Prominent gallbladder enlargement: Kawasaki disease or other congenital or acquired gallbladder disease? A case report

Liang Zhao¹,²,³,⁴, Yimin Hua¹,²,³,⁴ and Kaiyu Zhou¹,²,³,⁴

Abstract
Kawasaki disease (KD) is a common systemic vasculitis in childhood that can result in damage to multiple body systems. However, prominent gallbladder (GB) enlargement in the acute stage is especially rare. A 5-year-old boy was admitted to the hospital with an 8-day history of a cervical mass, 7-day history of fever, and 5-day history of abdominal pain and rash. The child was diagnosed with KD. After treatment with high-dose intravenous immunoglobulin therapy (2 g/kg), all clinical manifestations were relieved except the abdominal pain. Enhanced computed tomography showed distinct enlargement of the GB, and a congenital choledochal cyst was strongly suspected. After high-dose glucocorticoid treatment, his obviously enlarged GB returned to normal size in the subacute phase. No abnormality was found during 2 years of follow-up. Prominent GB enlargement may emerge in the acute stage of KD. The enlarged GB can return to normal size within the subacute stage by standard treatment for KD. Proper diagnosis, thorough differential diagnosis, and active anti-inflammatory treatment of KD are crucial to avoid surgery.

¹Department of Paediatric Cardiology, West China Second University Hospital, Sichuan University, Chengdu, Sichuan, China
²The Cardiac Development and Early Intervention Unit, West China Institute of Women and Children’s Health, West China Second University Hospital, Sichuan University, Chengdu, Sichuan, China
³Key Laboratory of Birth Defects and Related Diseases of Women and Children (Sichuan University), Ministry of Education Chengdu, Sichuan, China
⁴Key Laboratory of Development and Diseases of Women and Children of Sichuan Province, West China Second University Hospital, Sichuan University, Chengdu, Sichuan, China

Corresponding author:
Kaiyu Zhou, Department of Paediatric Cardiology, West China Second University Hospital, Sichuan University, No. 20, 3rd Section, South Renmin Road, Chengdu 610041, China.
Email: kaiyuzhou313@163.com
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Introduction
Kawasaki disease (KD) is a common systemic vasculitis in childhood. KD is the most common cause of acquired heart disease in the pediatric age group and results in permanent damage to coronary arteries in up to 25% of untreated children. Although inflammation of the coronary arteries results in the most important clinical outcomes, KD is characterized by systemic inflammation in all medium-sized arteries and in multiple organs and tissues during the acute febrile phase, leading to associated clinical findings. In addition to the skin, mucosa, and lymph nodes, multiple other body systems can be damaged in patients with KD, including the cardiovascular system, nervous system, urinary system, and digestive system. In patients with KD-induced digestive system damage, the gastrointestinal tract, liver, gallbladder (GB), pancreas, and spleen can all be adversely affected. Few reports of KD have mentioned prominent GB enlargement. We herein report a case of prominent GB enlargement in the acute stage of KD.

Ethical approval was obtained from the Ethics Committee of West China Second University Hospital, Sichuan University. Written informed consent was obtained from the parents of the patient for publication of this case report and any accompanying images. The reporting of this study conforms to the CARE guidelines.

Case report
A 5-year-old boy was admitted to the hospital with an 8-day history of a cervical mass, 7-day history of fever, and 5-day history of abdominal pain and rash. His medical history and family history were unremarkable. Eight days before admission, a mass of unknown cause with a diameter of 3 × 3 cm was found in the right neck. A high fever developed 7 days before admission, peaking at 41°C. The cervical lymph nodes were significantly enlarged (about 6 × 6 cm) and hard, and the skin temperature was elevated. Ultrasound examination of the neck showed cervical lymphadenitis, for which amoxicillin infusion was ineffective. Five days before admission, the child had developed a trunk rash, right abdominal pain, nonsuppurative conjunctival congestion in both eyes, red and cracked lips, “strawberry tongue,” edema of both lower limbs, and a cough; he had no jaundice or vomiting. Intensive anti-infection treatment with ceftriaxone was ineffective. Routine blood examination demonstrated a leukocyte count of 31.5 × 10⁹/L, neutrophil percentage of 97%, and C-reactive protein concentration of >170 mg/L. The child was diagnosed with KD and received high-dose intravenous immunoglobulin (IVIG) therapy (2 g/kg). After treatment, all of his clinical symptoms were improved except for the persistent abdominal pain. Abdominal B-ultrasound showed distinct GB enlargement; therefore, the child was transferred to our hospital for further diagnosis and treatment.

Physical examination on admission showed that the patient was acutely ill-looking and had hard, swollen hands and feet; red and chapped lips; a strawberry
tongue; and a palpable hard, gently tender 3-× 3-cm enlarged lymph node in the right neck. His heart rate was 109 beats/minute, and his heart sounds were low and blunt. His abdomen was soft, and the inferior margin of the liver was 8 cm below the right rib and 5 cm below the xiphoid process (subsequent computed tomography (CT) showed that the inferior margin of liver was actually the enlarged GB). The liver was soft, and Murphy’s sign was positive. Blood examination showed the following: leukocyte count, 16.5×10⁹/L; neutrophil percentage, 84%; hemoglobin concentration, 94 g/L; platelet count, 272×10⁹/L; C-reactive protein concentration, >170 mg/L; albumin concentration, 27 g/L; sodium concentration, 127 mmol/L; troponin I concentration, 0.451 μg/L; brain natriuretic peptide concentration, 12,700 pg/mL; and normal transaminase and bilirubin concentrations. An electrocardiogram showed first-degree atrioventricular block. Echocardiography showed heart enlargement, moderate tricuspid regurgitation, and no abnormality in the left and right coronary arteries and branches. Abdominal enhanced CT showed extremely large cystic lesions (55 × 52 × 120 mm) in the GB fossa (Figures 1(a), 1(b), and 2(a)), and a congenital choledochal cyst was strongly suspected based on the imaging findings.

After admission, the patient was still diagnosed with KD and received further high-dose IVIG therapy (1 g/kg) and 3 days of high-dose methylprednisolone therapy (20 mg/kg per day), followed by prednisone (1 mg/kg per day) and high-dose aspirin (30 mg/kg per day). With these treatments, all of the patient’s clinical symptoms and signs, including the abdominal pain, gradually resolved, and the echocardiography findings, electrocardiography findings, and routine blood parameters also gradually returned to normal. Abdominal enhanced CT re-examination (9 days later) showed that the GB size was normal (23 × 30 × 73 mm) but that the GB wall was still thickened (Figure 2(b)). The child recovered in good condition and was discharged with a satisfactory clinical status. He was treated with prednisone (0.5 mg/kg per day) for 1 week and aspirin (4 mg/kg per day) for 1 week.

Figure 1. Prominent gallbladder enlargement (arrow) in the (a) coronary position and (b) sagittal position before treatment.
per day) for 2 months after discharge. Follow-up at 1 week, 1 month, 2 months, 6 months, 1 year, and 2 years after discharge showed no abnormalities either overall or in the GB and coronary artery examinations.

Discussion

This patient had all six clinical manifestations of complete KD, and his laboratory examination findings also supported KD; therefore, the diagnosis of KD was very clear. This case was characterized by persistent abdominal symptoms and prominent GB enlargement, which introduced difficulties in the clinical diagnosis and treatment. The most common causes of excessive GB enlargement are congenital choledochal cysts, acquired cholecystitis, lithiasis, and tumors. Based on the laboratory and clinical characteristics of this case, chronic cholecystitis, cholelithiasis, and tumors were easily excluded. KD should be carefully differentiated from a congenital choledochal cyst complicated by infection or obstruction and acute cholecystitis, which would directly lead to completely different treatment schemes (anti-inflammatory therapy, anti-infection therapy, surgery, or combined treatment) and different results. Considering the patient’s medical history, ineffective antibiotic treatment, and effective IVIG infusion, the obviously enlarged GB was highly suspected to be an inflammatory reaction caused by KD. Therefore, we treated the patient with high-dose methylprednisolone (20 mg/kg per day) and high-dose aspirin (30 mg/kg per day). The treatment was very effective: all clinical manifestations disappeared, and the enlarged GB returned to normal size in the subacute stage. This outcome confirmed that the GB enlargement had been caused by KD and was not a result of the other causes mentioned above.

According to the literature, GB enlargement caused by KD usually manifests as GB hydrops. The incidence rate of GB hydrops ranges from 4% to 21%, and it is generally mild or moderate. The pathogenesis of KD complicated by GB hydrops remains unclear, but it might be related to vasculitis and inflammation, bile duct compression, and bile duct dysfunction. The present case confirms that

Figure 2. (a) The largest diameter of the enlarged gallbladder (arrow) was located in the third lumbar plane in the axial view before treatment. (b) The gallbladder (arrow) decreased to normal size in the axial view after treatment, with the largest diameter in the second lumbar plane.
active anti-inflammatory treatment can have a significant effect on the regression of GB hydrops caused by KD.

The literature suggests that severe GB hydrops mostly occurs in patients with incomplete KD and often leads to a delayed diagnosis. When KD is accompanied by severe GB hydrops, a delayed diagnosis or inadequate treatment may lead to GB perforation and the need for surgery. In one study investigating KD-related acute abdomen among 219 children, surgical operations were performed in 10 children with severe abdominal symptoms, 5 of whom also had obvious GB hydrops. This suggests that when KD is complicated by obvious GB hydrops, more active medical treatment is often needed to avoid disease progression and consequent surgery.

KD is the most common cause of coronary artery dilatation in children. Whether the coronary artery becomes damaged is related to many factors, such as the severity of inflammation, age, sex, opportunity to undergo IVIG therapy, and genetic background. The inflammatory reaction in the present case was serious, but there was no coronary dilatation; this might have been related to the patient’s low-risk age, timely use of IVIG treatment, and good response to anti-inflammatory treatment. GB distension is reportedly not a significant risk factor for coronary artery dilatation. Our patient had no coronary artery dilatation, which is consistent with the literature.

The present case serves as a reminder that KD should be considered as a differential diagnosis when a patient has manifestations of cholecystitis accompanied by unexplained clinical manifestations such as cervical lymph node swelling, conjunctival congestion, or rash. When a sufficient differential diagnosis has been made and it is determined that the significantly enlarged GB has been caused by KD, active anti-inflammatory treatment is needed.

To our knowledge, this is the first report with imaging evidence showing that a prominently enlarged GB caused by KD rapidly returned to normal size after effective anti-inflammatory treatment.

Conclusion
Prominent GB enlargement may emerge in the acute stage of KD and can be confirmed by abdominal CT examination. The enlarged, inflamed GB can recover to normal within the subacute stage of KD by standard treatment of KD. In clinical practice, a proper diagnosis, thorough differential diagnosis, and active anti-inflammatory treatment of KD are crucial to avoid surgery.

Declaration of conflicting interest
The authors declare that there is no conflict of interest.

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ORCID iD
Kaiyu Zhou https://orcid.org/0000-0002-4783-4243

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