

Ventricular arrhythmia as an initial sign in acute Kawasaki disease

A case report

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Abstract

Rationale: Coronary artery lesion is the most prominent cardiac manifestation in Kawasaki disease. However, few cases of life-threatening cardiac arrhythmia were reported in the acute phase of Kawasaki disease.

Patient concerns: A 1-year-old girl presented in the hospital with ventricular premature beats and ventricular tachycardia after 2 days of fever.

Diagnosis: On the fifth day of fever, the diagnosis of Kawasaki disease was achieved.

Interventions: Immunoglobulin was administered.

Outcome: The temperature became normal and ventricular arrhythmia disappeared.

Lessons: This case suggests that Kawasaki disease has various clinical manifestations besides typical features, and it can cause life-threatening cardiac arrhythmia in the acute phase with normal coronary artery and normal cardiac function.

Abbreviations: CAL = coronary artery lesion, CRP = C-reactive protein, EKG = electrocardiogram, KD = Kawasaki disease, VPB = ventricular premature beat, VT = ventricular tachycardia, WBC = white blood cell.

Keywords: Kawasaki disease, ventricular premature beat, ventricular tachycardia

1. Introduction

Kawasaki disease (KD) is a type of febrile systemic vasculitis. Coronary artery lesion (CAL) is the most prominent cardiac manifestation.^[1,2] In addition, other relatively infrequent heart complications, such as myocarditis,^[3] pericardial effusion,^[4] and cardiac arrhythmias, have been noted. Life-threatening cardiac arrhythmias, such as ventricular tachycardia (especially torsades de pointes), ventricular fibrillation, and atrioventricular heart-

block, were reported in long-term follow-up patients, especially those who had reduced left ventricular function^[5–7] and CALs, including large coronary aneurysm, coronary artery stenosis, and thrombosis. However, few cases of life-threatening cardiac arrhythmia were reported in the acute phase of KD.

Here, we report a case of a 1-year-old girl with KD who presented with ventricular premature beats (VPB) and sustained ventricular tachycardia (VT) with good early prognosis.

The ethics committee of Sichuan University approved this study.

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Informed consent was obtained from the parents of the patient (a kid) included in the study. The patient's parents gave their permission to be included in the manuscript.

The authors report no conflicts of interest.

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2. Case presentation

A 1-year-old girl presented in the pediatric outpatient department of a local hospital with 2 days of fever $>39^{\circ}\text{C}$. She was diagnosed with tonsillitis and was treated with acetaminophen and 125 mg bid cefaclor for 1 day. Auscultation revealed arrhythmia, and subsequent electrocardiogram (EKG) revealed VPB trilogy. The girl was subsequently transported to our hospital. There was no history and family history of arrhythmia.

2.1. Physical examination

She presented normal consciousness. Body temperature was 39°C with a respiration rate of 38/min, heart rate of 158 beats/min, and blood pressure 91/55 mm Hg. Rash, bulbar conjunctival injection, cervical lymphadenectasis, swelling of extremities, changes in lips and oral cavity, perianal desquamation, and abnormalities at the Bacille Calmette–Guérin inoculation site were not observed. Physical examination of the lung and abdomen was normal.

She exhibited an increased white blood cell (WBC) count of $13.5 \times 10^9/\text{L}$ with a neutrophilic cell count of $8.09 \times 10^9/\text{L}$,

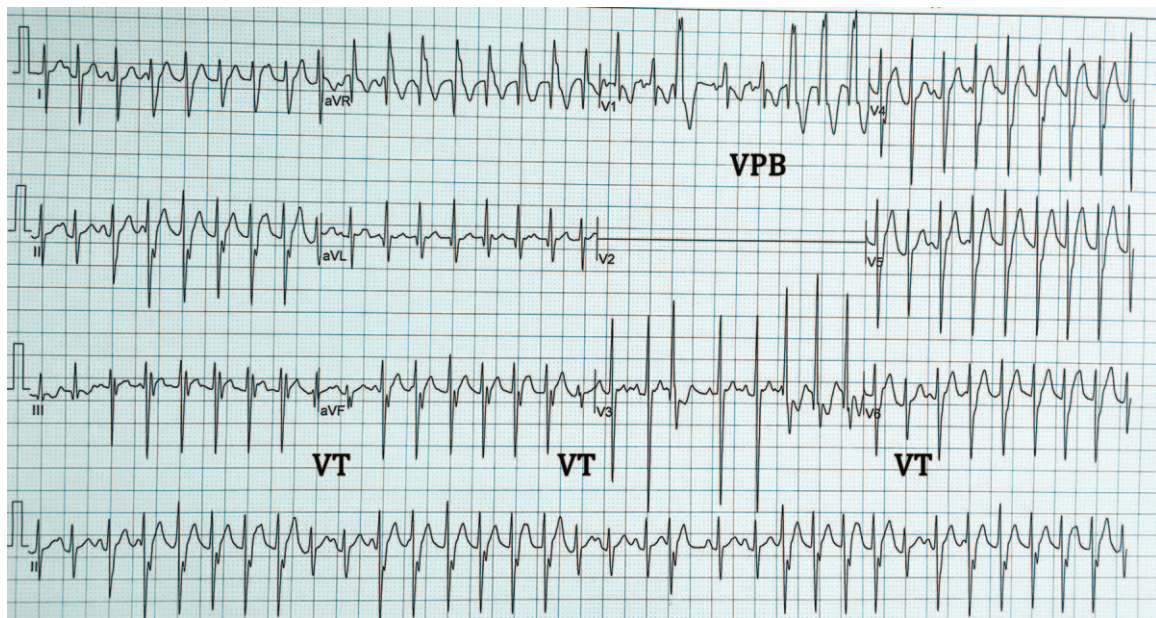


Figure 1. VPB and VT in EKG, lead V2 was omitted due to no enough space on the chest wall for electrode slice.

hemoglobin of 119 g/L, and platelet count of $375 \times 10^9/L$. Increased inflammatory markers, including 21 mg/L C-reactive protein (CRP) and 52 mm/h erythrocyte sedimentation rate (ESR), were noted. Cardiac troponin I and myoglobin were normal. Her liver function, thyroid function, and electrolytes, including phosphate, calcium, magnesium, potassium, and sodium, were normal. She was negative for immunoglobulin M of coxsackievirus and adenovirus. Feces and urine tests were normal.

After admission, VPB and short-onset VT were observed in the EKG (Fig. 1). Echocardiogram suggested normal heart structure with normal ejection fraction and fractional shortening. Chest X-ray revealed increased lung markings. Holter was arranged for further examination.

The first impression of the patient's condition was cardiac arrhythmia accompanied with infection. The remote cause of arrhythmia was fever and infection, especially septicemia infection according to the increased WBC and CRP. Blood culture was performed. Before the results were available, cefoperazone-sulbactam was administered. We did not administer anti-arrhythmia drugs immediately because the blood pressure was normal after admission and the child did not exhibit other signs of hemodynamic change. In addition, EKG monitor revealed frequent sinus capture. However, 2 days after drug administration (on the 4th day of fever), the girl still had fever with VPB and VT. EKG monitoring revealed persistent VT, which could persist for greater than 1 hour. A maculopapular rash appeared on the left shoulder and left chest wall and was attributed to allergic reaction of the electrode slice of the EKG monitor. Considering the hemodynamic risk of VT, which repeatedly occurred for a relatively long period of time, we administered 50 mg mexiletine q8 h (her body weight was 10 kg).

On the 3rd day after admission (5th day of fever), her temperature reached 40.5°C with increased rash on the face, chest, and limbs. Erythema of the lips and "strawberry tongue" were observed. The bulbar conjunctiva was injected in both eyes. The extremities of fingers and toes were red and swollen. VPB and VT were still prominent in the EKG. In total, 115,833 beats/24 h of VPB and 5459 instances of VT (consisting of at least 3 VPBs)

were recorded by Holter. The longest VT included 8830 VPBs. (Fig. 2). Blood test revealed an elevated WBC count of $19.9 \times 10^9/L$ with neutrophilic cells count of $14.01 \times 10^9/L$, platelet of $365 \times 10^9/L$, and slightly decreased hemoglobin of 102 g/L. In addition, CRP levels were increased to 39 mg/L. On the basis of these findings, the diagnosis of KD was considered, and 2 g/kg immunoglobulin was administered immediately followed by aspirin (50 mg/kg/day). Cefoperazone-sulbactam was cancelled as soon as KD was diagnosed.

On the 4th day of hospitalization, her temperature returned to normal, and VPB was dramatically reduced with no obvious VT. Mexiletine was canceled. On the next day, blood test indicated that WBC levels reduced to $5.1 \times 10^9/L$, platelets increased to $459 \times 10^9/L$, and hemoglobin decreased to 94 g/L. In addition, CRP levels were decreased to 16 mg/L. Furthermore, blood culture results were negative, which additionally excluded septicemia.

On the 5th day of hospitalization, no ventricular arrhythmia was noted in the EKG and repeated Holter. The patient was discharged and sent to local hospital following the conventional dual referral.

The aspirin dosage was reduced to 5 mg/kg/day 1 week after discharge with normal WBC and CRP levels. The patient accepted routine echocardiography (once a week during the first month and once every 2 weeks during the second month) in a local hospital. During the 2 months of follow-up, the echocardiogram did not suggest CALs. Holter was arranged 2 weeks and 2 months after discharge, separately. No cardiac arrhythmia was observed in the 2 Holter examinations (Fig. 3). The administration of aspirin was canceled 2 months after discharge due to normal echocardiogram and normal EKG and the lack of inflammatory signs. One-half-year follow-up was completed this month with normal Holter and echocardiogram findings.

3. Discussion

KD is a type of vasculitis, which often occurs in infants and young children.^[8] The etiology of this disease has not been clearly established.



Figure 2. VPB and VT in Holter before administration of immunoglobulin. Totally, 115,833 beats/24 h of VPB and 5459 times of VT (consisted by at least 3 VPBs) were recorded. (A) Sinus rhythm in Holter; (B) ventricular trigeminy was recorded; (C) 5459 times of VT were recorded with the longest VT consisted by 8830 VPBs.

Classic KD is diagnosed on the basis of the presence of fever ≥ 5 days and the presence of ≥ 4 of the 5 principle clinical features, including rash, bilateral bulbar nonexudative conjunctival injection, oral changes, extremity changes, and cervical lymphadenopathy.^[9] However, the clinical features are not often present at the beginning of this disease, and other clinical findings

are reported except the principle features.^[10] The incomplete or atypical clinical course of KD often causes delayed diagnosis and increases the risk of CALs.^[11]

The most important cardiovascular problem of KD is CALs. However, cardiac arrhythmia has been recognized a life-threatening manifestation.^[3,4] As a life-threatening cardiac



Figure 3. No VPB or VT was found in Holter after discharge. The heart rhythm was normal sinus rhythm.

arrhythmia, VT may occasionally present in long-term follow-up patients with compromised left ventricular function and CALs, including large coronary aneurysm, coronary artery stenosis, and thrombosis.^[12,13] However, in the acute phase, VT is a rare

clinical manifestation. Haney et al^[14] reported a case of VT in the subacute stage of KD with a normal echocardiogram in 1995. Of note, in that case, VT occurred 3 weeks after the administration of immunoglobulin.

Table 1

Summary of the clinical course of the disease.

	Fever	Lymph nodes	Oral cavity	Extremities fingers and toes	Rash	Conjunctiva	EKG	Treatment
Day 1	+	No enlargement	—	—	—	—	NA	Acetaminophen and cefaclor
Day 2	+	No enlargement	—	—	—	—	NA	Acetaminophen and cefaclor
Day 3	+	No enlargement	—	—	—	—	VT and VPB	Cefoperazone-sulbactam
Day 4	+	No enlargement	—	—	Maculopapular rash appeared on the left shoulder and left chest wall	—	VT and VPB	Cefoperazone-sulbactam and mexiletine
Day 5	+	No enlargement	Erythema of the lips and "strawberry tongue"	Red and swollen	Increased rash on the face, chest, and limbs	Bulbar conjunctival injection	VT and VPB	Immunoglobulin, aspirin, and mexiletine
Day 6	—	No enlargement	Relieved	Relieved	—	Relieved	Reduced VT and VPB	Aspirin and mexiletine
Day 7	—	No enlargement	—	—	—	—	Sinus rhythm	Discharged with aspirin

NA=not available, VPB=ventricular premature beat, VT=ventricular tachycardia.

VT as a prominent, initial presenting in the acute phase of KD is misleading. In our case, differential diagnosis was challenging given that VPB and VT appeared on the 2nd day of fever with no other principle features of KD. Fortunately, the correct diagnosis was made on the 5th day of fever with repeated assessment, monitoring, and accurate judgment (Table 1). Finally, the appropriate treatment management was performed. In addition, VPB and VT disappeared soon after immunoglobulin treatment, further suggesting that cardiac arrhythmia was caused by immune injury. In addition, this case reminds us that cardiac arrhythmia represents another heart risk in addition to CALs in patients with KD.

Given that the etiology of KD is unknown, the mechanism of cardiac arrhythmia in the acute phase of KD could not be well explained. Admittedly, VPB and VT could be caused by myocarditis,^[15] and KD is reported as a cause of myocarditis.^[3] However, in this case, it is difficult to diagnose myocarditis with normal heart chamber, normal ejection fraction, normal cardiac troponin I levels, and normal myoglobin levels. On the contrary, as an inflammatory disease, KD can lead to the release of a series of inflammatory factors that might possibly cause immune injury of the conduction system, contributing to cardiac arrhythmia,^[16] which is a probable cause of VT in our case. Finally, more relative basic research and clinical data accumulation will contribute to elucidation of the mechanism of cardiac arrhythmia complicated with KD and the increasingly noted accompanying symptom spectrums.

4. Conclusion

To our knowledge, this is the first case of KD initially presenting as VT in an early stage. KD can cause life-threatening cardiac arrhythmia in the acute phase with normal coronary artery and normal cardiac function and should be recognized for anti-diastole, especially presenting as initial symptoms.

Author contributions

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Funding acquisition: Yimin Hua.

Investigation: Fan Hu.

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References

- [1] Genizi J, Miron D, Spiegel R, et al. Kawasaki disease in very young infants: high prevalence of atypical presentation and coronary arteritis. *Clin Pediatr (Phila)* 2003;42:263–7.
- [2] McCrindle BW, Li JS, Minich LL, et al. Coronary artery involvement in children with Kawasaki disease: risk factors from analysis of serial normalized measurements. *Circulation* 2007;116:174–9.
- [3] Sato T, Somura J, Maruo Y. Steroid pulse therapy for Kawasaki disease complicated with myocarditis. *Indian Pediatr* 2016;53:1015–6.
- [4] Okada S, Hasegawa S, Suzuki Y. Acute pericardial effusion representing the TNF- α -mediated severe inflammation but not the coronary artery outcome of Kawasaki disease. *Scand J Rheumatol* 2015;44:247–52.
- [5] Tsuda E, Hirata T, Matsuo O, et al. The 30-year outcome for patients after myocardial infarction due to coronary artery lesions caused by Kawasaki disease. *Pediatr Cardiol* 2011;32:176–82.
- [6] Hirofumi W, Masataka K, Mamoru A. Potentially fatal arrhythmias in two cases of adult Kawasaki disease. *Cardiol Young* 2016;26:602–4.
- [7] Halliday B, Murgatroyd F, Whitaker D. Sudden cardiac arrest in adolescence: the case of ventricular fibrillation 11 years after presenting with Kawasaki's disease. *Heart* 2012;98:1756.
- [8] McCrindle BW, Rowley AH, Newburger JW, et al. Diagnosis, treatment, and long-term management of Kawasaki disease. *Circulation* 2017;135:e927–99.
- [9] McCrindle BW, Rowley AH, Newburger JW, et al. Diagnosis, treatment and long-term management of Kawasaki disease: a scientific statement for health professionals from the American Heart Association. *Circulation* 2017;135:e927–99.
- [10] Adib A, Fazel A, Nabavizadeh SH, et al. Atypical desquamation in a 2.5-year-old boy with Kawasaki disease: a case report. *Electron Physician* 2017;9:3764–7.
- [11] Satoh K, Wakejima Y, Gau M, et al. Risk of coronary artery lesions in young infants with Kawasaki disease: need for a new diagnostic method. *Int J Rheum* 2018;21:746–54.
- [12] Tsuda E, Arakaki Y, Shimizu T, et al. Changes in causes of sudden deaths by decade in patients with coronary arterial lesions due to Kawasaki disease. *Cardiol Young* 2005;15:481–8.
- [13] Sumitomo N, Karasawa K, Taniguchi K, et al. Association of sinus node dysfunction, atrioventricular node conduction abnormality and ventricular arrhythmia in patients with Kawasaki disease and coronary involvement. *Circ J* 2008;72:274–80.
- [14] Haney I, Beghetti M, McCrindle BW, et al. Ventricular arrhythmia complicating Kawasaki disease. *Can J Cardiol* 1995;11:931–3.
- [15] Mattsson G, Magnusson P. Electrical storm in the inflamed heart: ventricular tachycardia due to myocarditis. *Clin Case Rep* 2017;5:1327–32.
- [16] Wang M, Li S, Zhou X, et al. Increased inflammation promotes ventricular arrhythmia through aggravating left stellate ganglion remodeling in a canine ischemia model. *Int J Cardiol* 2017;248:286–93.