CASE REPORTS

Huge Chronic Pericardial Effusion
Caused by Toxoplasma gondii

J. Sagristá-Sauleda, M.D., G. Permanyer-Miralda, M.D., C. Juste-Sánchez, M.D.,
M. L. de Buen-Sánchez, M.D., R. Pujadas-Capmany, M.D., L. Arcalís-Arce, M.D.,
and J. Soler-Soler, M.D.

SUMMARY Two patients who had a huge pericardial effusion of at least 9 and 14 years’ duration caused by cardiac toxoplasmosis are reported. Toxoplasma gondii were seen in the pericardial fluid, and serologic evidence also demonstrated the activity of the infection. These cases illustrate both the need to exclude toxoplasmosis in chronic pericardial effusion of unknown cause and the possibility of seeing toxoplasma in the pericardial fluid of patients with active toxoplasmic pericarditis. Moreover, in endemic areas, cardiac toxoplasmosis may not be an exceptional cause of chronic pericardial effusion.

TOXOPLASMOSIS is known to cause several types of heart disease, including myocarditis, chronic myocardial disease, arrhythmias, and both acute and subacute pericarditis.1-5 In this report, we present two patients who had a huge pericardial effusion caused by Toxoplasma gondii that persisted for several years. Pericardial effusion caused by toxoplasma infection has not, to our knowledge, been reported. In both patients, the protozoon was seen in the pericardial fluid, thereby confirming the diagnosis. This finding, too, has not been described, as far as we know.

Methods

Immunofluorescent antibodies (IFA)6 were detected in plasma and pericardial fluid by using as antigen a suspension of toxoplasma obtained in our laboratory; the pericardial fluid had been centrifuged at 500 rpm for 5 minutes. Specific IgM antibodies were detected (Remington’s test)7 with labeled antiserum (Biotrol) against the problem serum and the supernatant pericardial fluid, both diluted to 1:40.

Investigation of toxoplasma in pericardial fluid was carried out by direct examination by phase contrast and indirect immunofluorescence. Pericardial fluid processed as follows was used as antigen. First, the fluid was centrifuged at 500 rpm for 5 minutes, followed by a second centrifugation at 3500 rpm for 30 minutes. Sediment was spread on an immunofluorescence slide, and a positive standard serum was used for the reaction. A negative serum without antitoxoplasma antibodies was used as a control. Intraperitoneal inoculation of white mice was carried out as follows. Six mice were inoculated with pure pericardial fluid, and another six mice were inoculated with the sediment obtained by centrifugation. After the first inoculation, blind passages of peritoneal fluid were carried out at weekly intervals. Smears of peritoneal exudates were examined by phase contrast, Giemsa stain and indirect immunofluorescence.

Case Reports

Case 1

A 44-year-old woman was admitted to the hospital on February 25, 1980, with a 6-week history of chest pain, low-grade temperature and malaise. At ages 30 and 40 years, cardiac enlargement was discovered at a routine radiographic examination. She had had left eye ophthalmitis at age 5 months followed by microphthalmia and enucleation, as well as three miscarriages. At admission, her heart rate was 80 beats/min and her blood pressure 110/60 mm Hg. Paradoxical pulse was not present, and there were no murmurs or gallop sounds. There was no edema, liver enlargement or jugular distention. The optic fundus (right eye) was normal.

Routine blood and urine tests were normal. T, and T, plasma levels were normal. Tuberculin skin test was negative. The chest radiograph (fig. 1) showed osensible cardiac enlargement and normal lungs. The echocardiogram suggested huge pericardial effusion as the only abnormal finding. Pericardiocentesis yielded straw-colored fluid with a protein content of 5.8 g/dl; its cellularity was scanty. Investigation for tubercle bacilli in pericardial fluid was negative. Specific investigations for toxoplasmosis showed (1) a high IFA titer in serum (240 IU) and in pericardial fluid (120 IU); (2) positive Remington’s test in serum and pericardial fluid; (3) visualization of toxoplasma by phase contrast and by indirect immunofluorescence (fig. 2) in pericardial fluid; and (4) positive inoculation to mice 45 days after the first inoculation with pure pericardial fluid.

Because adequate medical treatment (spiramycin 500 mg four times a day and pyrimethamine 75 mg on the first day and 25 mg/day thereafter, both for 1 month) was unsuccessful, the patient was subjected to subtotal pericardiectomy. The pericardium was slightly thickened and there were no adhesions. Investiga-
tion for toxoplasma in pericardial tissue was negative. Microscopic examination of the pericardium showed nonspecific changes consistent with chronic pericarditis. One year after operation, radiographic examination showed normal heart size, and the patient's clinical condition was good. The IFA titer was significantly lower (25 IU) than the initial value (240 IU).

Case 2
The patient, a 53-year-old woman, was the aunt of the case 1. At age 44 years, an important increase in heart size, which persisted on later examinations, was discovered at a routine radiographic examination. At age 49 years, an echocardiogram performed in another hospital showed a huge pericardial effusion. She had normal pregnancies at ages 25 and 30 years. Dyspnea and chest pain were not present. At our request she was admitted to the hospital on March 18, 1980, after we confirmed the presence of huge pericardial effusion by echocardiogram. At admission, her heart rate was 56 beats/min and her blood pressure 120/85 mm Hg; paradoxical pulse was not present. Cardiac auscultation was normal. The optic fundi were normal.

Routine blood and urine examinations were normal, except a fasting blood sugar of 115 mg/dl. Tuberculin skin test was negative, and plasma T₃ and T₄ levels were normal. The ECG showed sinus rhythm and low QRS amplitude. The chest radiograph (fig. 3) and the electrocardiogram suggested a huge pericardial effusion without other abnormalities. Pericardiocentesis was unproductive. Specific investigations for toxoplasmosis showed a high IFA titer (120 IU) and positive Remington's test in serum.

Treatment with pyrimetamine and spiramycin failed to influence the size of pericardial effusion. Twelve days after admission she developed progressive tamponade. Pericardieotomy was performed on April 18, 1980. The pericardium was slightly thickened, and 2700 ml of serosanguineous fluid were obtained. Specific toxoplasmosis investigations in pericardial fluid showed a high IFA titer (120 IU) and a positive Remington's test. Toxoplasma organisms were seen by phase contrast and indirect immunofluorescence. Inoculation to mice was negative. No parasites were seen in pericardial tissue, which had microscopic features of chronic nonspecific pericarditis. Two weeks after operation, the IFA titer in serum was 60 IU. Eighteen months after discharge she remained in good health, and there were no signs of pericardial effusion in the echocardiogram.
Serologic determination of IFA was performed in 12 first-degree relatives. Two had a titer of 100 IU, with negative Remington’s test; in one, the titer was 50 IU, and in the remaining nine it was 25 IU.

**Discussion**

These two cases are noteworthy for two reasons: they illustrate the possibility of long-standing, huge pericardial effusion due to cardiac toxoplasmosis, and the diagnosis of toxoplasmosis was confirmed by direct visualization of the protozoon in the pericardial fluid of both patients.

Huge chronic pericardial effusion as an isolated finding is not an exceptional occurrence in clinical practice, and is probably a manifestation of a spectrum of diseases affecting the pericardium. Commonly, a thorough study fails to discover the cause of the condition. In the largest review of the literature, in 73 cases out of 134 with chronic pericardial effusion the etiologic diagnosis could not be established. Toxoplasmosis was not even mentioned as a possible etiologic factor in this review or in others dealing with chronic pericardial effusion. This fact may be accounted for by the usually low suspicion index of toxoplasmosis among cardiologists. Indeed, correct diagnosis of our cases was made because our protocol study of pericardial disease includes routine determination of IFA.

We think, therefore, that the present report illustrates the possibility that toxoplasmosis may be one of the diseases responsible for chronic pericardial effusion and that it may represent a not uncommon occurrence in endemic areas.

These two cases represent instances of chronic cardiac toxoplasmosis with episodes of acute reactivation. After congenital or acquired primary infection, toxoplasmas are spread throughout the body by the bloodstream: they may reach any organ and can persist there as a cyst for the entire life span of the subject. Rupture of cysts gives rise to asymptomatic parasitemia or to clinical symptoms of organ damage, resulting in acute reactivation of the disease. In both of our cases, the laboratory findings are consistent with acute reactivation. However, the persistence of pericardial effusion for several years strongly suggests the possibility of previous active cardiac toxoplasmosis as the cause of chronic effusion.

The diagnosis of cardiac toxoplasmosis is rarely made with confidence, as it is usually based on indirect evidence such as serologic methods and the demonstration of the parasite in organ tissues other than the heart. In these instances, evidence for active toxoplasmosis is sound, but the cardiac involvement can only be assumed by excluding other causes of the cardiac findings, although in occasional patients with unrelated diseases, the parasite has been found in a biopsy or autopsy specimen. Serologic diagnosis of active toxoplasmosis is based upon the finding of a significant titer of 19 S (IgM) antibodies in the patient’s serum (Remington’s test), or on the falling or rising IFA titers. The finding of a slightly raised, stable IFA titer has a questionable significance, as low titers are very common in certain communities with a high prevalence of infection; in Spain, more than 50% of the asymptomatic population has a low titer of antitoxoplasma antibodies (unpublished data). This fact makes the diagnosis of chronic cardiac toxoplasmosis difficult when nonspecific findings of heart disease coexist with a slightly raised IFA titer. Although toxoplasmosis has been seen at autopsy, our patients are the first reported cases where the parasite has been recovered from pericardial fluid of a living patient. Our finding, therefore, emphasizes the need for routine attempts to visualize the parasite.

In our patients, the classic medical treatment was unsuccessful. Pericardectomy seems to have controlled the disease, as no evidence of pericardial effusion was detected 1 year and 18 months later, respectively. Surgery may, therefore, play a role in the management of this disease.

**References**


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