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Case Report

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Acute Appendicitis: A Rare But Probable Manifestation of Kawasaki Disease

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Conflict of Interest
No potential conflict of interest relevant to this article was reported.

ABSTRACT

Kawasaki disease (KD) is an acute, systemic inflammatory disorder that often targets coronary arteries. Being the common cause of acquired heart disease in children, timely diagnosis and intravenous immunoglobulin treatment are crucial. However, it is challenging for physicians to diagnose KD if it presents with atypical manifestations. We report the case of a 5-year-old boy who initially presented with appendicitis; after an appendectomy, he had a prolonged fever. He was finally diagnosed with atypical KD and successfully recovered after intravenous immunoglobulin treatment. Through a literature review, we found 21 cases of appendicitis associated with KD. In most cases, the patients were male with a mean age of 5.3 years. Most had higher proportions of incomplete KD and coronary artery complications than expected for typical KD. In conclusion, appendicitis could be a rare complication of KD; therefore, multidisciplinary cooperation and early recognition of atypical KD are essential for timely diagnosis.

Keywords: Abdomen, Acute; Appendicitis; Child; Mucocutaneous lymph node syndrome

INTRODUCTION

Kawasaki disease (KD) is an acute, systemic inflammatory disorder that predominantly occurs in children younger than five years of age, and it manifests as vasculitis, often in the coronary arteries.[1] Since the exact etiopathogenesis of KD has not been identified and no pathognomonic test has been developed, KD diagnosis is still dependent on clinical findings. Typically, patients with KD manifest high spiking fevers with five principal clinical findings: bilateral nonexudative conjunctival injection; strawberry tongue or red, cracked lips; erythematous edema of the hands and feet; various forms of skin rashes; and nonsuppurative cervical lymphadenopathy.[1] A diagnosis of KD is established if four of the five principal clinical criteria are met along with a fever. However, besides these principal symptoms, various atypical manifestations can precede or occur with KD, and these can prevent timely diagnosis. An acute abdomen can also be the first presentation of KD. Gallbladder hydrops with cholangitis is most often reported, followed by paralytic intestinal obstruction or pseudo-obstruction.[2,3] We report the case of a 5-year-old boy who was diagnosed with KD after appendectomy.

Author Contributions

Conceptualization: Choi W, Park JY; Data curation: Choi W, Hong M, Suh SW; Formal analysis: Choi W; Investigation: Hong M, Suh SW; Methodology: Choi W; Supervision: Yun SW, Hong M, Suh SW, Yi DY, Park JY; Visualization: Choi W, Yun SW, Hong M, Suh SW, Park JY; Writing - original draft: Choi W; Writing - review & editing: Park JY.

CASE

A previously healthy 5-year-old Korean boy visited the emergency room with intermittent fever up to 39.4°C and progressive abdominal pain. The fever began on the day the patient visited the hospital. A dull pain had begun two days before in the periumbilical area. However, by the day of the hospital visit, the pain had migrated to the right lower abdomen. Upon physical examination, the patient complained of tenderness on his right lower quadrant. Initially, his vital signs were stable: blood pressure, 100/60 mmHg; respiratory rate, 20/min; body temperature, 36.4°C; and slight tachycardia (120 beats/min). The following laboratory findings were determined: white blood cell (WBC) count, 13,210/mm^3 with dominated by neutrophils (79.1%); hemoglobin, 12.7 g/dL; platelet count, 305,000/mL; and C-reactive protein (CRP) concentration, 13.7 mg/dL. Enhanced abdomen computed tomography (CT) was performed to rule out a surgical abdomen. The patient underwent a CT scan because acute appendicitis was suspected. CT indicated the diameter of the appendiceal tip was 6.5 mm. The appendiceal wall showed enhancement and thickening, and a small amount of periappendiceal fluid collection was noted. A right internal iliac lymph node was enlarged. Several other small lymph nodes of the right lower mesenteric nodal station were enhanced. In summary, the CT findings were consistent with acute appendicitis (**Fig. 1A**). Thus, the patient was admitted to the Department of Surgery (hospital day [HD] 1), and intravenous piperacillin/tazobactam was initiated. A laparoscopic appendectomy was then performed on HD 1. The intraoperative findings included dilatation of the whole bowel and several enlarged lymph nodes with small amounts of inflammatory ascites in the ileocolic area. The tip of the appendix was also dilated, but there was no appendicolith (**Fig. 2A**).

The high, spiking fever continued despite surgery and administration of intravenous antibiotics. An itchy, maculopapular rash developed throughout the trunk and extremities from HD 3. The surgeon requested a consultation with the Division of Pediatric Infectious Disease. We recommended changing from piperacillin/tazobactam to cefotaxime and metronidazole with an antihistamine because of the suspected drug rash. Also, we recommended administration of antibiotics for a few more days to evaluate the effectiveness of the antibiotics for the fever. Even with the new antibiotics, the fever and rash continued until HD 7. Thus, the patient was transferred to the Department of Pediatrics. In the Department of Pediatrics, physical examination revealed a bilateral nonexudative

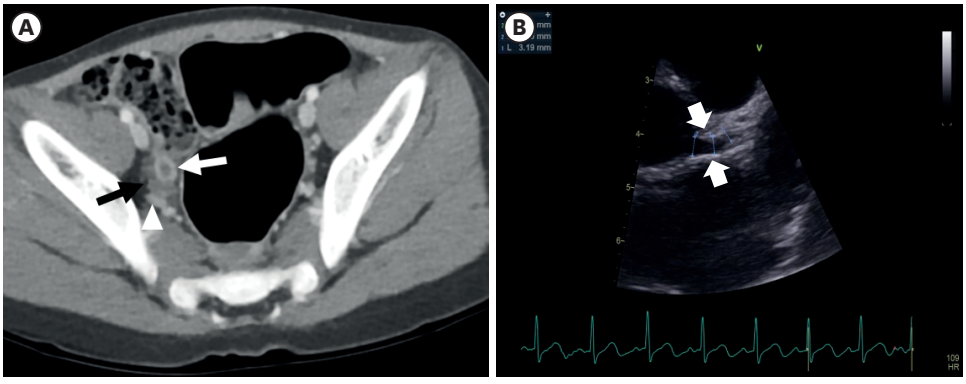

Fig. 1. Images during diagnosis. (A) Abdominal CT: the enhanced CT scan shows enhanced wall thickening of the appendiceal tip (white arrow), periappendiceal fluid collection (black arrow), and an enlarged right internal iliac lymph node (white arrowhead); (B) Echocardiography: left main coronary artery shows mild ectasia with intimal wall irregularity and echo brightness. The Z value of the left main coronary artery is 3.14.
Abbreviation: CT, computed tomography.

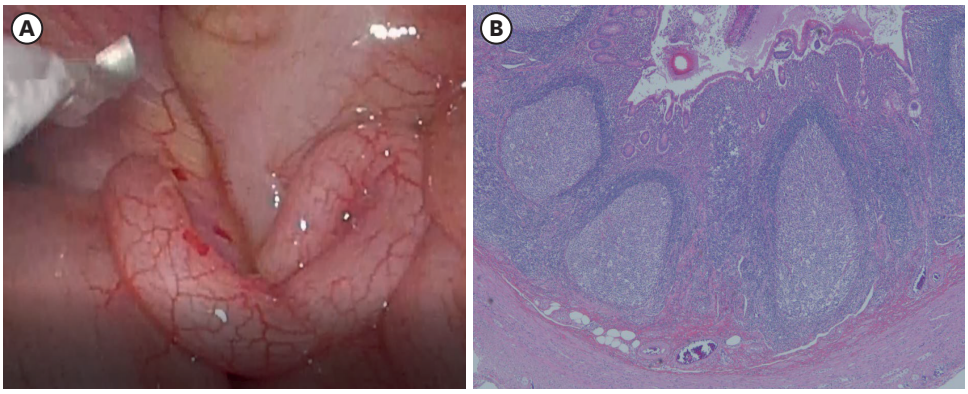

Fig. 2. Photos captured during laparoscopy and biopsy. (A) Operative findings: the tip of the appendix is dilated, but there is no appendicolith; (B) pathological findings: reactive follicular hyperplasia and serositis of the appendix are shown. Hematoxylin and eosin stain, 40× magnification.

conjunctival injection, and laboratory findings revealed elevated WBCs (11,820/mm^3; 76.0% neutrophils and 3.6% eosinophils), erythrocyte sedimentation rate (ESR, 88 mm/h), and CRP (12.8 mg/dL). The level of N-terminal pro-B-type natriuretic peptide was 438 pg/mL (normal range: 5–391 pg/mL), and negative results were obtained for. all culture studies. Because atypical KD was suspected, echocardiography was performed on HD 10, which revealed mild ectasia of the left main coronary artery (**Fig. 1B**).

Once the KD diagnosis was obtained, antibiotics were discontinued, and intravenous immunoglobulin (IVIG) (2 g/kg) and aspirin (50 mg/kg/d) were administered beginning on HD 10. On HD 12, the patient became afebrile, and the inflammatory biomarkers ESR and CRP had decreased to 86 mm/h and 1.52 mg/dL, respectively. On HD 12, fingertip desquamation was initiated, and the patient was discharged from the hospital with a prescription for aspirin (4 mg/kg/d). Two weeks later, follow-up echocardiography at an outpatient clinic showed full recovery without coronary artery complications. After discharge, the final pathologic findings revealed reactive follicular hyperplasia and serositis of the appendix without suppurative changes (**Fig. 2B**).

This study was approved by the Institutional Review Board of Chung-Ang University Hospital (no. 2305-013-19470), which waived the need for informed consent.

DISCUSSION

According to nationwide survey data from the Kids Inpatient Database to study trends in KD hospitalizations in the United States of America, children younger than 5 years had the highest annual hospitalization rates, and children of Asian and Pacific Islander ancestries had the highest rates among all racial groups.[4] Although coronary artery abnormality is the most important complication, KD itself is a systemic disease, affecting all body organs. Gastrointestinal symptoms are common in the acute phase of the disease; Baker et al.[5] reported that 61% of 198 KD patients presented with one or more gastrointestinal symptoms in the 10 days before diagnosis. KD sometimes even presents as an acute surgical problem. In a retrospective cohort study in Italy, 4.6% of 219 patients with KD presented with acute surgical abdomens, and most patients were diagnosed postoperatively with gallbladder hydrops, followed by small intestinal occlusions and paralytic ileuses.[2,3]

Acute appendicitis is a very rare presentation of KD. We conducted a literature review for appendicitis associated with KD using the search terms "appendicitis" and "Kawasaki disease" on PubMed. From 1998 to 2023, we found 18 cases of KD patients whose symptoms mimicked, or actually were due to, acute appendicitis.[2,6-18] In Korea, we found an additional two KD-related appendicitis cases reported in a presentation at the Congress of the Korean Pediatric Society.[19,20]

In total, 21 cases were identified by the literature review. In cases that provided information about age and sex, the mean patient age was 5.3 years old (range: 3–8 years), and most patients were male (14/16). For this age group, acute appendicitis is a relatively rare cause of a febrile surgical abdomen because its peak incidence is between 10 and 19 years of age.[21] Physical examinations showed signs of peritonitis in all patients; 90% (19/21) received an appendectomy, 52% (11/21) were diagnosed with appendicitis according to histologic reports, and 29% (6/21) were diagnosed with symptoms mimicking those of appendicitis. The most common cause of symptoms mimicking appendicitis was mesenteric adenopathy (3/6), followed by appendicular vasculitis (2/6) and serositis (1/6). In two cases in which surgery was not performed, appendicitis improved along with KD after IVIG treatment.[15,20] At the time of KD diagnosis, 60% (12/20) of patients fulfilled all diagnostic criteria for complete KD, whereas 40% (8/20) satisfied less than four criteria, which was classified as incomplete KD. Nonexudative conjunctival injections were present in all cases (16/16). Dysmorphic skin rashes on the body and swelling or erythema of the hands and feet were the second most common symptoms (13/16), followed by lip and tongue changes (12/16) and cervical lymphadenopathy (3/16). Although IVIG treatment was initiated within 10 days of fever in 13/14 of cases, 21% exhibited coronary artery complications (dilation or aneurysms) during follow-up echocardiography. Compared with a study by Newburger et al.[1] showing that IVIG treatment within the first 10 days reduces the incidence of coronary artery complications to less than 5%, the incidence of coronary artery complications appeared to be higher in patients with KD accompanied by appendicitis (**Supplementary Tables 1-3**).

The 6th edition of the Japanese Society of Kawasaki Disease guidelines, published in 2020, contained important changes for early diagnosis of KD.[22] To emphasize the importance of early diagnosis, the concept of incomplete KD and its possibility were introduced. It was recommended that KD be suspected even when only one or two diagnostic criteria were satisfied if no other disease could be diagnosed. Because incomplete KD and atypical KD have higher risks of complicating coronary artery lesions than typical KD,[22] it is especially important to become familiar with atypical clinical manifestations of KD.

Surgeons may be less familiar with KD than pediatricians; thus, if a patient manifests symptoms after surgery, an accompanying fever could be mistaken for postoperative fever, and unnecessary treatments and delayed diagnoses could occur. In our case, postoperative fever and drug rash presented as the first differential diagnosis, and bilateral nonexudative conjunctival injection was recognized after transfer to the Department of Pediatrics on HD 7. Incomplete KD was finally diagnosed on HD 10, but only after echocardiography revealed coronary artery dilation.

In addition, KD can mimic the multisystem inflammatory syndrome in children (MIS-C) after coronavirus disease 2019 (COVID-19) infection, and MIS-C with acute appendicitis was recently reported.[23] Thus, a careful differential diagnosis is warranted. In October 2020, when the patient in this case study was admitted to the hospital, COVID-19 was not

very prevalent in Korea, and the PCR results of the patient were negative for severe acute respiratory syndrome-coronavirus-2. Also, the patient had no contact or travel history. Thus, MIS-C was excluded, and the patient was diagnosed with KD.

The results of this study lead us to recommend physicians consider KD as a rare cause of acute appendicitis in early childhood. We should also suspect KD when a prolonged fever occurs after an appendectomy, especially when a bilateral conjunctival injection, skin rash, or changes in the hands and feet follow. In this case, we recommend multidisciplinary cooperation for diagnosing KD to prevent further cardiac complications.

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SUPPLEMENTARY MATERIALS

Supplementary Table 1

Details of 21 cases of appendicitis–mimicking Kawasaki disease: appendicitis aspect

Click here to view

Supplementary Table 2

Details of 21 cases of appendicitis–mimicking Kawasaki disease: Kawasaki disease aspect

Click here to view

Supplementary Table 3

Treatment detail and response of 21 cases of appendicitis-mimicking Kawasaki disease

Click here to view

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요약

가와사키병은 종종 관상동맥을 침범하는 급성 전신적 염증 질환이다. 소아에서 가장 흔한 후천성 심장병의 원인으로 알려져 있으며, 적절한 시기에 빠른 진단과 정맥 면역글로불린 치료가 중요하다. 그러나 비정형적인 증상으로 나타나면 의사들은 진단에 있어 어려움을 느낀다. 본 저자들은 5세 남아가 복통으로 응급센터를 내원하여 급성 충수돌기염으로 진단받아 충수돌기 절제술을 시행받은 이후에도 발열이 지속되어 소아감염분과로 전과된 케이스를 공유하고자 한다. 환아는 응급센터 내원 당시 발열없이 우하복부 복통으로 내원하여 컴퓨터 단층촬영에서 급성 충수돌기염으로 진단받았으며, 응급실 재실 중 발열이 처음 발생하였다. 환아는 충수돌기 절제술을 시행하였으나 이후에도 발열 호전없고 발진 동반되어 소아감염분과 의뢰되었고, 최종적으로 가와사키병으로 진단받았다. 이 환아가 약간의 결막 충혈이 보여 소아감염분과 의사는 진단 과정에서 적극적으로 수술의와 수술 소견, 병리과 의사와의 병리 소견에 대한 상의를 통하여 비정형 가와사키병을 의심할 수 있었다. 결국 비정형 가와사키 진단을 받고 면역글로불린 정맥주사로 성공적으로 회복됐다. 또한, 문헌 검토를 실시하여 가와사키와 관련된 충수염 21건을 확인하였다. 대부분의 환자는 평균 연령이 5.3세인 남성이었다. 대부분은 불완전 가와사키 및 관상 동맥 합병증의 비율이 전형적인 가와사키에 대해 예상되는 것보다 더 높았다. 결론적으로 맹장염은 가와사키의 드문 합병증이다. 따라서 다학제간 진료를 통한 비정형 가와사키의 조기 인식은 시기 적절한 진단에 필수적이었다.

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