MYOPERICARDITIS ASSOCIATED WITH ECHO VIRUS TYPE 3 INFECTION
— A Case Report —

TAKEHISA FUKUHARA, M.D., MASAHIKO KINOSHITA, M.D., KEIZO BITO M.D.
MATSUHIKO SAWAMURA, M.D., MASAKAZU MOTOMURA, M.D.
SEIICHI KAWAKITA, M.D., AND KATSUYUKI KAWANISHI, M.D.*

A case with myopericarditis caused by type 3 ECHO virus was reported. The diagnosis was based on a significantly increased hemagglutination-inhibiting antibody titer (from 4:6 to 4:516) against type 3 ECHO virus in the acute and the convalescent phase. A 29-year-old male was hospitalized for chest pain and fever. The patient had congestive heart failure, pericardial effusion and temporarily appearing abnormal Q waves on his electrocardiogram in the acute phase all of which gradually improved within about 3 weeks. Cardiac catheterization performed on the 21st day of hospitalization disclosed normal coronary arteries, but a partially hypokinetic region was found in the left ventricular free wall. A right ventricular endomyocardial biopsy study revealed histological features of a small number of mononuclear cell infiltrations, myocardial cell necrosis and early fibrosis associated with an increased number of fibroblasts and ultrastructural changes including myocytolysis, vacuolation in sarcoplasm and dissociation of some intercalated discs. The endomyocardial biopsy study, and the electrocardiographic and cineangiographic findings in this case suggest that viral infection may induce clinical signs of myocardial infarction in the heart with normal coronary arteries.

ALTHOUGH the etiology of myopericarditis cannot be ascertained in many cases, a wide variety of causes have been reported. Viruses are known to damage the myocardium, thus usually causing myocarditis1, endocarditis2, valvulitis3, 4 or pancarditis4. Myocarditis is caused by a great number of viruses, among which group B Coxsackie viruses are the most common5. The pathogenetic role played by RNA viruses, especially the picornavirus (including Coxsackie A and B, ECHO and Polio), in acute cardiac disease at all ages is now well established6. There is abundant evidence that ECHO virus causes cardiitis7—12. Among 34 known serotypes of ECHO virus, types 6, 9, 11 and 30 have been chiefly linked with pericarditis or myocarditis. The association of these diseases with types 1, 3, 5, 12, 14, 16, 17, 20, 21 and 25 of this virus has also been reported, but less frequently in the large volume of data which have been consolidated and analyzed by the WHO Virus Unit (WHO data 1967—1974).13

To our knowledge, only one case has been reported as myocarditis associated with type 3 ECHO virus in all the available literature written in English14. A patient with acute myopericarditis, who had significantly increased antibody

Key Words:
Myopericarditis
ECHO virus
Myocardial infarction
Abnormal Q wave
Myocardial biopsy

(Received August 2, 1982; accepted May 24, 1983)
The First Department of Internal Medicine, and *the Department of Radiology, Shiga University of Medical Science, Ohtsu, Japan
Mailing address: Takehisa Fukuhara, M.D., the First Department of Internal Medicine, Shiga University of Medical Science, Seta, Ohtsu 520-21, Japan

1274 Japanese Circulation Journal Vol. 47, November 1983
titer of type 3 ECHO virus and about whom detailed clinical and laboratory studies could be performed, will be described.

CASE PRESENTATION

On June 18, 1981 a 29-year-old male office worker was transferred to Shiga University of Medical Science from another hospital for evaluation of myocardial infarction, because his electrocardiogram had shown an elevation of the S-T segments in leads I, aVL and V_2-3. There was a sudden onset of vague anterior chest sensations and palpitations on June 14, 1981, and his temperature rose to 38.6°C on June 15, 1981. He was not preceded by fever, chills, headache, convulsions, dizziness, vomiting, diarrhea and eruption. He had no history of heart disease, tuberculosis, rheumatic fever, hypertension, hyperlipidemia, obesity or alcohol abuse except for the consumption of 20 cigarettes/day.

Physical Examination: His pulse was 88 regular beats per minute with a blood pressure of 122/60 mmHg. There were no skin lesions, edema, lymphadenopathy or nuchal rigidity. His lungs were clear to percussion and auscultation. On auscultation of the heart, the first heart sound was normal. The second heart sound was widely splitting and normal respiratory movement was present. The third and the fourth sounds galloped and a grade 1/6 mid-systolic murmur was heard at the apex. Overt pericardial friction rub was not heard. The liver was tender and measured 4 cm below the right costal margin.

Urinalysis revealed slight proteinuria. The patient had no anemia. C-reactive protein (CRP) was +2. Total white blood cell (WBC) count was 8,000/mm (23% band-form granulocytes, 33% segment-form granulocytes, 18% monocytes and 1% eosinophil). Several blood cultures were all negative. The serum glutamic oxalacetic transaminase (GOT) was 146 IU and creatine phosphokinase (CPK) was 679 IU. The lactic dehydrogenase (LDH) was 915 IU, with isoenzymes of 65.3% for LDH_1, 27.5% for LDH_2 and 1.5% for LDH_5.

Clinical Course

Japanese Circulation Journal Vol. 47, November 1983
Fig. 3. Serial echocardiograms.
(A): A normal left ventricular dimension but a decreased percent fractional shortening were observed on admission.
(B): Pericardial effusion, an enlarged left ventricular dimension and a decreased percent fractional shortening were found on 6th day of hospitalization.
(C): An enlarged left ventricular dimension and a decreased percent fractional shortening were still found about one month later, but pericardial effusion had disappeared.

His chest roentgenogram showed clear lung fields and normal cardiac size on admission (Fig. 1). On the 5th day of hospitalization, his chest roentgenogram showed mild pulmonary congestion, pleural effusion and mild cardiomegaly with a cardio-thoracic ratio (CTR) of 53%. On the 10th day of hospitalization, his chest roentgenogram disclosed a reduction in the size of the cardiac silhouette (CTR 46%) and in pleural effusion.

His electrocardiogram revealed a complete right bundle branch block, elevated S-T segment in I, aVL, V₁₋₅ and abnormal Q waves in aVL on admission (Fig. 2). Although the complete right bundle branch block disappeared, R waves vanished in V₃ on the 6th day of hospitalization but reappeared 2 weeks later (Fig. 2).

Echocardiograms were taken serially throughout his clinical course (Fig. 3). His echocardiogram revealed normal left ventricular dimension and the slightly decreased percent fractional shortening (ΔD, the difference between the end-

Japanese Circulation Journal Vol. 47, November 1983
systolic and end-diastolic diameters divided by the end-diastolic diameter, normal value 35.5 ± 3.9%) was 25% on admission. On the 6th day of hospitalization his echocardiogram revealed left ventricular enlargement with ΔD of 22.0% and the presence of approximately 200 ml of pericardial effusion. Four weeks later the pericardial effusion disappeared and ΔD improved, but left ventricular enlargement was still present.

The elevated CPK, GOT, LDH and WBC values, and fever gradually fell to normal levels and CRP became negative (Fig. 4).

Myocardial perfusion scintigraphy using thallium-201 was performed at rest both on the 7th day of hospitalization and 6 months later in his chronic course. The scintigraphy disclosed the presence of an area of reduced tracer concentration in the anterior wall of the left ventricle in the early stage and an improvement of the perfusion defect in that area in the chronic phase.

Cardiac catheterization was performed on July 13, 1981. The coronary arteries were normal angiographically (Fig. 5). Left ventriculogram and cardiac catheterization findings revealed hypokinesis of left ventricular anterior wall but normal left ventricular end-diastolic pressure (9 mmHg) and normal left ventricular contractility (peak positive dp/dt 2100 mmHg/sec, end-diastolic volume 162 ml, end-systolic volume 54 ml, ejection fraction 66.3%).

Right ventricular endomyocardial biopsy was performed using a Konno-Sakakibara biopom, and 2 specimens were obtained from right ventricular septum. One tissue specimen was processed for light microscopy and another one for electron microscopy (Fig. 6). Light microscopy revealed a small number of mononuclear cell infiltrations with some plasma cells, eosinophils and histiocytes and myocytolysis with focal myocyte necrosis. Early fibrosis with fibroblasts was found. Electron microscopic studies showed mitochondrialosis with various shapes of mitochondria, disruption and mild disarray of the myofibrils, vesiculation and vacuolation in the

**Fig. 5.** Left ventricular and coronary angiograms at 30-degree right anterior oblique view.

(a): The coronary arteries are normal angiographically.
(b): The localized hypokinetic region is seen on the left ventricular free wall (arrow).
sarcoplasm and a widening of the intercalated discs.

Virological studies of the serum disclosed a significant increase in hemagglutination-inhibiting antibody titers against type 3 ECHO virus (from 4:6 to 4:512) in the acute and the convalescent period. No enterovirus was isolated from the faecal and throat washing specimens during the first week of the illness.

DISCUSSION

Despite a variety of clinical features attributable to ECHO virus infection, the details of cardiovascular involvement have not been clearly documented in contrast with the group B Coxsackie virus infection. The ECHO virus may often be associated with myopericarditis during the course of an acute pleurodynia-like illness12 but an apparent myocardial involvement is clinically rare. Haynes11 has described clinical and laboratory data on an outbreak of type 3 ECHO virus infection, in which only one of the 29 children infected had myopericarditis.

Criteria for determining the infectious agent in viral myopericarditis have been described by Lerner and Wilson16: 1) viral isolation and identification during the first few days of the illness, 2) direct tissue examination for viruses or pathognomonic changes using light and electron microscopic techniques and 3) at least a fourfold rise in specific antibody (neutralizing and hemagglutination-inhibiting antibodies) in paired acute and convalescent serum specimens by serological examination. Our patient met condition 3) mentioned above. Namely, the hemagglutination-inhibiting antibody titer for type 3 ECHO virus increased significantly during his clinical course.

Electrocardiograms are helpful for evaluating cardiac involvement caused by viral infection, i.e., the presence of S-T segment elevation, flattening and inversion of T wave, ventricular or atrial arrhythmia, conduction disturbance, or persistent or temporary abnormal Q waves suggests this disorder.17–23 Smith24 has reported that 3 of 41 patients with myopericarditis due to Coxsackie B virus infection showed abnormal Q waves, which, however were observed only temporarily.

Fig. 6. Histological findings of the right ventricular specimens obtained using an endomyocardial biopsy on 21st day of hospitalization.

(a): Light micrograph shows a small degree of mononuclear cell infiltration, early fibrosis and interstitial edema (hematoxylin and eosin stain, x 200).
(b): Electron micrograph shows mitochondriosis, vacuolation and mild disarray of the myofibrils in the sarcoplasm (x 3800).
in 2 of them as in our case.

Myocardial cell viability was assessed by an intracoronary injection of thallium-201. Myocardial uptake of thallium-201 depends on both the blood flow delivering the thallium to the myocardium and the viability of the myocardial cells which extract and concentrate it. An improvement of the regional perfusion was observed in our case 6 months later, suggesting the recovery of the jeopardised myocardium. This was indicated by the disappearance of the Q waves on his electrocardiogram.

In our case, echocardiographic findings showed a persistent left ventricular dilatation even after the normalization of his electrocardiogram and of his myocardial perfusion scintigram. Focal hypokinesis of the left ventricular anterior wall was noticed on his left ventriculogram. El-Khatib et al. have found aneurysmal dilatation of the left ventricle in suckling mice with acute myocarditis due to group B Coxsackie viruses. Deguchi has studied the ultrastructural changes of the myocardium in mice with Coxsackie virus group B-3 myopericarditis. In the chronic phase some myocardial cells showed various degenerative changes, including myofibrillar disorientation and lysis as also observed in our case.

Although the presence of abnormal Q waves and abnormal left ventriculographic findings may indicate myocardial infarction, acute myocarditis due to type 3 ECHO virus was diagnosed on the basis of normal coronary angiograms and a significant increase of the antibody titer against type 3 ECHO virus in our patient. Miklozeck has reported that viral infection may play a poorly defined pathogenic role in the production of myocardial infarction in patients with normal coronary arteries. Sohal et al. have described electron microscopic findings on the cardiac capillaries of Coxsackie B-4 virus infected mice, in which the capillary lesions due to Coxsackie viruses probably played an important role in the production of the heart disease. The pathological changes of the endothelial cells described in their report, which consisted of overt swelling of cytoplasm or of contact of opposing endothelial cells across the lumen, were not found in our case.

Viral myopericarditis is of clinical importance from at least 2 different points of view. One is whether or not myocardial infarction may occur due to viral myocarditis without any risk factors manifestation of prior coronary heart disease. The other is whether or not viral myopericarditis develops into dilated cardiomyopathy in its chronic phase.

REFERENCES