
Successful Treatment by Pericardiectomy

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Although cholesterol pericarditis is usually associated with myxedema, it may occur as a result of tuberculous infection or hemopericardium. Cardiac constriction is apparently an uncommon feature of the condition. A case of chronic constrictive cholesterol pericarditis was treated by pericardiectomy with complete relief of symptoms. Neither bacteriologic nor histologic studies of the resected pericardium revealed the etiologic basis for cholesterol accumulation within the pericardial sac.

CHOLESTEROL PERICARDITIS is a rare condition and usually occurs in association with myxedema. The first instance of pericardial effusion with large quantities of cholesterol was reported by Alexander¹ in 1919. This fluid contained 0.61 Gm. of cholesterol per liter and had a “gold paint” appearance. Although Alexander recognized that the patient was myxedematous, he did not associate the pericarditis with this condition. The occurrence of pericardial effusion in patients with myxedema was subsequently emphasized by Gordon² and others. In the case reported by Harrell and Johnston,³ the serum cholesterol was 270 mg. per 100 cc. and the cholesterol content of the pericardial fluid 92 mg. per 100 cc. Bullrich and associates⁴ found that the pericardial fluid from a patient with myxedema contained slightly more cholesterol than the blood. In 1946 Howard⁵ reported the necropsy findings of a patient with myxedema. The pericardium contained 4000 cc. of dark, green fluorescent fluid in which were bright, sparkling yellow cholesterol crystals. Chemical examination of the fluid revealed a cholesterol content of 76 mg. per 100 cc. The pericardial fluid from five patients with myxedema was examined by Bustamente and Perez-Stable⁶ and cholesterol was found in all, but in quantities much below the blood levels. In the case of cholesterol pericarditis reported by Merrill⁷ the etiology was obscure although the clinical manifestations and the patient’s response to thyroid extract suggested hypothyroidism.

Other conditions besides myxedema have been reported to be of significance in the production of cholesterol pericarditis. Tuberculosis has been suggested by Daniel and Puder⁸ as an etiologic factor on the basis of the necropsy findings in one case. They postulated that hemopericardium may have occurred as a result of tuberculous involvement of the pericardium. Subsequent hemolysis of erythrocytes and absorption of a portion of the fluid accounted for the high cholesterol content of the pericardial fluid.

In a case of hemorrhagic pericarditis described by Voldet,⁹ microscopic examination of the epicardium revealed numerous collections of cholesterol crystals surrounded by giant cells.

In 1950 Ada¹⁰ reported a case of cholesterol pericarditis proved by biopsy and without demonstrable etiology. The pericardial fluid was golden yellow, opalescent, and contained 120 mg. of cholesterol per 100 cc. The blood cholesterol was 167 mg. per 100 cc. At thoracotomy several cholesterol plaques were noted on both the visceral and parietal pericardial surfaces. Since there was no evidence of cardiac constriction, only a biopsy was done. Microscopic examination revealed fibrous tissue containing masses of cholesterol, large numbers of foreign body giant cells and some regenerating fat cells.

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Recently we have treated a patient with chronic pericardial effusion of unknown etiology that progressed to constrictive pericarditis. Pericardiectomy was performed with complete relief of symptoms. Histologically, the resected pericardium revealed chronic cholesterol pericarditis. Because of the apparent rarity of this condition and since no reports of pericardiectomy for cholesterol pericarditis have appeared, this case is recorded in some detail.

**Case Report**

J. O. S., a 32 year-old white man, was admitted to the Houston Veterans Administration Hospital on Aug. 28, 1953 with the history of having been in good health until April, 1952, when he rather abruptly developed constant, dull, aching precordial pain and a sensation of fullness and tenderness in the epigastrium. The pain was markedly accentuated on deep inspiration. He had no other symptoms and the pain subsided within a short time. He was then well until the end of May, 1952, when similar symptoms recurred and he noted a temperature elevation to 102 F. At that time in a local hospital, his physician noted enlargement of the cardiac silhouette on fluoroscopy. On June 7, 1952 he was referred to another hospital where he remained for three weeks.

Physical examination at that time revealed a normal temperature, blood pressure of 116/76 and pulse rate of 72 beats per minute. There was enlargement of the area of cardiac dullness to the right and left. The heart sounds were faint, and no murmurs or thrills were noted. The lung fields were clear. The remainder of the physical examination was not remarkable. Laboratory studies revealed an erythrocyte count of 3,820,000, hemoglobin of 11.3 Gm. per 100 cc., hematocrit of 42 percent and erythrocyte sedimentation rate of 36 mm. in 1 hour. The venous pressure was 16 cm. of saline and the circulation time, arm to tongue, was 30 seconds (Decholin).

On June 11, 1952, pericardial aspiration yielded 20 cc. of deep yellow fluid. Immediately after paracentesis, the venous pressure dropped to 8 cm. of saline. In the fluid there were no erythrocytes, the leukocytes could not be counted, and the differential count revealed 7 per cent neutrophils and 93 per cent lymphocytes. The total protein was 5.8 Gm. per 100 cc. Acid fast organisms were noted on direct smear of the fluid; however, guinea pig studies were negative at six weeks.

On June 16, 1952, the patient was started on 1 Gm. of dihydrostreptomycin and 12 Gm. of para-aminosalicylic acid daily. After five weeks the dosage of para-aminosalicylic acid was reduced to 6 Gm. daily because of nausea and vomiting, and the dihydrostreptomycin to 1 Gm. twice a week. After four months para-aminosalicylic acid was discontinued, and for the following four months he received streptomycin, 1 Gm. twice a week, and isonicotinic acid hydrazide. The patient remained ambulatory during the period of streptomycin therapy and was apparently asymptomatic.

He was seen again on Feb. 24, 1953, when he complained of slight cough and minimal temperature elevation. He was advised to re-enter the hospital but did not do so as the symptoms subsided in a short time.

He continued relatively asymptomatic until three weeks prior to admission to this hospital when he developed a constant, aching pain that began under the left scapula and radiated anteriorly into the chest. This was associated with a substernal feeling of fullness, exertional dyspnea, and a mild non-productive cough. He lost 6 pounds of weight during the month prior to admission. A chest roentgenogram on Aug. 7, 1953 again revealed a large cardiac silhouette. Streptomycin and para-aminosalicylic acid therapy was restarted and he was advised to re-enter a hospital.

The past history was entirely negative for tuberculosis, chest trauma or symptoms suggestive of hypothyroidism.

At the time of examination the patient was thin, well-developed, and did not appear ill. The temperature was 98.6 F., respirations 20, pulse rate of 72 per minute and blood pressure 110/70 mm. Hg. The skin was warm and moist. A few small posterior cervical lymph nodes were noted. The lung fields were clear. The heart was enlarged by percussion to the left anterior axillary line. The heart sounds were distant, and no murmurs were heard. There was no pulsus paradoxus. Except for slight tenderness in the mid-epigastrium, the remainder of the physical examination was essentially negative.

Laboratory studies were as follows: Urinalysis negative; erythrocytes 4,650,000; hemoglobin 14.3 Gm.; leukocytes 7,900 with 6 per cent stab forms, 54 per cent segmented neutrophilic granulocytes, 25 per cent lymphocytes, 2 per cent monocytes, 12 per cent eosinophils, 1 per cent basophils; and sedimentation rate 20 mm. in 1 hour. The serology was negative. The blood urea nitrogen was 36 mg. per 100 cc., serum cholesterol 154 mg. per 100 cc., and the basal metabolic rate was plus 8 per cent. Three gastric washings were negative for acid fast bacilli on culture. A tuberculin skin test was positive. The venous pressure was 15 cm. of saline and circulation time (arm to tongue) was 11 seconds. The initial electrocardiogram was within normal limits. The chest roentgenogram (fig. 1A) revealed clear lung fields but a marked increase in the size of the cardiac silhouette. Fluoroscopy showed minimal pulsations of all cardiac borders.

Pericardial aspiration on September 1 yielded 250 cc. of turbid, red-orange fluid which contained many erythrocytes, epithelial cells and cholesterol
crystals. The total protein was 8.5 Gm. per 100 cc. and the sugar was 19 mg. per 100 cc. Smear and culture of the fluid were negative for miscellaneous organisms as well as for acid fast bacilli. Several hours after the pericardial aspiration, the patient began to complain of substernal discomfort and epigastric pain which was accentuated by inspiration. The symptoms were progressive, and on Sept. 3 examination revealed distention of the neck veins, pulsus paradoxus, a pleural friction rub over the left lower anterior chest and clicking and bubbling sounds of air and fluid in the pericardial space. There was no pericardial friction rub. The venous pressure was 34.8 cm. of saline. Electrocardiogram revealed S-T segment elevation consistent with pericarditis. Pericardial aspiration yielded 1250 cc. of reddish iridescent fluid similar to that obtained previously. Examination of this fluid showed a specific gravity of 1.025, 1300 white blood cells per cubic millimeter, 450 erythrocytes per cubic millimeter, total protein 7.2 Gm. per 100 cc., sugar 12 mg. per 100 cc., and total cholesterol 263 mg. per 100 cc. (cholesterol content of supernatant fluid was 156 mg. per 100 cc.). Smears and cultures for miscellaneous organisms and acid fast bacilli, as well as guinea pig inoculations, were again negative.

Immediately following the pericardial aspiration, symptoms subsided somewhat, but over the next several days he again developed pain in the precordial region. Rales were noted in the left lung base and the liver became palpable 4 fingerbreadths below the right costal margin. On Sept. 7, 1700 cc. of brown-yellow fluid, which did not have the same iridescent appearance, were removed. Bacteriologic studies were again negative. At the time of aspiration, 850 cc. of air were injected into the pericardial space. A roentgenogram of the chest (fig. 1b) showed a large amount of air about a normal sized heart and the pericardium appeared thickened.

Over the following two weeks a pericardial friction rub and splashing sounds were noted intermittently. During the seven weeks following the last aspiration, the patient had an intermittent low grade fever. Because of the possibility of tuberculous pericarditis, streptomycin 1 Gm. daily, and isonicotinic acid hydrazide, 100 mg. three times a day, were started on Sept. 9 and two weeks later sodium para-aminosalicylic acid, 4.0 Gm. four times a day, was added. On Sept. 9, 131 uptake studies revealed a decreased iodine uptake (5.4 per cent in 3 hours, 5.3 per cent in 6 hours, 5.6 per cent in 24 hours) compatible with hypothyroidism. However, three repeat 131 uptake studies after para-aminosalicylic acid had been discontinued were normal, the one on Nov. 17 being 8.6 per cent in 3 hours, 10.0 per cent in 6 hours, 18.9 per cent in 24 hours, and 19 per cent in 48 hours. Repeat chest roentgenograms on November 13, (fig. 2), revealed marked diminution of the pericardial air, and the fluid level was again noted. On Dec. 1 the patient was transferred to the Surgical Service.

On Dec. 3 a left thoracotomy was performed through the fourth intercostal space anteriorly. The pericardium was gray-yellow and intimately adhered to the surface of the heart. The mediastinal pleura was incised and the phrenic nerve mobilized and retracted away from the pericardium. A longitudinal incision was made over the left lateral aspect
CHOLESTEROL PERICARDITIS

FIG. 2. Roentgenogram of the chest two months after admission, showing persistence of a pericardial fluid level.

of the pericardial sac and carried down to the myocardium. There was a layer of fibrous connective tissue intimately adherent to the epicardium and between this layer and the thickened pericardium there were numerous cyst-like spaces containing straw-colored fluid and numerous yellow plaques. The pericardium varied in thickness from 0.6 cm. over the ventricles to 0.2 cm. over the atria. Dissection of the pericardium was carried superiorly to the atrioventricular groove, laterally to include the surface of both right and left ventricles, and over the diaphragmatic surface of the heart. As the thickened, constricting pericardium was removed from the surface of the ventricles there was a noticeable increase in heart size. Upon completion of the pericardectomy an intercostal catheter was inserted for underwater drainage of the chest and the thoracotomy wound was closed.

The patient’s convalescence was uneventful and he was discharged on December 18, 1953.

Pathologic Findings: The specimen consisted of multiple portions of soft membranous tissue of varying thickness, the largest 10 by 8 cm. All surfaces were ragged with adhesions and here and there were bright yellow plaques up to 2 by 1.5 cm. The cut surfaces were firm, shiny white with some hemorrhagic areas.

Microscopic examination (fig. 3) revealed hyalinized connective tissue focally infiltrated with lymphocytes, plasma cells, and large mononuclear cells, with occasional aggregations of lymphocytes amounting to lymph follicles. In many areas foam cells were interspersed with lymphocytes and occasional giant cells of the foreign body type. There were a few slit-like spaces resembling cholesterol clefts. Sudan IV stains were positive for lipid in the

FIG. 3. Microscopic appearance of pericardium. In a dense hyalinized fibrous connective tissue are aggregates of slit-like spaces, few giant cells of the foreign body type, many foam cells and some lymphocytes and plasma cells. X 100.
foam cells. The substance contained in the cells was isotropic.

On Aug. 20, 1954, about nine months after operation, the patient was asymptomatic and chest roentgenogram revealed a normal cardiac silhouette (fig. 4).

**COMMENT**

The etiology of the constrictive cholesterol pericarditis is obscure in this case. Although acid fast organisms were noted on one direct smear of the pericardial fluid, subsequent studies failed to confirm this. Repeated cultures and guinea pig inoculations were negative, and there was little if any clinical response to long-term anti-microbial therapy during the first year of the patient’s illness. Furthermore, histologic examination of the resected specimen failed to disclose any changes indicative of tuberculosis. While continued antibiotic therapy might have eradicated all evidence of tuberculous, this seems inconsistent with the course of the disease.

There were no clinical manifestations suggestive of hypothyroidism, though there was an initial low $^{131}$I uptake. However, para-aminosalicylic acid was being administered at the time this test was performed thus invalidating the results. Several subsequent $^{131}$I uptake studies after discontinuation of para-aminosalicylic acid were normal and no other laboratory studies were compatible with a diagnosis of hypothyroidism.

No history of chest trauma was obtained and neither the fluid removed by paracentesis nor the findings at operation suggested hemopericardium.

Recent observations by Ehrenhaft indicate that lipids in high concentration within the pericardial sac may produce constrictive pericarditis. He injected autogenous whole blood into the pericardial sac of one group of dogs and in another the blood lipid fraction alone was injected. When sacrificed at intervals of one to six months later, in all of the animals there were changes in the pericardium and epicardium, but only those having intrapericardial injection of lipids had advanced constrictive pericarditis. These changes consisted of pericardial and epicardial thickening, areas of granulation tissue and adhesions. Fat stains revealed lipid material in cells within the thickened pericardium and epicardium.

In view of this experimental study, it is postulated that a high cholesterol content of the pericardial fluid was responsible for the constrictive pericarditis in this case. However, the factors responsible for the accumulation of cholesterol within the pericardial sac are not apparent.

**SUMMARY**

Pericardial effusion with a high cholesterol content is usually associated with myxedema. Tuberculosis and hemopericardium have also been considered of etiologic significance in cholesterol pericarditis.

The successful treatment of a case of chronic constrictive cholesterol pericarditis by pericardectomy is reported. On the basis of experimental studies it appears that high concentrations of lipids in the pericardial fluid may produce pericarditis.

**SYNOPSIS IN INTERLINGUA**

Ben que pericarditis cholesterolic es usualmente associate con myxedema, illo pote occurrer in consequentia de infecciones tubere-
lotic o de hemopericardio. Il pare que constriction cardiac es un tracto unusual del condition.

Un caso de chronic constrictive pericarditis cholesterolic esseva tractate per pericardiectomia con complete alleviamento del symptommas. Studios bacteriologic e histologic del resectionate pericardio non revelava le base etiologic del accumulation de cholesterol intra le sacco pericardial.

REFERENCES

Cholesterol Pericarditis: Successful Treatment by Pericardiectomy
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doi: 10.1161/01.CIR.12.2.193
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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