Case Report

A Case of Kawasaki Disease Accompanied by Encephalitis and Several Kinds of Arrhythmia during the Acute Phase

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1.Introduction

Kawasaki disease (KD) is acute vasculitis of unknown etiology that was first described by Dr. Tomisaku Kawasaki in 1967 [1]. The most common sites of end-organ damage are the coronary arteries; however, an inflammatory response is induced in medium and small vessels throughout the body. Furthermore, complications of the central nervous system (CNS), including convulsions, disturbance of consciousness, aseptic meningitis, encephalopathy, and facial palsy, have been reported in patients with KD although CNS complications are uncommon in KD [2–4].

Arrhythmia severe enough to be clinically problematic during the acute phase of KD is rare [5] although pancarditis including the inflammation of the conduction systems in KD has been reported [6]. This case report describes the post-operative case of a newborn with Taussig–Bing anomaly with coarctation of the aorta who experienced encephalitis and various types of problematic arrhythmias during the acute phase of KD.

2. Case Report

One day after birth, the male newborn was transferred to Hiroshima Citizen’s Hospital in a state of shock and was diagnosed with Taussig–Bing anomaly with coarctation of the aorta. After maintenance therapy for shock recovery, the patient, aged 4 days, underwent aortic arch reconstruction and pulmonary arterial banding. After coronary angiography which revealed that his coronary
arteries were Shaher type 1, he underwent an arterial switch operation and ventricular septal defect closure at the age of 2 months. As his pulmonary branch stenosis progressed severely, the patient underwent percutaneous transluminal pulmonary angioplasty followed by surgical progression. The patient's heart rhythm was regular with a systolic murmur of Levine IV/V, which was consistent with previous findings. Both his cerebral lymph nodes were swollen and painful. The patient was expressionless with a consciousness level of E4V3M5, as determined by the Glasgow Coma Scale.

Laboratory blood tests performed at admission demonstrated the following: white blood cell count, 3,300/μL; hemoglobin, 13.5 g/dl; hematocrit, 0.38; platelets, 81 × 10^3/mm^3; C-reactive protein, 6.6 mg/dl; sodium, 133 mEq/L; aspartate aminotransferase, 186 IU/L; alanine aminotransferase, 137 IU/L; and serum albumin, 3.7 g/dl. Examination of the patient's cerebrospinal fluid (CSF) demonstrated a glucose level of 57 mg/dl, protein level of 28 mg/dl, and a white blood cell count of 3/μL.

A standard 12-lead electrocardiogram (ECG) was performed at admission, which demonstrated a regular sinus rhythm and complete right bundle branch block, which was consistent with the findings of a previous ECG (Figure 1(a)). A chest roentgenogram demonstrated mild cardiomegaly (cardio thoracic ratio, 0.60), which was also consistent with previous results, without pleural effusion. An echocardiogram demonstrated the following: left ventricle end diastolic dimension, 33.6 mm (105% of normal range); left ventricle end systolic dimension, 18.8 mm; left ventricle ejection fraction (LVEF) and fractioning shortening (SF), 83% and 44%, respectively; mild mitral regurgitation; mild tricuspid regurgitation; mild pulmonary regurgitation; and pulmonary stenosis, 3.6 m/s, without coronary arterial lesions and pericardial effusion. No significant differences were detected between these results and previous echocardiogram findings.

Electroencephalogram (EEG) indicated diffuse disorganized high-voltage slow waves. Magnetic resonance imaging (MRI) at admission detected mild cerebral edema. The patient was diagnosed with KD-associated encephalitis and subsequently received methylprednisolone pulse therapy (30 mg/kg for 3 days), high-dose intravenous immunoglobulin (IVIG, 2 g/kg), and flurbiprofen (5 mg/kg/day). Consequently, his fever resolved, his consciousness level improved, and the other KD symptoms were also resolved. However, the fever recurred on day 10 of the illness, and the patient’s level of consciousness deteriorated; therefore, additional 2 g/kg of IVIG and edaravone (1 mg/kg/day) were administered (Figure 2).

Abnormal ECG findings were subsequently detected (Figure 1(b)). Sinus arrest and junctional escape rhythm were detected on day 10 of the illness, followed by a short burst of atrial tachycardia. The patient was not administered any specific treatment for arrhythmia, as the sinus arrest had no significant influence on hemodynamics.

Mild pleural effusion was detected on the left side on day 12 of the illness; however, no novel abnormal findings were detected on echocardiography, including pericardial effusion. He regained his consciousness completely, and EEG showed normal findings on day 17. An oral steroid, edaravone, was administered for 7 days, after which the dosage was gradually reduced and discontinued.

Although the LVEF declined to 72% on day 9 transiently, it improved over 80% on day 15 of the illness and there was no sign of coronary arterial lesion.

An atrial flutter was detected on day 20 of the illness (Figure 1(c)). The atrial rate was 310 bpm, with a resultant 2:1 to 4:1 atrioventricular conduction block. Cardioversion was performed, as the atrial flutter continued for >18 hours. The patient was subsequently administered flecainide to prevent atrial flutter; however, this treatment was discontinued due to a significant sinus arrest of 5.7 seconds (Figure 1(d)). Sinus arrest gradually attenuated and was alleviated 3 days later.

Coronary angiography performed on day 25 of the illness demonstrated no dilatation or stenosis of the coronary arteries, and the sinus node artery was seen in normal origin from the right coronary artery (Figure 3). A myocardial biopsy was simultaneously performed. Myocardial cells exhibited variation in size and irregular adhesion, and fibrosis was detected between the muscular fibers (Figure 4). These findings may be attributed to the pressure overload on the right ventricle due to pulmonary arterial stenosis. Pathological findings of myocardium detected no evidence of myocarditis because the timing of biopsy was late to observe the findings of the acute phase of myocarditis.

Cerebrospinal fluid and serum cytokine data at admission are presented in Table 1. CSF and serum levels of interleukin (IL)-2 and IL-10 were elevated, while the CSF and serum levels of IL-6 and interferon-γ were significantly increased. The CSF level of IL-6 was two times higher than the serum level of IL-6. The patient was discharged without significant sequelae of cardiac and central nervous system complications.

3. Discussion

In the acute stage, about 10% of patients of KD show neurological disorders such as irritability and lethargy, which are caused by encephalitis [1]. Inflammation of the microvessels of the entire body can be observed by pathological inspection and by magnetic resonance imaging.
during this period, and this inflammation of the micro-
vesseles causeencephalitis [7]. Histopathological find-
ings of the central nervous system (CNS) of KD patients with en-
cephalitis revealed aseptic chorio and/or leptomenigitis [8].
The inflammatory cells in the CNS were mainly lymphocytes
and mononuclear cells, and such were corresponding to the
findings in the CSFs [8] although our case did not have
pleocytosis of the CSF. On the other hand, several reports
revealed that IL-6 and tumor necrosis factor-α levels are
extremely high in both the CSF and serum or in the CSF of
KD [9, 10]. And, Aiba et al. reported that in addition to
peripheral T cells, IL-6 is produced by oligodendrocytes,
astrocytes, and other glial cells in the brain, and this IL-6
induces encephalitis [11]. We infer that IL-6 was associated
with the encephalitis observed in the present patient, as the
CSF and serum levels of IL-6 were extremely high.

It has previously been reported that although sinus
node disturbances induced by KD are not easily identified
by body surface electrocardiogram, they are prolonged to
a high rate if they are assessed by an electrophysiological
study [12]. Previous studies have suggested that vasculitis
of the sinus node artery causes disturbance in blood
perfusion to the sinus node, resulting in a disturbance in
sinus node function [12]. Other studies have indicated
that the inflammatory cells infiltrate the sinus node and
neighboring ganglion; therefore, inflammation spreads to
the sinus node [6].

Concerning the present patient, it is important to
consider the influence of the previous operation for the
congenital heart disease. Arrhythmias have been detected in
60/624 (9.6%) patients who underwent the arterial switch
operation for transposition of the great arteries, and sick
sinus syndrome (SSS) was detected in 6/624 (0.96%) pa-
tients. Furthermore, approximately half of all these cases
developed SSS >5 years after the arterial switch procedure
[13]. We hypothesize that subclinical sinus node dysfunction
was induced by the arterial switch operation for the
Taussig–Bing anomaly, and the disturbance of the blood
perfusion of the sinus node and the inflammation of the
sinus node occurred during the acute phase of KD, which in
combination induced SSS.

Following transposition of the great arteries in patients
who underwent arterial switch operation, all episodes of
syncope were caused by complete atrioventricular block or
SSS [13]. Pacemaker implantation (PMI) must be considered
if SSS or complete atrioventricular block was not transient.
Even though the present case met the criteria of PMI during
the acute stage of KD, sinus node function returned to normal
and special treatment was not required for arrhythmia after
recovery from KD. However, the possibility of progression to

Figure 1: Electrocardiograms (a). Sinus arrest was detected (b-1), junctional rhythms (↓) were pointed with retrograde P waves (▲), and short bursts of atrial tachycardia were detected (★). Atrial flutter occurred with a resultant 2:1 to 4:1 atrioventricular conduction block (c). Sinus arrest occurred (maximum, 5.7 s) (d).
SSS as the sequela of inflammation and the influence of arterial switch operation in the future cannot be denied.

In conclusion, the present study described a case of KD accompanied by encephalitis and various types of arrhythmias during the acute phase. Both KD-induced vasculitis and arterial switch operation may have influenced the sinus node dysfunction. Although normal sinus node function was recovered, the possibility of progression to SSS should be considered. Therefore, it is essential the patient be continuously observed.
Disclosure

The gist of this case report was presented at the 11th International Kawasaki Disease Symposium, Honolulu, USA, February 03–06, 2015.

Conflicts of Interest

All authors have no conflicts of interest to disclose.

Acknowledgments

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References


**Table 1: Cerebrospinal fluid and serum cytokine data.**

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<th>IL-2 (pg/ml)</th>
<th>IL-4 (pg/ml)</th>
<th>IL-6 (pg/ml)</th>
<th>IL-10 (pg/ml)</th>
<th>IFN-γ (pg/ml)</th>
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<td>CSF</td>
<td>5.81 (&lt;2.6)</td>
<td>4.00 (&lt;6.6)</td>
<td>234.27 (&lt;6.2)</td>
<td>3.55 (&lt;2.8)</td>
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<td>Serum</td>
<td>3.78 (&lt;3.9)</td>
<td>4.26 (&lt;3.8)</td>
<td>126.63 (&lt;9.5)</td>
<td>7.76 (&lt;6.8)</td>
<td>658.25 (&lt;21.1)</td>
<td>3.03 (&lt;3.9)</td>
</tr>
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**Figure 4:** Histopathology of myocardium (on day 25 of the illness). There was no finding of the infiltration of the inflammatory cells. The myocardial cell had variation in the size and irregular adhesion, and fibrosis was seen between the muscular fiber. These were not findings of the acute phase but chronic stage, which were delivered by the pressure overload of the right ventricle due to the pulmonary arterial stenosis. Hematoxylin eosin, ×160.