Case Report
A misdiagnosed atypical Kawasaki disease: a case report

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Abstract: The diagnosis of atypical Kawasaki disease is a clinical challenge. Misdiagnoses or missed diagnoses for patients with atypical Kawasaki disease can potentially result in severe clinical outcomes. We report a rare case of atypical Kawasaki disease presenting symptoms similar to those of appendicitis and fulminant viral myocarditis but without any classic clinical features during the whole illness. A 4.5-year-old boy presented with acute abdominal pain and fever for 10 days. Exploratory laparotomy and appendectomy were performed after failed treatment with intravenous antibiotics, yet the persistent abdominal pain was not relieved, and cardiac arrest occurred after surgery. The echocardiography examination revealed a giant coronary artery aneurysm and reduced cardiac output in the third week after onset. Then the patient was diagnosed with atypical Kawasaki disease. Even after treatment with intravenous immunoglobulin, anticoagulation drugs and diuretics, the patient’s heart dysfunction still progressed, and he had to undergo a coronary artery bypass graft. At the 2-year postoperative follow-up evaluation, the patient’s heart function remained at New York Heart Association (NYHA) class I and normal growth was sustained. Improving the understanding of Kawasaki disease as a vasculitis syndrome may be helpful in reducing the misdiagnosis.

Keywords: Kawasaki disease, coronary artery aneurysm, myocardial infarction, coronary artery bypass graft

Introduction
Kawasaki disease (KD) is an acute systemic vasculitis disease of unknown etiology commonly in infants and young children [1]. The incidence rate varied in different regions in China, which was from 7.1 per 100,000 children in Sichuan Province to 74 per 100,000 children in Hong Kong [2]. Although the etiology of KD remains unclear, factors of infection, immune response and genetic predisposition are considered to associate with pathogenesis of KD [3]. Unlike complete KD, atypical KD might present many clinical signs like perineal desquamation, sterile pyuria, peripheral arthritis and hydrops of gall bladder which would confuse the clinicians. Although several common and novel laboratory methods were evaluated for diagnosis of atypical KD, none of them own enough specificity [4, 5]. The diagnosis of atypical KD is still a challenge [6], and missed diagnoses for patients with atypical KD often occurred in clinical practice. Severe complications and even death can occur if KD patients do not receive reasonable and timely treatment. In this paper, we report a case of atypical Kawasaki disease misdiagnosed as appendicitis and fulminant viral myocarditis.

Case report
The 4.5-year old boy was admitted to a community clinic after experiencing fever and abdominal pain with a peak temperature of approximately 39°C for 10 days. No signs of rash, chapped lips, glossitis, limb swelling, or desquamation occurred. The routine blood test and C-reactive protein (CRP) test showed a white blood cell count (WBC) of 21.1×10⁹/L, neutrophil percentage (NEUT) of 86%, hemoglobin (HGB) of 97 g/L platelet count (PLT) of
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After routine antibiotic treatment for 6 days, his temperature returned to normal, but the abdominal pain was still not relieved. Then the boy was transferred to a municipal hospital and acute appendicitis was suspected. An exploratory laparotomy was performed, and appendix showed the status of mild hyperemia. He subsequently underwent an appendectomy. The preoperative electrocardiogram (ECG) revealed no abnormalities. Three days after surgery, he presented with sudden cardiac arrest and underwent cardiopulmonary resuscitation, ventilator-assisted ventilation, and anti-infective treatment using meropenem combined with metronidazole for 7 days. After recovering consciousness, the patient still complained of abdominal pain; his family requested to be discharged and took him to the Department of Pediatric Surgery, West China Medical Center, Sichuan University for further diagnosis and treatment.

After the boy was admitted to the West China Medical Center, his temperature was 36.7°C, blood pressure was 120/80 mmHg, heart rate was 72 beats/min and respirations was 20 breaths/min. The edge of the heart extended towards the lower left. The heart rhythm was normal. Dull S1 and II/6 systolic murmurs in the mitral valve area were detected.

A full biochemical blood screening test was performed. Routine blood testing showed a WBC of 11.0×10⁹/L, NEUT of 36% HGB of 97 g/L and PLT of 485×10⁹/L. The inflammation parameters showed a CRP of 8 mg/L, ESR of 25 mm/h and procalcitonin of 0.07 ng/ml. The myocardial parameters showed an NT-BNP of 577 pg/ml, cTnl of 0.061 g/L, cTnT of 109.1 ng/L and Mb of 8.2 g/L; DIC screening showed a DDI of 3.27 mg/L, FDP of 12.6 g/L, Fg of 126 mg/dl, PT of 13.1 s and APTT of 32.1 s.

The ECG showed sinus tachycardia with sinus arrhythmia, abnormal Q-waves (V2 and V3 in QS type, V4 and V5 in QRS type), T wave inversion (V2 and V3) and T wave flat (V4 and V5) (Figure 1). Transthoracic echocardiography (TTE) revealed no abnormality. Chest X-ray showed an enlarged heart shadow mainly in the left ventricle. Multiple abdominal ultrasonography evaluations showed no abnormality.

Eight days after admission, the boy complained of pain in the left upper abdomen. The ECG examination showed no abnormality. The pediatric general surgeon then consulted us for a diagnosis. After reviewing the patient’s history, we suspected that the boy suffered from cardiac complications of atypical KD, and ordered another cardiac echocardiography examination, which showed a giant coronary aneurysm (16 mm) complicated with a massive thrombus in the left anterior descending branch (LAD). The other manifestations visualized by TTE included an initial dilation in the right coronary artery with a maximal diameter of 6.7 mm (Figure 2). Then atypical KD complicated by thrombosis, myocardial infarction and ischemic cardiomyopathy was diagnosed.

Low-molecular-weight heparin and warfarin were initially given, and then a combination of clopidogrel and warfarin was prescribed after the patient became stable. Captopril and β blockers were used to mitigate cardiac dysfunction and myocardial remodeling. The routine blood examination upon discharge was normal: WBC 6.6×10⁹/L, N 28.5%, Hb, 107 g/L, PLT 385×10⁹/L, CRP 6 mg/L and INR 2.08. The echocardiography findings were as follows: left coronary artery (LCA) and right coronary artery (RCA) dilatation complicated with

![Figure 1. ECG represented ischemic changes in the left anterior descending branch. The red arrows indicate the pathological Q waves in V2-V5.](image-url)
Figure 2. Transthoracic echocardiogram examination six months after discharge. A. A giant aneurysm in the left anterior descending branch (LAD) with a maximum diameter of 17.2 mm. The red arrows show a mural thrombosis of 11.8×12.5 mm; B. Dilated right coronary artery at the beginning with a maximum width of 6.73 mm; C. Enlarged left ventricle (LV) with abnormal segmental movement. AO, Aorta; RV, Right Ventricle; LA, Left Atrium; RA, Right Atrium.
LCA thrombosis, incoordinate left ventricular wall motion, and a slightly decreased left ventricular ejection fraction of 55%. After discharge, the patient received long-term oral warfarin, clopidogrel, and captopril treatment. It was suggested that the patient would have to undergo follow-up evaluations monthly. However, he has not been regularly examined by physicians.

Six months after discharge, the child developed a severe cough, accompanied by limited physical activity, difficulty breathing and palpitations. The heart function grade based on the NYHA criteria was class II-III. TTE showed coronary dilatation with a thrombosis in the LAD of 21 mm and the left ventricular systolic function EF was 38%. Coronary angiography showed the following: the CAA had a diameter of 21.5×19.7 mm and was located at the end of the left main trunk causing visible filling defects, suggesting the formation of a thrombosis; the opening of the RCA was normal; a coronary aneurysm was noted right after the opening of the RCA (12.3 mm in length and 6 mm in width); and the distal branch formed multiple collateral branches (Figure 3).

Based on the condition of left heart dysfunction, coronary artery bypass graft (CABG) was performed. The hemodynamic analysis performed immediately after surgery showed that the cardiac output improved compared with the preoperative cardiac output. No surgical complications occurred after surgery.

At the 2-year postoperative follow-up evaluation, the patient had normal growth without limited exercise. The coronary CT examination showed an open left anterior descending branch and left circumflex artery (Figure 4).

Discussion

When we reviewed the patient’s history at the first time, we considered that there would be three most likely diagnoses: myocarditis, sepsis and KD. Based on the guidelines for diagnosing myocarditis established by Subspecialty Group of Cardiology, the Society of Pediatrics Chinese Medical Association, the main criteria for myocarditis are as follows: (1) Cardiac dysfunction, cardiogenic shock or Adams-Stoke syndrome; (2) Cardiomegaly; (3) Increased serum cardiac troponin T or I (cTnI or cTnT) or serum creatine-kinase isoenzyme (MB, CK-MB); (4) Significant ECG changes (ECG or 24 h Holter); (5) Cardiac magnetic resonance imaging presents typical myocardial inflammation. If the patient’s manifestations meet three of them, the diagnosis of myocarditis can be clinically decided [7]. The boy’s clinical findings including cardiac arrest, enlarged heart shadow, increased troponin T and troponin I, and abnormal Q wave in ECG match 4 of those criteria seemingly. But considering that myocarditis is mainly caused by virus, the significant increases of white blood cell and CRP at the beginning are most unlikely expected in myocarditis. Arrhythmias are commonly seen in patients with myocarditis, but we have not seen any arrhythmia throughout the course of the boy, except for cardiac arrest.

Sepsis caused by bacteremia could be suspected, which could explain fever, abdominal pain, high WBC and CRP, and elevated troponin. But sepsis leading to cardiac arrest should be very severe, and often was accompanied by shock and dysfunction of multiple organs. Therefore, sepsis couldn’t explain why cardiac arrest happened after temperature went back to normal, and why only heart was involved.
Complete Kawasaki disease (KD) could be diagnosed through classic clinical features (diffuse mucosal inflammation, bilateral nonpurulent conjunctivitis, dysmorphic skin rashes, indurative angioedema over the hands and feet, or cervical lymphadenopathy), but not all patients would meet these criteria. According to the statement from the American Heart Association, patients who were in a fever ≥ 5 days and with 2 or 3 clinical symptoms together with CRP ≥ 3.0 mg/dL and/or ESR ≥ 40 mm/hour, positive echocardiogram and any 3 or more following laboratory criteria: (1) anemia for age; (2) platelet count ≥ 450,000 after the seventh day of fever; (3) albumin ≤ 3.0 g/dL; (4) elevated ALT level; (5) WBC count ≥ 15,000/mm³; (6) urine ≥ 10 WBC/hpf; or patients with a fever ≥ 7 days and without or only 1 clinical symptom mentioned above together with positive echocardiogram, should be referred to as atypical KD [8]. In this case, KD could explain fever, high WBC and CRP, abdominal pain, cardiac arrest and abnormal ECG, but without positive echocardiogram. Considering the abnormal heart shadow in the left ventricle in chest X-ray examination, we ordered another cardiac echocardiogram and then confirmed the diagnosis.

The diagnosis of appendicitis is difficult to obtain in infants or preschool children, because the classical features often do not exist, although fever, diffuse abdominal pain, elevated WBC, absolute neutrophil count and CRP could diagnose up to 50% of children with appendicitis in the acute stage [9]. In this case, the persistent abdominal pain lasted for 16 days, but only mild appendiceal hyperemia was shown. The mild lesion on the appendix was not consistent with the clinical manifestations of the patient, so it was suggested that another disease should be considered instead of appendicitis. KD is the most common systemic vasculitis disorder affecting middle-sized blood vessels in childhood, so it can affect multiple systems, including the cardiovascular system, respiratory system, musculoskeletal system, gastrointestinal system, nervous system and genitourinary system. Appendiceal hyperemia can result from vasculitis of the appendix, so the lesion is very mild.

The clinical symptoms of myocarditis vary greatly. Patient with heart function insufficiency, elevated troponin I, abnormal electrocardiogram finding or abnormal echocardiogram finding without structural cardiac lesions and

Figure 4. Coronary computed tomography angiography examination 18 months after coronary artery bypass graft. The results showed an open left anterior descending branch and left circumflex artery. AO, aorta; LAD, left anterior descending branch; LCA, left coronary artery; LCX, left circumflex artery; RCA, right coronary artery.
the premonitory symptoms of fever should be suspected to have a myocarditis [10]. In this case, the patient showed the similar symptoms to those mentioned above, which may be the reason why the pediatric general surgeon considered the patient to have fulminant myocarditis. However abnormal Q waves usually suggested myocardial infarction, and did not appear in the early stages of fulminant myocarditis [11]. And the cardiac symptoms might just be explained by the cardiac coronary lesions caused by systemic vasculitis of KD.

In conclusion, as Kawasaki disease might result in multisystem damage, if a child has a fever for more than 5 days and abnormal routine blood test, Kawasaki disease should be considered even if the classic clinical symptoms are absent. Furthermore, strengthening the training of doctors in local hospitals and improving the understanding of Kawasaki disease as a vasculitus syndrome may be helpful in reducing the misdiagnosis rate.

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Disclosure of conflict of interest

None.

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