

# Cholelithiasis Associated to Acute Pancreatitis and Chronic Cholecystitis; A Case Report

Addina Irawan<sup>1</sup>, Yusri Dianne Jurnalisa<sup>2</sup>, Jon Efendi<sup>3</sup>

<sup>1</sup>Department of Pediatrics, Faculty of Medicine, Andalas University, Indonesia

<sup>2</sup>Neurologic Subdivision, Department of Pediatric, Faculty of Medicine, Andalas University, Indonesia

<sup>3</sup>Pediatric Surgery Subdivision, Department of Surgery, Faculty of Medicine, Andalas University, Indonesia

Corresponding Author: Addina Irawan

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## ABSTRACT

**Background:** Cholelithiasis is a condition in which rare in children but in recent years has been increasing due to ultrasound used. This problem associated to inflammation, infection, obesity, children who received long total parenteral nutrition, resection of bowel, chronic liver disease or genetic. Most of cholelithiasis in children are asymptomatic. Gallstones are divided into cholesterol stones and pigment stones, could be on lucent or opaque description in abdominal x-ray. There are no special guidelines defined indications for medical or surgical treatment in children with cholelithiasis.

**Case Presentation:** A 7 years 2 months old boy complaint of abdominal pain getting worse since 6 hours before admission; colicky pain, does not spread to other region of abdominal, and especially after eating. Vomit was frequently after eating. Symptoms are repeated for 3 times hospitalization and established as acute pancreatitis in second hospitalization but confirmed as cholelithiasis in recent admission.

**Conclusion:** Cholelithiasis in children could be related to inflammation and/ or infection of organs around the gallbladder.

**Keywords:** Cholelithiasis, acute pancreatitis, chronic cholecystitis, case report

## INTRODUCTION

Cholelithiasis is a condition in which stones form in the gallbladder.<sup>1</sup> This condition is rare in children<sup>2</sup> but in recent years there has been an increasing.<sup>3,4</sup> In population based

studies, the prevalence of cholelithiasis in children is about 1.9%.<sup>3,5,6</sup> Other study explain that this case's prevalence was 0.15-0.22 with male:female ratio are 2.3:1. Median age for boys was 5 years (3 months-14 years) and the median age for girl is 9 years (7 months-15 years).<sup>7</sup> Fifty six percent of case were solitary stones.<sup>7</sup> The increasing of incidence may also be due to the increased use of ultrasound.<sup>1,9</sup>

Eighty to ninety five percent of cholelithiasis cases in children are asymptomatic.<sup>7</sup> One study reported the prevalence of symptomatic cholelithiasis between 0.13% of which 0.27% occurred in women.<sup>10,11</sup> Clinical symptoms that often appear in cholelithiasis are abdominal pain (34%), jaundice (18%), and vomiting (8%).<sup>12</sup> Another symptoms found are nausea and Murphy's sign.<sup>8,13</sup>

This study aimed to report a case of cholelithiasis associated to acute pancreatitis and chronic cholecystitis.

## CASE PRESENTATION

A 7 years 2 months old boy admitted to emergency room with chief complaint abdominal pain was getting worse since 6 hours before admission. The pain was colicky, not spread to other region of abdominal and especially exist after eating. Vomit after eating, frequency 3-4 times a day which each volume quarter of drinking glass, consist of food and yellowish fluid. Abdominal trauma history was declined.

Defecation and micturition were in normal limit. No fever or seizure. Previously patient was hospitalized in other district hospital for 6 days due to the same symptoms. Abdominal sonography result 5 months before admission was suggestive loculated ascites at left iliac region to suprapubic, no abnormality on liver, spleen, gallbladder, kidney bilateral, vesica urinary, and no enlargement of paraaortic lymphnode. Abdominal sonography result 2 weeks before admission was in homogeneity and irregularity of pancreas head, suggestive acute pancreatitis. The patient has no past illness since birth nor family illness history of the same disease. The patient's birth by sectio caesarean delivery, a term with birth weight 2.700 gram vigorous, with no congenital abnormalities found.

On physical examination, the patient was moderately ill presentation, blood pressure 105/65 mmHg, heart rate 100 beats per minute, respiratory rate 22 times per minute, and body temperature was 36,8°C. The patient was on undernourished nutritional status with bodyweight (BW) 18 kg, body length (BL) 125 cm, weight for length was 75%. There were no jaundice nor pallor skin. The conjunctiva was not anemic with isochor pupil (diameter of 2 mm/2 mm). Lung and heart on physical examination was normal. There was no abdominal distension, liver and spleen was not palpable. Pain at right hypochondrium area but no Murphy's sign. Percussion was tympany, peristaltic sound was normal. Extremities was warm with good capillary refilling.

Laboratory investigation revealed haemoglobin count of 13,3 gr/dL, leucocyte 10.170/mm<sup>3</sup>, platelets 364.000/mm<sup>3</sup>, erythrocytes 3,67 million/mm<sup>3</sup>, hematocrit 37 %, differential count 0/0/0/88/6/6. MCV 75 fl, MCH 27 pg, MCHC 36%, sodium (Na) 137 mmol/L, potassium (K) 4 mmol/L, chloride 107 mmol/L, albumin 4,1 gr/dL, random blood glucose 76 mg/dL, AST 21 U/L, ALT 10 U/L, urea 28 mg/dL, creatinine 0,5 mg/dL. Total bilirubin 0,3 mg/dL, indirect bilirubin 0,2 mg/dL, direct bilirubin 0,1 mg/dL, urea 28 mg/dL,

creatinine 0,5 mg/dL, uric acid 7,3 mg/dL. Isothermal molecular SARS-CoV-2 test negative. Impression blood examination in normal limit. The urinalysis showed yellow colour, turbidity positive, pH 5, leucocyte 1-2/HPF, erythrocyte 0-1/HPF, cylinder hyalin negative, epitel (+), protein (+3), reduction (-), bilirubin (-), urobilinogen (-), impression was proteinuria. Chest and abdominal x-ray examination were normal. (Figure 1)



Figure 1. Chest and abdominal X-ray examination.

Patient was diagnosed as acute pancreatitis due to symptom of abdominal pain with differential diagnosis H.Pylori infection. Temporary fasting was performed while waiting for result of amylase and lipase enzyme's level. Total parenteral nutrition, antibiotic, analgetic and proton pump inhibitor was given to the patient. On the 5th day of admission, amylase and lipase enzyme's level was normal and H.Pylori antibody result was normal. Abdominal sonography (figure 2) and scanning with contrast (figure 3) impression was multiple cholelithiasis.



Figure 2. Abdominal sonography result.

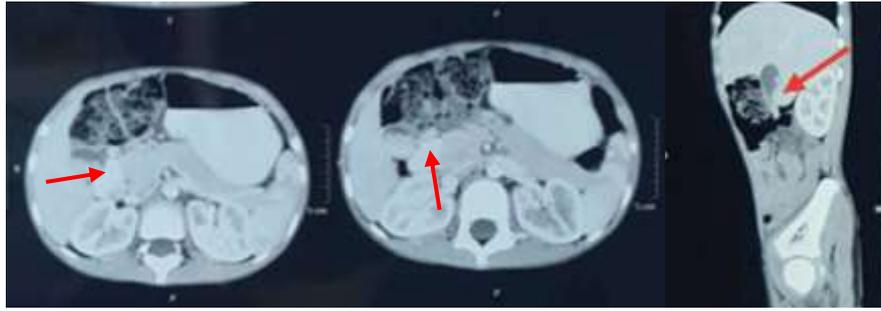


Figure 3. Abdominal scanning with contrast.

Laparoscopy cholecystectomy procedure (figure 4) was performed in this patient and patient discharge on 6 days after the surgery. Gallstones analysis revealed that the stone was brown pigmen stone with

irregular rough edge, multiple (>10 stones), each stone's size <0,5 cm, in which 93,97% Calcium bilirubinate and 6,03% Calcium carbonate. (figure 4)

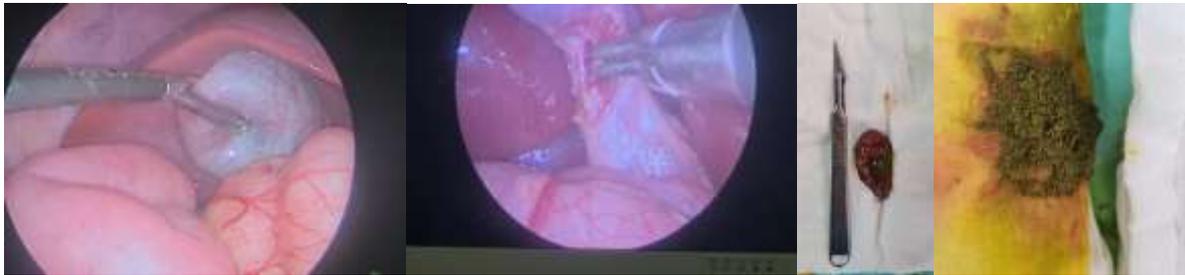


Figure 4. Laparoscopy cholecystectomy procedure and gallstones.

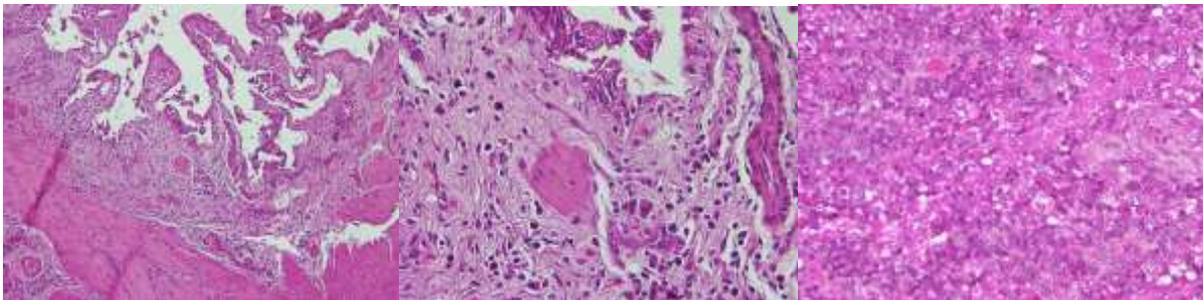


Figure 5. Histopathology of patient's gallbladder.

Anatomical pathology examination (figure 5) result was vesica felea tissue with a mucosal surface lined with columnar epithelium which is partly eroded, partly forming villi and crypts. Rokitansky-Aschoff sinuses in muscularis mucosa, lymphocyte cells, plasma cells and hyperemic capillaries. Impression of this result was chronic cholecystitis.

## DISCUSSION

There have been reported case a 7 years 2 months old boy has hospitalized with a diagnosis suspected acute pancreatitis, differential diagnosis was H. Pylori

infection. The working diagnosis was established based on the detailed history of abdominal pain, in this period and last hospitalized, which are the same symptom and has been known by abdominal sonography a month ago. Repeated abdominal sonography in recent hospitalized found multiple cholelithiasis and confirmed by abdominal scanning with contrast.

Most of cholelithiasis in children are asymptomatic<sup>7</sup> and only 0.13% cases which is symptomatic; abdominal pain (34%), jaundice (18%), and vomiting (8%).<sup>10-12</sup> The most common complaints in younger

children are nausea and vomiting. The classic right hypochondriac pain is more common in adolescents than younger children. This classic pain includes sharp abdominal pain radiating to right shoulder and scapula, most often appears after eating fatty foods and can last several hours.<sup>14</sup> Cholelithiasis can be symptomatic if it causes cholestasis, cholecystitis, and cholangitis.<sup>8,13</sup> In accordance with these clinical findings, this patient with classic complaints of abdominal pain and vomiting. Idiopathic cholelithiasis, with no identifiable risk factors, has been reported for 23.2% - 52.5%.<sup>5</sup> On the other hand comorbidities that are often found in cholelithiasis patients are hepatitis (30.8%), choledocholithiasis (16.9%), cholecystitis (16.9%), and acute pancreatitis (6.2%).<sup>12</sup> Acute pancreatitis was found through abdominal ultrasound examination. Cholecystitis condition was found by anatomic pathology examination after surgery procedure. Several studies have found that gallstones, especially cholesterol stones, are associated with obesity in children<sup>12</sup> but patient was malnourished whose not related with cholelithiasis. Another risk factor associated with cholelithiasis is children who received long total parenteral nutrition, resection of bowel, girls taking hormonal contraceptives,

hemolytic disease (sickle cell anemia, spherocytosis), cystic fibrosis, chronic liver disease, Crohn disease, prematurity with surgical or nonsurgical complications, and cancer treatment in child.<sup>7,15,16</sup> Ethnic factor also play a role in the development of gallbladder stones, for example the incidence of cholelithiasis is high in the Pima Indians of America and the indigenous peoples of Chile and Peru.<sup>7</sup> Another factor that is associated with cholelithiasis and cholecystitis is the presence of Helicobacter pylori infection in gallbladder tissue and bile fluid. This patient's H.Pylori's antibody was negative either only Helicobacter DNA in gallbladder tissue has statistically significant relationship with the incidence of cholelithiasis, which means it must be examined by PCR method.<sup>7</sup> Gallstones are divided into two types; cholesterol and pigment stones. Pigment stones are further divided into two, namely black and brown stones (table 1)<sup>1,2,7</sup> The composition of cholelithiasis is a mixture of cholesterol, bile pigments, calcium and inorganic matrix.<sup>7</sup> The risk factors affect the formation of different stones according to stone's type. This patient with brown pigment stones which are related to inflammation and infection.

**Table 1. Difference of cholesterol stone, black pigmen stone and brown pigmen stone.<sup>7</sup>**

Characteristic	Cholesterol Stone	Black pigmen stone	Brown pigmen stone
Color	Light yellowish, brownish	Black	Brown-orange
Consistency	Hard, layered crystal, dark core	Hard, shiny	
Amount, size and sharpness	Multiple: 2-25 mm, small Soliter: 2-4 cm, small	Multiple: <5 mm,irregular shape, small	Multiple: 10-30 mm, round, small
Composition	Monohidrat cholesterol >50%, glycoprotein, Ca salt	Pigmen polymer 40%, Ca salt 15% (carbonat, phosfat), Cholesterol 2%, other composition 30%	Bilirubinatan Ca 60%, Palmitat Ca fatty acid soaps-stearate 15%, Cholesterol 15%, other composition 10%
Radiodensity	Lucent	Opaque 50%	Lucent
CT Scan (Hounsfield unit)	<20-60	>40	60-140
Location in biliary system	Gall bladder, biliary ductal	Gall bladder, intrahepatic biliary ductal	Ductal
Clinical association	metabolic, no infection, no inflammation	Hemolysis, sirosis, parenteral nutrition	Infection, infestation of parasite, inflammation

The chemical composition and the presence of lipids in bile play an important role in process of stone formation. Both are insoluble to water, in bile bound to bile salts

with 70-80% of bile lipids. Approximately 8% of bile lipids are in the form of cholesterol and 15-20% are phospholipids. Pigment stones are a mixture of insoluble

calcium salts, consisting of calcium bilirubinate, calcium phosphate and calcium carbonate. Cholesterol in pigment stones is small amounts; 10% in black pigment stones and 10-30% in brown pigment stones.<sup>7</sup> No cholesterol was found in this patient's gallstone.

Black pigment stones are commonly found in patients with cirrhosis or chronic hemolytic diseases such as thalassemia and sickle cell anemia. Composition of the stones in this patient are calcium bilirubinate (93,97%) and calcium bicarbonate (6,03%) (Picture 4). Brown pigment stones are often associated with infection, in accordance this patient had greenish brown stone and history of acute pancreatitis. This type of stone also causes a lucent radiodensity and not seen on abdominal X-rays due to lower calcium phosphate and carbonate levels.<sup>6,7</sup>

The diagnosis of cholelithiasis is obtained from anamnesis, physical examination, and supporting examinations.<sup>5,8</sup> Cholelithiasis is often diagnosed incidentally on ultrasound.<sup>8,13</sup> Transabdominal ultrasound is the diagnostic imaging option with a sensitivity and specificity of more than 95% for detecting stones. The sensitivity of ultrasound to detect gallstones in children is lower than in adults due to the difficulty in examining an uncooperative child. In addition, ultrasound can identify hepatic and common duct involvement, other abnormalities of the liver and pancreas. Endoscopic ultrasound can help identify stones that are not visible on transabdominal ultrasound.<sup>7,8,14</sup>

Treatment of cholelithiasis is influenced by several factors, such as anatomical status of the stone, level of symptoms in the children, underlying cause of stone formation, inflammatory changes in the bile, and the age of the child.<sup>8,12</sup> Stones located in the common bile duct (CBD) or around the pupillary sphincter can cause cholangitis, bile flow obstruction, and jaundice in children, which definitely requires stone removal.<sup>8</sup> In addition, for symptomatic cases of cholelithiasis, treatment is usually

curative, ie by surgery.<sup>5,14</sup> In the case of cholecystitis and cholangitis, after administration of antibiotics, serum therapy, and monitoring of vital signs, it is advisable to remove gallstones (preferably by laparoscopy) as soon as possible.<sup>8</sup> Laparoscopic cholecystectomy has been shown to be safe and efficient. Cholecystectomy is appropriate in cases requiring acute gallbladder drainage and in severe cases.<sup>5,8</sup>

Whereas in asymptomatic patients or patients who have small stones, given the low complication rate, it is sufficient to monitor the child's clinical periodically and also serial ultrasound examinations every 3 months for at least 1 year. In most cases, gallstones will resolve spontaneously.<sup>5,8</sup> In the case of a child receiving TPN, the child should be supervised because of the time limit for using TPN. Discontinuation of TPN and initiation of oral nutrition will resolve the gallstone gradually. However, in more severe cases, where TPN must be continued, the therapeutic approach of cholecystectomy is chosen.<sup>8</sup>

The criteria for treatment with Ursodeoxycholic acid (UDCA) are cholesterol rich, noncalcified gallstones <20 mm in diameter, and patent cystic ducts.<sup>12</sup> It decreases cholesterol by inhibiting intestinal absorption and biliary cholesterol secretion.<sup>16</sup> However, their use is limited due to prolonged treatment and side effects such as diarrhea and liver disorders.<sup>5,8</sup> Use of UDCA should be continued for 3 months after the stone is crushed to ensure there are no microscopic stones that might not be detected by ultrasound.<sup>12</sup>

Administration of hydroxyurea has been shown to be useful in reducing the frequency of cholelithiasis in some hemolytic diseases, such as in thalassemia. Extracorporeal shock-wave lithotripsy (ESWL) is another method that can be applied to either asymptomatic patients or radiolucent stones. Although this procedure gives satisfactory results in adults, it appears that children are faced with some limitations regarding its side effects, such as

intravenous hemolysis, duodenitis, nausea, and vomiting.<sup>8</sup>

There are no special guidelines have defined indications for medical or surgical treatment in children with cholelithiasis. Therapeutic approach for cholelithiasis were seen in table 2.<sup>10</sup> Medical treatment could dissolve of stone until 30,8% in 1-6 months therapy.<sup>12</sup> Cholecystectomy is gold standard therapy for cholelithiasis.<sup>7</sup> Indications for cholecystectomy are cholelithiasis, complicated obstructive disease (cholelithiasis with pancreatitis or choledocholithiasis or dilatation of common bile duct, and icteric condition), and abdominal pain in right upper quadrant that persisted despite receiving medical treatment for more than one week.<sup>12</sup> Indication of laparoscopy cholecystectomy in this patient was multiple cholelithiasis with persistent abdominal pain more than one week.

The complication rate in cases of cholelithiasis is quite low at 8.6%. Complications of cholecystitis are cholecystitis and pancreatitis, which are caused by obstruction of the gallstones.<sup>8,13</sup> Complications of cholecystectomy such as bleeding, infection, bile duct injury, ileus, and pancreatitis.<sup>3</sup> Stones with a larger size will be at risk for causing gallbladder carcinoma.<sup>8</sup> The incidence of relapse in cholelithiasis reaches 10.8%.<sup>12</sup>

## CONCLUSION

The case initially suspected as acute pancreatitis due to symptom and previous sonography examination. Normal level of amylase and lipase enzyme rescinded this diagnosis. Repeated abdominal sonography examination inadvertently found multiple cholelithiasis in accordance with the study about the increasing incidence of cholelithiasis by increasing use of ultrasound. Abdominal scanning with contrast leads the multiple cholelithiasis confirmed.

Cholelithiasis could not be known certainty through symptoms and physical examination but we could use

complementary modality to confirm it. Faster diagnosis will reduce morbidity and accelerate which therapeutic approach will be taken. Education related to feeding habit and intake of fat soluble vitamins must be conveyed in detail to children and parents because this condition will last a lifetime especially for children after cholecystectomy.

## Declaration by Authors

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