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Case Report

A rare case report of acute acalculous cholecystitis in active chronic hepatitis C virus infection

Putu Indri Widiani*, Nyoman Angga Santosa, I. Made Suma WIrawan

Department of Internal Medicine, Wangaya Regional Hospital, Denpasar, Bali, Indonesia

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***Correspondence:**
Dr. Putu Indri Widiani,
E-mail: indriiwidiani@gmail.com

ABSTRACT

Acute acalculous cholecystitis (AAC) is an inflammation of gallbladder with absence of gall stones or bile sludge. Daily cases reported about 90-95% of the acute cholecystitis present with gall stone, while only 5-15% occur without gall stones obstruction. AAC is reported associated with Epstein bar virus infection, hepatitis B virus and hepatitis A virus. Hepatitis C-induced AAC cases still rare. This case report presents a 49-years-old female patient with epigastric pain, nausea, yellowish sclera, tea urine color, pale stool and there was a history of the patient's husband with hepatitis C. On physical examination there was epigastric and right hypochondriac pain, and positive murphy sign. There was leukocytosis, hyperbilirubinemia and an increase in SGPT (1.360 U/L) and SGOT (1.720 U/L). Antibodies to HCV were positive. Abdominal ultrasonography showed cholecystitis with no biliary duct dilatation and no parenchymal liver disease appearance The patient was diagnosed with acute chronic hepatitis C and cholecystitis. Pathophysiology of hepatitis C induced AAC is not fully understood, but is thought to be due to complexes immune, directly infect gallbladder and proximal biliary epithelial cells uncontrolled, increased portal/septal myofibroblasts activity and inflammation. The presence of AAC with an increase in serum levels of SGOT and SGPT 5-10 times the normal limit should be suspected due to acute hepatitis viral infection. Further research still needs to be done to determine the relationship between hepatitis C and the incidence of AAC.

Keywords: Acute acalculous cholecystitis, Active chronic hepatitis C, Hyperbilirubinemia

INTRODUCTION

Cholecystitis is an inflammation of the gallbladder, which may occur acute or chronically. It is usually due to ductal obstruction by the gall stone which leads to distension and edema of the gallbladder.

From studies, it is said that 90-95% of the acute cases are calculous cholecystitis (ACC), only 5-15% of the cases occur with absence of stone obstruction or sludge, namely AAC.[1] AAC cases usually associated with risk factors, such as immunosuppression, ampullary stenosis, choledochal cyst, severe hypotension, sepsis, ischemia, and total parenteral nutrition.[2,3] The cases of AAC with underlying infection which mostly reported are associated with Epstein bar virus, hepatitis B virus and hepatitis A virus. While AAC cases associated to hepatitis C virus (HCV) infection are still rarely reported.[4] Studies stated that ischemic injury of gallbladder epithelium due to ongoing inflammation and the detergent effects of bile on the epithelium play a major role in the pathogenesis of acalculous cholecystitis.[2] In condition of occurring acute hepatitis, the parenchymal inflammation may lead gallbladder wall edema which may induces ischemia event and slowing the bile clearance which may lead to the formation of bile sludge. In radiologic examination, gallbladder wall thickening may be seen.[3,4] It is hypnotized that hepatitis B virus (HBV) infection may trigger the immune complex deposits located in the vessel walls of the gallbladder which may lead to necrotizing

vasculitis, same principal is thought to occur in HCV infection as well, therefore further studies are needed.[2,3]

Acalculous cholecystitis case associated with acute viral hepatitis may have different outcomes. Case studies stated that some of these are mild which self-limiting and heal spontaneously, while a limited number of cases progress to a chronic cholecystitis or even severe condition such as gallbladder perforation, gangrenous state, and death.[2,4] In this report, we present a case of AAC associated with hepatitis C virus (HCV) infection, especially active chronic hepatitis C case.

CASE REPORT

A 49-years-old female patient referred to emergency department in Wangaya general hospital, Bali, Indonesia on September 21st 2021 with epigastric pain. The symptom began for 10 days before referred to hospital, it was come and go by itself so the patient didn't take any medicine to treat it. The modifying factors of her symptom were unclear. For two days before hospitalized, she said that her sclera turned yellowish. Epigastric pain was getting worse and persist followed by nausea since morning before admission to the hospital. There was no fever or vomiting, but she said that the urine color was like tea and her stool was pale coloured.

There was no history of same symptom before, history of systemic disease or surgery were denied. Any smoking or alcohol consumption habit was denied as well. She has neither skin piercings nor tattoos. History of using injection drugs was denied. She often consumes fatty foods which made from pork. The patient work as a "Canang" (prayer equipment) seller in the market in daily living. She is a widow, her husband passed away about 10 years ago from suffering chronic hepatitis C. Recent months sexual activity history is denied. The patient said that she rarely gets sick, even if she sick, she usually takes oral medicine, no history of treatment using injection drugs. The last time she had an injection was during COVID-19 vaccination, using AstraZeneca vaccine, together with other sellers in the market about 2 months ago.

The patient was in good contact but seemed physically weak. Vital signs examination showed the blood pressure was 130/82 mmHg, pulse rate 92 bpm, respiratory rate 18 times per minute, axillary temperature was 36.6 degree Celsius, oxygen saturation was 98% on room air. On physical examination, her sclera and palm were icteric, pain in palpation in epigastrium and right hypochondrium region (positive Murphy's sign), remainder of physical examination was within normal limit. On complete blood count evaluation showed thrombocytosis (thrombocytes count $414x10^3$/ul), blood glucose and electrolytes evaluation within normal limits. Other laboratory test (Table 1) known that liver function test showed elevated bilirubin level followed by highly elevated transaminase enzymes, blood urea nitrogen and serum creatinine level were within normal limits, abdominal ultrasonography (Figure 1) showed a thickening gallbladder wall which was suggestive of inflammation process, no biliary duct dilatation, no sign of obstruction or bile sludge, and no parenchymal liver disease appearance. Serologic test was positive for anti-HCV.

Table 1: Laboratory investigation result.

Lab investigation	Result	Units	Reference range
Total bilirubin	8.24	mg/dl	0.20-1.20
Conjugated bilirubin	7.36	mg/dl	0.00-0.50
Unconjugated bilirubin	0.88	mg/dl	0.00-0.07
SGPT/ALT	1.360	U/l	5-34
SGOT/AST	1.720	U/l	0-55
BUN	10.75	mg/dl	6.5-17.8
Creatinine	0.88	mg/dl	0.55-1.02
Anti-HCV	Positive	-	Negative
HBSAg	Negative	-	Negative

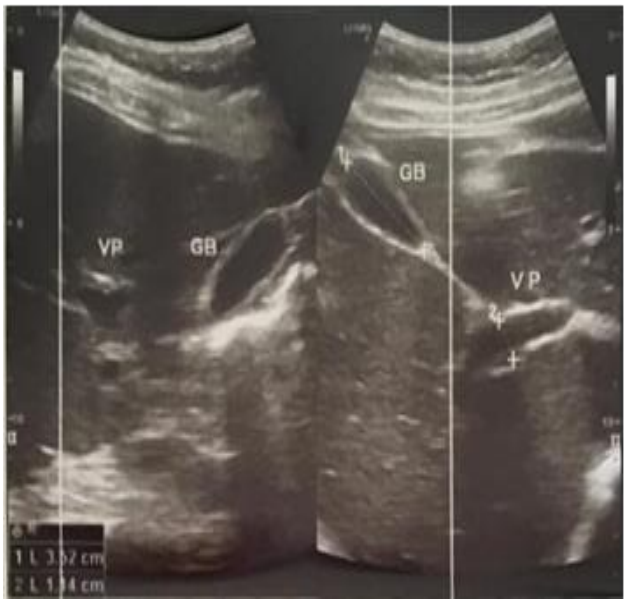

Figure 1: Abdominal ultrasonography of a thickening gallbladder (GB) wall with no sign of obstruction or bile sludge.

According to history taking, physical examination, laboratory and radiology evaluation, the patient was diagnosed with AAC and active chronic hepatitis C. Thus, she was treated with supportive treatment with intravenous fluid NaCl 0.9% with maintained drops, ondansetron and pantoprazole, third-generation cephalosporin antibiotic intravenously, hepatin tablet (contain curcuminoid, silymarin phytosome, echinacea extract, choline bitartrate, and vitamin B6). Ursodeoxycholic acid (UDCA) to treat hyperbilirubinemia. Gradually, the epigastiric pain and nausea got better on following days and the patient

started to eat well. The icteric got better as well after four days of hospitalization, no more yellowish color on her palms only seemed just a little look on her eyes. Liver enzymes level was decreased by more than half compared to the initial laboratory result after seven days of hospitalization. She was able to discharge from hospital and undergo outpatient treatment. The patient was planned to undergo HCV RNA test as well and get antiviral treatment according the result of it.

DISCUSSION

This case report is discussed about patient with active chronic hepatitis C which inducing AAC. Hepatitis C is a dangerous disease of liver, it is caused by hepatitis C virus (HCV). This virus is an RNA virus and the member of the *Flaviviridae* family. In acute hepatitis C virus does not give fulminant complaints, so many people are underdiagnosed and viral infections are only known when they have given serious complaints which caused liver damage.[5-7]

In this case report, the patient complained of yellowish sclera, nausea, vomiting, epigastric pain, urine colour was like tea and her stools was pale. On physical examination and ultrasound of the abdomen showed cholecystitis. High level of SGOT and SGPT indicate to evaluate the viral infection in patient then we got antibody against HCV is positive. Her husband died 10 years ago because of hepatitis C, so there is a possibility of sexual transmission to patient. In this case, SGPT (1.360 U/L) and SGOT (1.720 U/L) liver enzymes in this case were very high which increased more than 10 times from normal limit. This indicates an active infection. In this case, the level of SGOT was higher than that of SGPT which indicated that mitochondria or liver parenchyma had been damaged and it is possible that the infection has been going chronically.[8]

AAC is inflammation of the gallbladder that occurs due to blockage of the cystic duct or impaired emptying of the gallbladder that is not caused by gall stones.[9] Cases of AAC are rare and the pathogenesis is yet to be studied. Based on studies, AAC may cause by hypoalbuminemia, hepatomegaly due to acute inflammation, and high portal venous pressure causing gallbladder wall oedema which can decrease perfusion of tissues. The inflammatory process that continues to occur in the gallbladder tissue can cause necrosis of the wall of the gallbladder.[10,11] On the histological picture that compares between ACC and AAC, the AAC shows biliary infiltration into the mucosa and muscular layers, leukocyte arterial margination with non-thrombotic hypoperfusion (ischemia), focal lymphatic dilatation with interstitial oedema, and less epithelial degeneration (necrosis).[12]

The most reported cases of AAC were associated with Epstein bar virus infection, hepatitis B virus and hepatitis A virus. Cases of AAC induced by hepatitis C virus infection are very rarely reported.[4,13,14] Pathophysiology of hepatitis C induced AAC is not fully understood. Hypothesis of immune complexes causing ischemic injury to the muscular and serous layers of the gallbladder described in cases of hepatitis B with cholecystitis, and is thought to occur in chronic HCV infection as well.[15-18] HCV is also suspected to directly infect gallbladder and proximal biliary epithelial cells because it has toll-like receptor-4 (TLR4) expression, which is associated with hepatic inflammation.[19,20] Therefore, it is further postulated that ongoing uncontrolled viral replication may result in increased portal/septal myofibroblasts activity and inflammation, resulting in AAC.[20]

AAC with increase serum levels of SGOT and SGPT which increases 5 to 10 times from normal limit, or more, should be susceptible caused by acute hepatitis viral infection. Pathophysiology and pathogenesis of AAC induced by HCV infection still requires further research.

CONCLUSION

AAC is inflammation of the gallbladder that occurs due to blockage of the cystic duct or impaired emptying of the gallbladder that is not caused by stones. Cases of AAC are very rare and the pathogenesis is yet to be studied. The presence of AAC with an increase in serum levels of SGOT and SGPT 5-10 times the normal limit should be suspected due to acute viral infection such as HCV infection. Pathophysiology and pathogenesis of AAC induced by HCV infection is not clear yet and still requires further research.

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