An Autopsied Case of a Two-month-old Infant with Granulomatous Pancarditis Having Severe Vasculitis and Valvulitis

SACHIO KAWAI, M.D., RYOZO OKADA, M.D., HARUNORI SUGIMOTO, M.D.*
MOTOI OKADA, M.D.** AND YOSHIRO FUKUDA, M.D.**

A 2-month-old female infant with pancarditis was reported. The patient died after a 26-day clinical course. The autopsy showed pancarditis, including inflammation in all 4 valves and chordae, fibrinoid vasculitis, pharyngolaryngitis and atrophy of the lymph nodes. Microscopic examination revealed proliferative inflammation in the endocardium, valve, myocardium, epicardium and coronary vessels. The histological findings suggested the etiology to be a rheumatic-type reaction at an extremely young age.

So-called "interstitial myocarditis" is known to occur even in infants. However, in most cases, primary focus of the infection is the myocardium, and endocarditis and epicarditis are either absent or only slight, if present. The authors studied an autopsied case of an infant with pancarditis, who had severe valvular lesions, suggesting the future development of valvular heart disease, had the patients survived.

CASE REPORT

The patient was a 2-month-old female weighing 2,800g at birth. She was born at a gestation period of 39 weeks and 4 days. The present disease began on September 17, 1981, with the symptoms of fever, cough, rhinorrhea, eruptions and diarrhea. Reddening of the throat appeared on the day following the onset. On the 8th day, pyretolysis occurred and the eruptions abated, but from the 11th day the fever recurred and the eruptions became aggravated. She was admitted on September 30.

Findings on Admission: She weighed 5,200g and had a regular pulse with a rate of 148/min. She had a blood pressure of 100/50 mmHg. Her face was wan, but cyanosis was not present. Patches of erythema marginatum, measuring 1.0–1.5 cm in diameter with a healthy skin area in the center, were observed on her trunk and extremities. Her lymph nodes were not palpable. Her chest X-ray on admission revealed slight extrusions (Fig. 1A). Her electrocardiogram (ECG) indicated slight ST-T changes, but P-Q intervals were not prolonged (Fig. 1B).

Laboratory Data: A white blood cell count of 16,700/ml, a red blood cell count of 392 x 10^4/ml, a hemoglobin content of 11.3g/100 ml, a hematocrit of 37%, a platelet count of 29 x 10^4/ml, a reticulocyte count of 31% and an eosinophil count of 56/ml were noted. Urine analysis showed a specific gravity of 1.029, a pH of 6.0, a protein level of 17 mg/100 ml. Glycosuria was not found and urinary sediments were within normal limits. Blood chemistry findings were as follows: glutamic-oxalactic transaminase, 15 u/ml; glutamic-pyruvic transaminase, 25 u/ml; alkaline phosphatase, 10.4 B.U.; lactic dehydrogenase, 291 u/ml; total protein, 5.8g/100 ml (albumin, 52.0%, gamma-globulin,
10.5%); sodium, 125 mEq/L; potassium, 4.7 mEq/L; chloride, 90 mEq/L; blood urea nitrogen 10 mg/100 ml and C-reactive protein, 6+. Anti-streptolysin O titer (ASO), anti-nuclear antibody titer, RA factor and various virus antibody titers were not tested.

From the above-mentioned findings, she was suspected of suffering from septicemia. Blood cultures were performed after a discontinuation of antibiotic treatment. Although the results of the cultures were negative, treatment against septicemia with ampicillin, piperacillin, human immunoglobulin and so on was commenced. Pyretolysis did not occur. Diuretics, adrenocortical steroid hormones and digitalis were administered concurrently. On the 24th day after the onset, apical holosystolic murmur appeared. The patient died from congestive heart failure on the 26th day.

**Autopsy Findings**

The patient was 59 cm tall and weighed 5.2 kg. Anasarca, widely disseminated vesicles and bullas of the skin, and pharyngolaryngitis were observed, but there were no findings suggesting septicemia. The lesions were found primarily in the cardiovascular system. The heart weighed 39 g, and an extrusion of the pulmonary conus was marked. The epicardium had become thick. Aneurysm of the coronary artery was not observed macroscopically. The mitral valve had become cloudy and thick; in the area around the anterior commissura, a prolapse of the posterior leaflet into the left atrium was observed (Fig. 2A). Histopathologically, pancarditis, including pericarditis, myocarditis and endocarditis in large areas, was present. Severe lesions were found in all 4 valves, including the pulmonary valve. The fundamental lesions were proliferative inflammations consisting of infiltrations of the inflammatory cells into each layer of the valve. The valve structure was partially disrupted, and fibrinoid deposits were observed in part of the spongiosa (Fig. 2B–E). Myocarditis was noted in 2 types of the disease manifestation: 1) myocarditis which spread or continued from the endocardial lesions or from the subepicardial connective tissue lesions and 2) myocarditis which formed nodular lesions around the small vessels. In these lesions, there were observed polymorphonuclear neutrophils, eosinophils, small round cells, plasma cells, fibroblasts and capillaries, as well as a relatively large number of large mononuclear cells having pleomorphism. Anitschkow-like cells and giants cells were found sparsely but diffusely. Frequent double nuclei

*Japanese Circulation Journal Vol. 47, November 1983*
were observed in the myocytes.

In the coronary vessels, several lesions were observed in the proximal segment. Marked infiltrations of the inflammatory cells were observed in the periadventitia and the adventitia, and the media was partially impaired to a certain extent. The internal elastic layer had totally disappeared in part of the coronary artery. The intima showed severe proliferative changes. Infiltration of the inflammatory cells into the adventitia and proliferative changes in the intima were also found in the mural coronary arteries. Furthermore, proliferative phlebitis was noted in some of the veins. As for the conduction system, the atrio-ventricular node and the bundle of His were affected by severe myocarditis in the vicinity of the upper segment of the ventricular septum and by inflammations of the connective tissue. Inflammatory changes were also observed in the aorta (Fig. 3) and in the pulmonary, periadrenal and perirenal arteries.

As for other organs, proliferative laryngitis, involving giant cells and a marked involution of the thymus weighing 4.5g, was present. Severe depletion of lymphocytes from the medulla and cortex of a parapancreatic lymph node was observed (Fig. 3D). The spleen and the bone marrow manifested similar proliferative changes.

An examination using an immunofluorescence method did not show any significant immuno-
globulin deposits in any area.

DISCUSSION

This was a case of proliferative inflammation having the main lesions in the heart and the vascular system, and unlike ordinary myocarditis, it was characterized by severe valvular lesions. The cells which were involved in the inflammations included many large mononuclear cells, which were believed to be histiocytes or similar cells, and few plasma cells. The pathological findings did not suggest septicemia. The authors believe that what lay at the basis of this case was an infection which first involved the pharyngolarynx rather than the heart itself, and that the secondary immune response resulting from this pharyngolaryngitis became strongly manifest in the heart. The valves as well as the chordae tendineae manifested severe inflammatory changes and thickening. If the patient had survived the acute stage, thickening, shrinkage and fusion of the valves and chordae would probably have developed into valvular heart disease.

Early Western literature has reported that rheumatic fever can occur in extremely young patients. In the West nowadays, rheumatic fever has become increasingly rare with the development of preventive procedures. In developing countries, however, it still poses a social problems, and juvenile rheumatic heart diseases and juvenile mitral stenosis are current problems. Some researchers are questioning whether or not such juvenile mitral stenosis in developing countries is the same as or a variant of

the rheumatic heart diseases observed in the West.

The pathological findings of the present case were of a chronic inflammation type. Although accumulation of large mononuclear cells in a spindle shape, primarily centered around the arteries, was present, typical Aschoff’s node manifestation was lacking and a tendency towards exudative changes was strong. Considering the age of the patient and the fact that ASO was not measured, it is hard to believe that the condition was rheumatic fever. However, infantile rheumatic fever has a rapid course, often leading to death in a short period of time, and its pathological findings lack discrete foci of fibrinoid necrosis. Furthermore, large number of granulocytes and occasionally lymphocytes are present. In some cases, Aschoff’s node is lacking, and as a result, it is known that the diagnosis of rheumatic fever cannot be made from pathological findings alone.

In Japan, Kawasaki disease, which sometimes involves the coronary arteries, is common and is known to be sometimes accompanied by myocarditis. However, based on the following reasons the present case was not considered to have had Kawasaki disease (Naoe, personal communication): 1) even 26 days after onset, neutrophils were still present in the coronary arteries; 2) the media was partially separated; 3) aortitis and pulmonary arteritis were present concurrently; 4) although it was 26 days after the onset, severe myocarditis and valvulitis were present concurrently and 5) the condition did not have the clinical characteristics of Kawasaki disease.

The present patient had pancarditis accompanied by severe valvulitis and coronary arteritis with lesions in the vascular system throughout the body, and she is believed to be a case of rheumatic-type reaction in a broad sense of the word.

Acknowledgements

The authors wish to express their profound thanks to Professor Emeritus Atsushi Okabayashi (Chiba University School of Medicine) and Professor Shiro Naoe (Research Laboratory of Pathology, Toho University Ohashi Hospital) for their kind and helpful advice.

REFERENCES

1. SAPHIR O, COHEN NA: Myocarditis in infancy. *AMA Arch Pathol* 64: 446, 1957
2. WOODRUFF JF: Viral myocarditis: A review.
3. POCCOCK FE: Case of acute rheumatism, occurring in a newly-born infant, treated with salicylate of soda. *Lancet* ii: 804, 1882
5. POYTON FJ: A contribution to the subject of rheumatism based upon a study of 52 cases in children under five years of age and an analysis in childhood. *Q J Med* 1: 225, 1908
15. ROY SB, BHATIA ML, LAZARO EJ, RAMALINGASWAMI V: Juvenile mitral stenosis in India. *Lancet* iii: 1193, 1963
16. ABDIN ZH, EIASSA A: Rheumatic fever and rheumatic heart disease in children below the age of five years in the tropics. *Ann Rheum Dis* 24: 399, 1965
21. NA AYUTHYA PS, RATANABANANGKOON K, PONGPANCH B: Juvenile rheumatic fever and rheumatic heart disease at Ramathibodi Hospital, Thailand. *Southeast Asian J Trop Med Publ Hlth* 7: 77, 1976
22. PADMAVATI S: Rheumatic fever and rheumatic heart disease in developing countries. *Bull World Health Organization*


*Health Org* **56**: 543, 1978