

Kawasaki Disease with Dilatation of the Common Bile Duct: A Case Report and Review of Literature

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Case Report

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Abstract

Background

Kawasaki disease (KD), which was first described by Tomisaku Kawasaki in 1967, is a syndrome that results in acute systemic vasculitis, affecting mainly infants and children, and is a major cause of acquired heart disease in developed countries. KD is diagnosed based on certain characteristic symptoms and echocardiogram results. It has been reported that neck and abdominal ultrasound is also reliable diagnostic method. Nevertheless, abdominal ultrasound is not a routine procedure in KD. Moreover, dilatation of the common bile duct (CBD) has been rarely reported in previous cases.

Case presentation:

A 4-year-old boy presented with fever and markedly high transaminase level (AST, 5,323 U/L, ALT, 1,554 U/L). The patient was diagnosed as having KD based on characteristic symptoms and echocardiogram findings. Neck and abdominal ultrasound revealed dilatation of the CBD as well as cervical lymphadenopathy resembling a cluster of grapes, thickening of the gallbladder wall, and increased periportal echogenicity throughout the liver parenchyma. The patient received initial treatment with intravenous immunoglobulin (IVIG) at day 4 of fever, following which, transaminase level decreased. The patient received second-line treatment with IVIG and prednisolone because of recurrent fever on day 6. Dilatation of the CBD was improved from 6.6 mm on day 4 to 3.1 mm on day 8. Although re-dilatation was observed, it gradually diminished and normalized (4.3 mm on day 28, 4.0 mm on day 63, 3.3 mm on day 105, and 2.8 mm on day 182).

Conclusion

This case highlights the usefulness of abdominal ultrasound and the importance of considering dilatation of the CBD as one of the complications of KD. Because abdominal ultrasound is not a routine procedure in KD, it is possible that dilatation of the CBD in KD is quite latent if not investigated thoroughly. Further prospective studies to support these findings are warranted.

Background

Kawasaki disease (KD) is a syndrome that results in acute systemic vasculitis, affecting mainly infants and children, and is a major cause of acquired heart disease in developed countries.¹ Although KD was first described by Tomisaku Kawasaki in 1967,²⁻⁴ the cause of the disease is still unknown. Therefore, to date, KD is diagnosed based on certain characteristic symptoms and echocardiogram results.⁵

It has been reported that neck and abdominal ultrasound is reliable diagnostic method; for instance, characteristics such as cervical lymphadenopathy resembling a cluster of grapes,⁶ severe dilatation of

the gallbladder called hydrops of the gallbladder,⁷ thickening of gallbladder wall,⁸ and segmental bowel-wall thickening⁹ support the diagnosis of KD. Nevertheless, abdominal ultrasound is not a routine procedure in KD. Moreover, dilatation of the common bile duct (CBD) has been rarely reported.

Herein, we report the case of a 4-year-old boy with KD, and with various ultrasound findings including dilatation of the CBD during acute phase of disease.

Case Presentation

A 4-year-old boy was admitted to our hospital because of markedly high level of transaminase. The patient had been well until 3 days before admission, when a runny nose and fever were noted. On the day of symptom onset, the patient was evaluated by his primary care pediatrician and was diagnosed as having bronchitis. After which, the patient experienced nausea and vomiting and was taken to the emergency department at another hospital. At the other hospital, the patient did not appear ill but had redness in the pharynx and cervical lymphadenopathy. The blood test results showed high transaminase level, after which he was transferred to our hospital.

On arrival, the patient was ill-appearing and febrile, with a body temperature of 40.4 °C. His blood pressure was 97/48 mmHg, pulse rate was 148 beats per minute, respiratory rate was 28 breaths per minute, with oxygen saturation of 96% while breathing ambient air. Physical examination revealed bilateral conjunctival congestion, erythema around the navel, reddening and indurative edema of palms, and cervical lymphadenopathy. There was no evidence of reddening of the lips, strawberry tongue, and redness at the site of Bacille Calmette-Guèrin (BCG) inoculation. The blood test results showed markedly high level of transaminase with acute inflammatory response (white blood cell count: 16,400 / μ L; erythrocyte sedimentation rate: 50 mm/h; C-reactive protein: 15.7 mg/dL; aspartate aminotransferase (AST): 5,323 U/L; alanine aminotransferase (ALT): 1,554 U/L; total bilirubin: 1.5 mg/dL; gamma-glutamyl transpeptidase: 149 U/L; and total bile acid: 381.1 μ mol/L). There was no evidence of viral hepatitis (negative results of hepatitis A virus antibody, hepatitis B surface antigen, hepatitis C virus antibody, and polymerase chain reaction for Epstein-Barr virus, cytomegalovirus, herpes simplex virus 1 and 2, and human herpes virus 6) or autoimmune hepatitis. No bacterial growth was detected in any of the cultures. Some cytokines were measured using cytokine bead assay (BD™ CBA kit); IL-6 level increased to 87.7 pg/mL, IL-10 increased to 32.0 pg/mL, whereas IL-1 β and TNF α levels were normal. Although the echocardiogram showed normal cardiac function with no evidence of valve regurgitation, slight dilatation of left main trunk was observed (Fig. 1). Ultrasonographic evaluation of cervical lymph nodes revealed multiple hypoechoic-enlarged nodes, which resembled a cluster of grapes (Fig. 2A). An abdominal ultrasound showed thickening of the gallbladder wall, increased periportal echogenicity throughout the liver parenchyma, and dilatation of the CBD with the maximum diameter of 6.6 mm at the intrapancreatic region (4-year-old standard value: 2.3 mm, upper limit: 3.7 mm)¹⁰ (Fig. 2B-2D). No evidence of biliary calculus and pancreatitis was observed.

After admission, intravenous administration of cefotaxime was initiated; however, it was ineffective. The next day of hospitalization (day 4 of fever), reddening of lips was observed and the patient was diagnosed with KD based on the presence of five principal symptoms.⁵ Intravenous immunoglobulin (IVIG) (2 g/kg) was administered as initial therapy. Oral aspirin (ASA) was not administered owing to high transaminase level. Kobayashi score of 8 suggested that the patient was at high risk of IVIG resistance.¹¹ Viral hepatitis could not be completely ruled out at this point; therefore, steroid administration was avoided. The patient defervesced rapidly with the initiation of treatment, and transaminase level gradually improved. However, the patient's fever relapsed on day 6; therefore IVIG (2 g/kg) and intravenous prednisolone (PSL) (2 mg/kg/day) were administered as second-line therapy. Flurbiprofen, which is used as an alternative to ASA in Japan when high transaminase levels are observed,¹² was also administered because transaminase level remained to be high (AST, 171 IU/L; ALT, 468 IU/L). The patient maintained a defervesced state after second-line therapy. Oral medication was switched from flurbiprofen to ASA (5 mg/kg/day) on day 10 (AST, 45 IU/L; ALT, 171 IU/L), and PSL administration was simultaneously changed from intravenous to oral because the patient's C-reactive protein level normalized. Following which, PSL administration was tapered as 5-day step—from 2 mg/kg/day to 1 mg/kg/day to 0.5 mg/kg/day. Membranous desquamation appeared on the fingertips on day 15.

The maximum diameter of the CBD reduced from 6.6 mm on day 4 to 3.1 mm on day 8. Although re-dilatation was observed, it gradually diminished and normalized (4.3 mm on day 28, 4.0 mm on day 63, 3.3 mm on day 105, and 2.8 mm on day 182). The thickening of the gallbladder wall was persistent on day 8; however, it improved after day 28. All abdominal ultrasound tests were performed in a fasting state (Fig. 2D). No exacerbation of coronary lesions was observed.

Discussion

Our patient was diagnosed with acute KD and showed dilatation of the CBD. Very few reports are available on biliary dilatation in KD patients (Table 1). To the best of our knowledge, only one Japanese paper (1987) has reported acute-phase KD (only available in the Japanese literature),¹³ and our case is the first report in an international journal.

A Japanese report evaluated the hepatobiliary system using abdominal ultrasound in 68 patients with KD every 3 or 4 days.¹³ Of the 68 patients, 20 had dilatation of the gallbladder, and among them, 4 patients had thickening of the gallbladder wall and 3 had dilatation of the CBD in acute phase. All 3 patients with dilatation of the CBD had high transaminase level and cholestasis. Dilatation of the CBD regressed spontaneously in 2 weeks to 1 month (Table 1, case A1-3). In present case, the peak value of ALT and the maximum diameter of the CBD were most severe, took longer to normalize.

In the subacute phase, which is also rare, a total of 3 cases of biliary dilatation have been reported.^{14,15} Petersen et al. reported a case of 10-year-old with painless jaundice and elevated amylase level, along with dilatation of the CBD and hydrops of the gallbladder. On endoscopic retrograde cholangiopancreatography (ERCP), the patient had string-like stenosis in the pre-papillary CBD (Table 1,

case S1).¹⁴ Cherry et al reported two cases; one was of a 6-year-old boy who experienced recurrent abdominal pain, jaundice, and persistent elevation of transaminases with dilatation of the CBD. On computed tomography (CT), the patient had CBD stenosis at the level of the pancreatic head (Table 1, case S2). The other case was of a 3-year-old boy who developed pancreatitis. On magnetic resonance cholangiopancreatography (MRCP), the patient had dilatation of the CBD with tapering near the ampulla of Vater, consistent with stenosis (Table 1, case S3).¹⁵ One of the three cases underwent CBD stent placement, the others spontaneously improved. It is not described whether dilatation of the CBD in the subacute phase was also present in the acute phase. Although abdominal ultrasound as well as CT, MRCP, and ERCP is not routine procedure for KD, past cases along with the present case suggest that the presentation of the CBD dilatation in KD may be quite latent if not investigated thoroughly.

Our patient also showed increased level of transaminase and gamma-glutamyl transpeptidase with thickening of the gallbladder wall, increased periportal echogenicity throughout the liver parenchyma, along with dilatation of the CBD detected by abdominal ultrasound, which suggested cholecystitis and intrahepatic/extrahepatic cholangitis. Although there have been few pathological investigations that consider hepatobiliary abnormalities in KD, it was reported that patients with dilatation of the gallbladder and thickening of the gallbladder wall showed neutrophil infiltration around the gallbladder wall, cystic duct mucosa, and bile duct epithelial cells.^{16,17} Actually, 62.7% of patients with acute phase KD show increased gamma-glutamyl transpeptidase level and 40.3% show an increase in alanine aminotransferase level.¹⁸ These evidences indicate that KD can lead to cholecystitis and intrahepatic/extrahepatic cholangitis. The relationship between these pathological conditions and ultrasound findings remains unclear. However, it is presumed that inflammation of the cystic duct results in obstruction, causing hydrops of the gallbladder.¹³ In addition, our case suggests that thickening of the gallbladder wall, increased periportal echogenicity throughout the liver parenchyma, and dilatation of the CBD also relate to inflammation and subsequent edema and obstruction at each location (Fig. 3).

Our patient demonstrated IL-6 elevation detected using Cytokine bead assay (BD™ CBA kit). IL-6 was discovered as a hepatocyte stimulating factor 2 induced in acute liver inflammation.¹⁹ IL-6 reduces gene expression of excretory transporters such as bile salt export pump (BSEP); ABCB11 and multidrug resistance-associated protein 2 (MRP2) in primary human hepatocyte cell lines,²⁰ which impair the secretion of bile acids into the bile ducts. Bile acids were also elevated in our patient. IL-6 elevation may have contributed to cholestasis and led to hepatobiliary abnormalities in KD.

Conclusion

This case of a 4-year-old with dilatation of the CBD in acute KD highlights the usefulness of abdominal ultrasound and the importance of considering dilatation of the CBD as one of the complications of KD. Because abdominal ultrasound is not a routine procedure in KD, it is possible that dilatation of the CBD in KD is quite latent if not investigated thoroughly. Further prospective studies to support these findings are warranted.

List Of Abbreviations

KD

Kawasaki disease

CBD

common bile duct

AST

aspartate aminotransferase

ALT

alanine aminotransferase

IVIG

intravenous immunoglobulin

ASA

oral aspirin

PSL

prednisolone

ERCP

endoscopic retrograde cholangiopancreatography

CT

computed tomography

MRCP

magnetic resonance cholangiopancreatography

Declarations

Ethics approval and consent to participate

This study was approved by the ethics committee of the University of Tsukuba Hospital. Written informed consent was obtained from the patient's parents.

Consent for publication

Written informed consent was obtained from the patient's parents.

Availability of data and materials

Not applicable.

Competing interests

None of the authors have any financial or non-financial competing interests to declare in relation to this manuscript.

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Author contributions

Substantial contributions to the conception or design of the work: AM and KI.

Acquisition, analysis, or interpretation of ultrasound findings for the work: AM and TI.

Acquisition, analysis, or interpretation of comprehensive data for the work: KI and MT.

Drafting the work: AM and KI.

Revising the work critically for important intellectual content: HT.

Final approval of the version to be published: AM, KI, TI, MT, and HT.

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Tables

Due to technical limitations, table 1 is only available as a download in the Supplemental Files section.

Figures

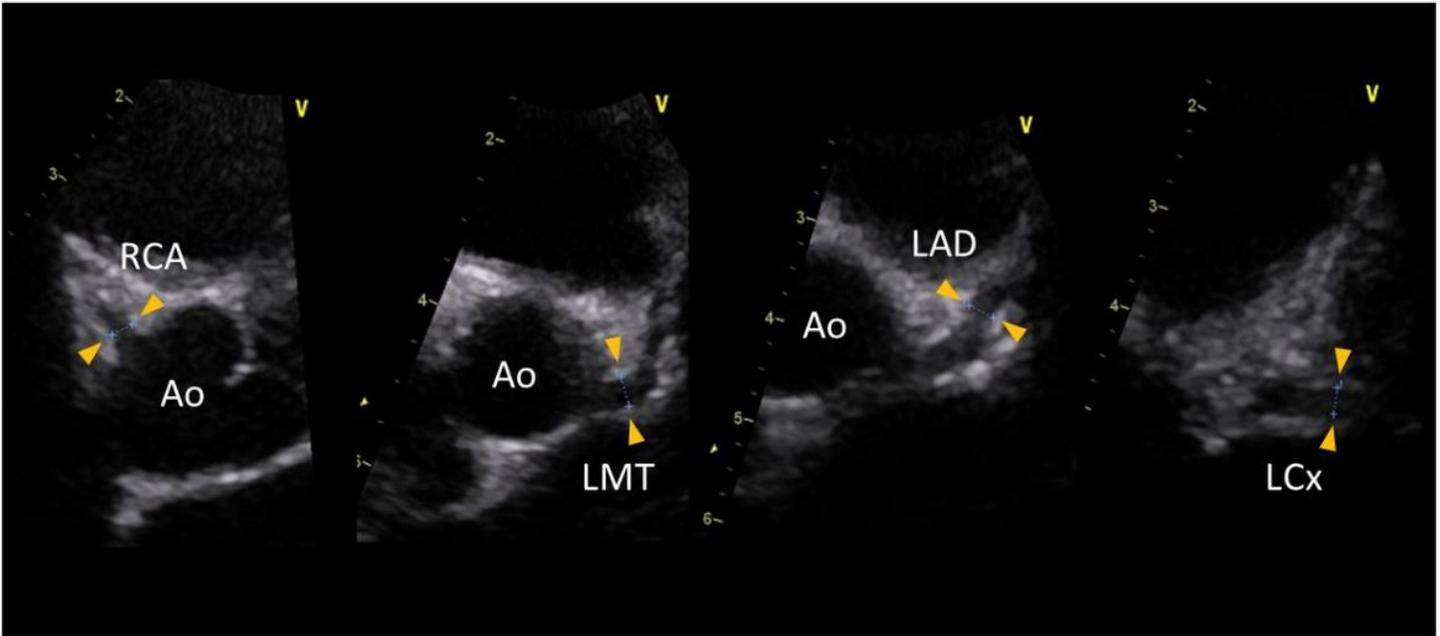


Figure 1

Echocardiogram of the patient Performed on day 4. Slight dilatation of the LMT were recognized. No evidence of valve regurgitation and cardiac dysfunction was observed. Each measured value was as follows: RCA (seg1): 2.2mm (Z=0.75), LMT (seg5): 3.4mm (Z=2.91), LAD (seg6): 2.6mm (Z=1.90), LCx (seg11): 2.5mm (Z=2.08). Ao: aorta, RCA: right coronary artery, LMT: left main trunk, LAD: left anterior descending artery, LCx: left circumflex artery, Z: Z score

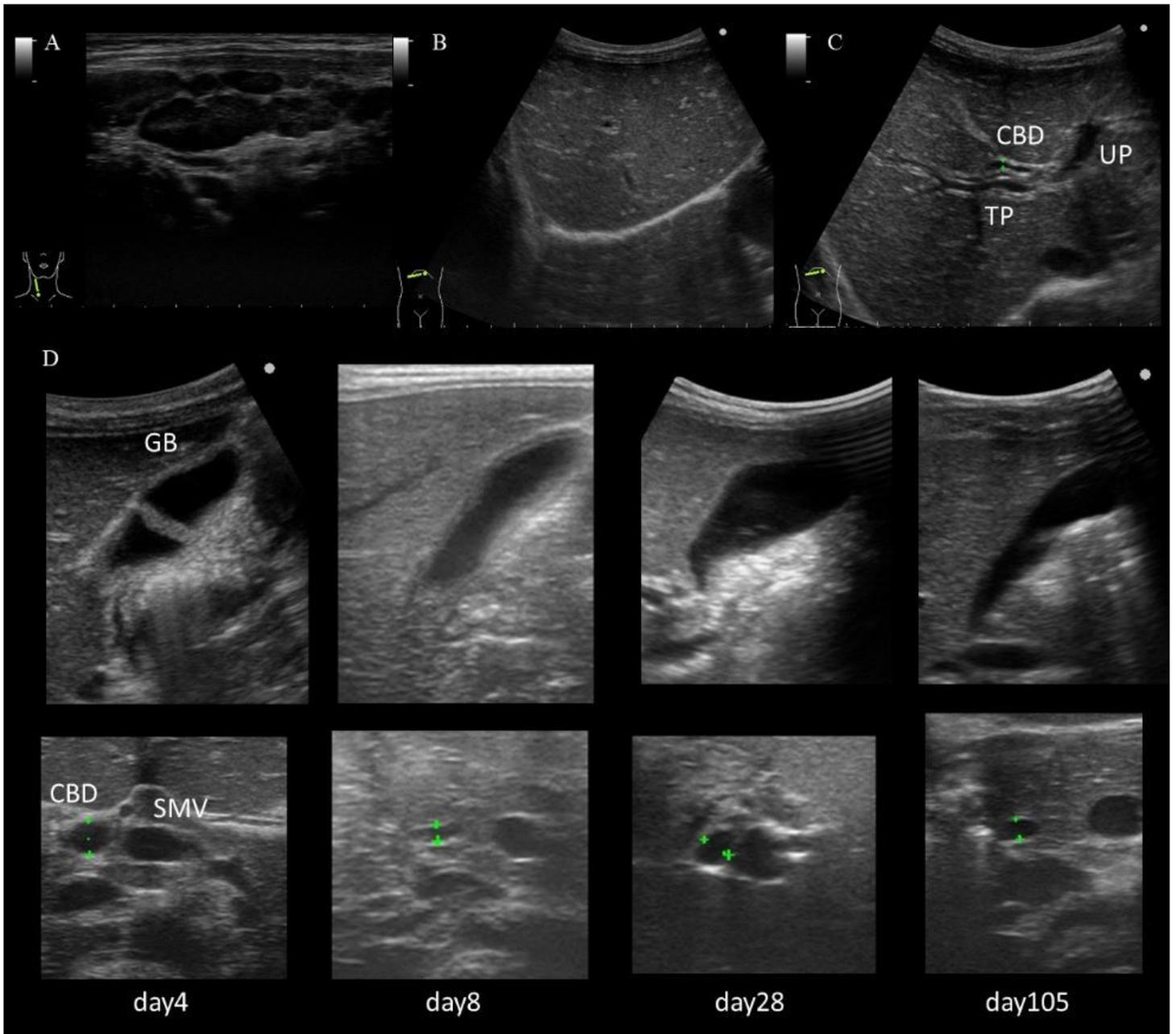


Figure 2

Neck and abdominal ultrasound and shift of maximum diameter of the common bile duct Performed on day 4. Neck ultrasound showed multiple hypoechoic-enlarged nodes which resembled a cluster of grapes (A). Abdominal ultrasound showed increased periportal echogenicity throughout the liver parenchyma (B), dilatation of common bile duct (C, D) and thickening of gallbladder wall (D). The maximum diameter of the common bile duct shifted as follows: day 4: 6.6 mm, day 8: 3.1 mm, day 28: 4.3 mm, day 63: 4.0 mm, day 105: 3.3 mm, day 182: 2.8 mm (4-year-old standard value is 2.3 mm, upper limit is 3.7 mm)⁹. All tests were performed in a fasting state. Thickening of the gallbladder wall remained on day 8, but it improved after day 28. CBD: common bile duct, UP: umbilical portion of the portal vein, TP: transverse portion of the portal vein, GB: gall bladder, SMV: superior mesenteric vein

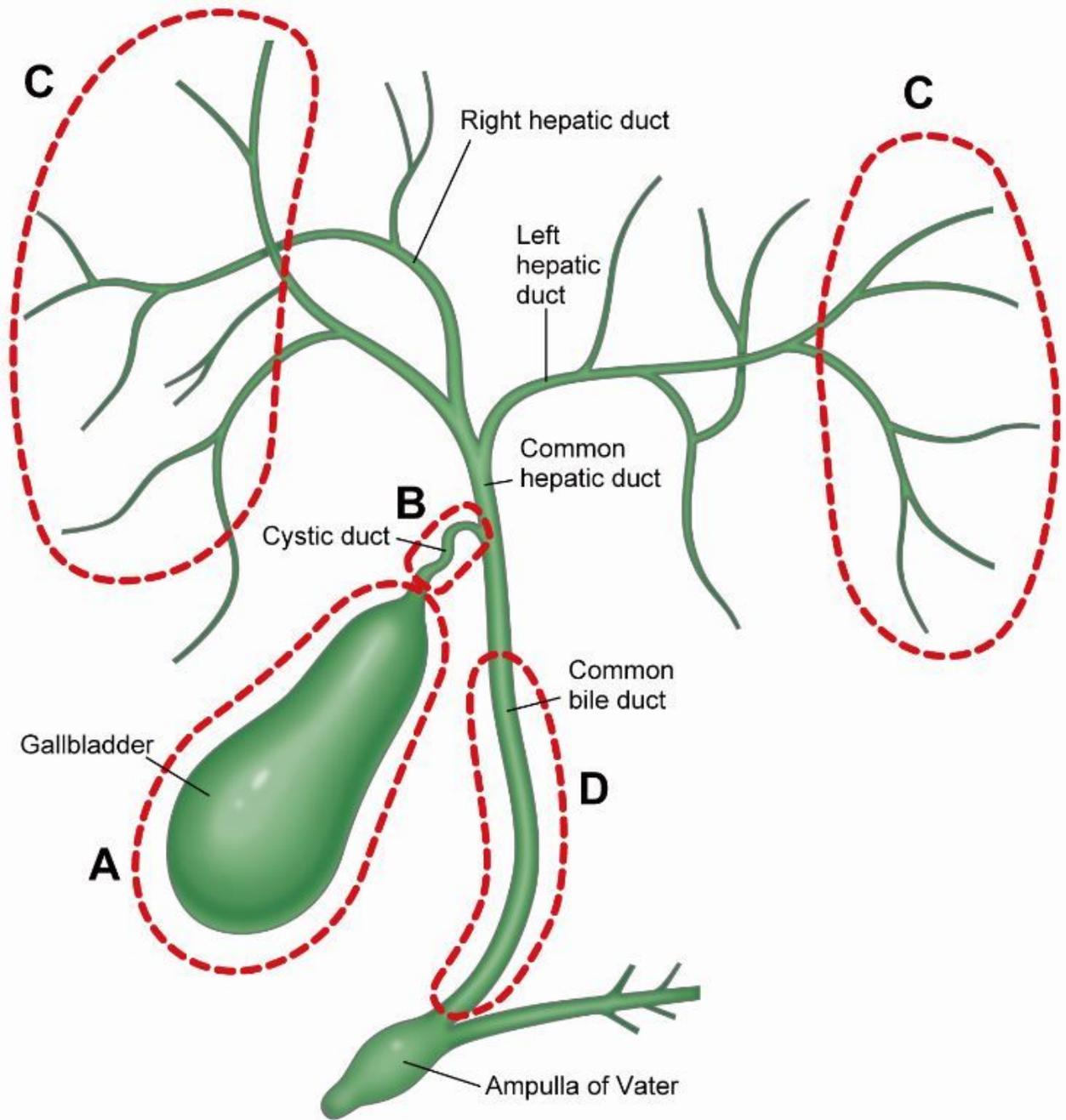


Figure 3

Hepatobiliary abnormalities and abdominal ultrasound findings in Kawasaki disease All abdominal ultrasound findings are presumed due to inflammation and subsequent edema and obstruction at each location. (A) Thickening of the gallbladder wall. Gallbladder swelling due to decreased contractility. (B) Hydrops of the gallbladder due to obstruction of cystic duct. (C) Increased periportal echogenicity throughout the liver parenchyma. (D) Dilatation of the common bile duct.

Supplementary Files

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- [Table1.jpg](#)