Mirizzi Syndrome in Gallstone Complication

*Ario Perbowo *, Dadang Makmun ***

* Department of Internal Medicine, Faculty of Medicine, University of Indonesia
Dr. Cipto Mangunkusumo General National Hospital, Jakarta
** Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine,
University of Indonesia/Dr. Cipto Mangunkusumo General National Hospital, Jakarta

ABSTRACT

Mirizzi syndrome is a rare complication of gallstone which is characterized by the presence of gallstone impaction in cystic duct that leads to inflammatory stricture in the biliary duct and results in obstructive jaundice. In this report, we highlighted the diagnostic approach and management of Mirizzi syndrome in a 58 year-old male complaining of nausea, vomiting, and appearing jaundice. The role of imaging such as abdominal ultrasonography in depicting the characteristics of Mirizzi syndrome was also discussed and compared the findings with the classification of the disease in the literature. In this patient, Mirizzi syndrome was suspected by the appearance acoustic shadow in the gallbladder with dilated cystic duct suggesting the impaction of common bile duct (CBD). We performed endoscopic retrograde cholangiopancreatography (ERCP) as both diagnostic and therapeutic modalities by which we allowed sphingterectomy to evacuate the gallstone. However, due to the risk of further stone evacuation, the procedure was followed by elective cholecystectomy.

Keywords: *gallstone, Mirizzi syndrome, complication*

ABSTRAK

Sindrom Mirizzi adalah komplikasi dari penyakit batu empedu yang jarang terjadi dengan karakteristik adanya impaksi batu empedu di duktus sistikus sehingga menghasilkan striktur inflamasi di saluran empedu dan menyebabkan ikterik obstruktif berkelanjutan. Dalam laporan kasus ini dibahas pendekatan diagnostik dan tata laksana sindrom Mirizzi pada pasien laki-laki berusia 58 tahun dengan keluhan mual, muntah, dan jaundice. Peran dari pencitraan seperti ultrasonografi abdomen dalam menggambarkan karakteristik sindrom Mirizzi juga didiskusikan dan membandingkan temuan pada kasus ini dengan klasifikasi penyakit pada literatur. Pada pasien ini, sindrom Mirizzi diduga dari penampilan bayangan akustik di kandung empedu dengan saluran cystic dilatasi yang mensugestikan impaksi dari saluran empedu. Endoscopic retrograde cholangiopancreatography (ERCP) dilakukan sebagai modalitas diagnostik dan terapeutik dimana sfingterektomi dapat mengevakuasi batu empedu. Namun dikarenakan risiko evakuasi batu lanjut, prosedur diikuti oleh kolesistektomi elektif.

Kata kunci: *penyakit batu empedu, Sindrom Mirizzi, komplikasi*

INTRODUCTION

Gallstone disease has been an important health problem in western countries. Estimated prevalence of gallstone disease is approximately 10-15% and increases in elderly. While in Indonesia, the number is still unclear due to the limited publications. Most gallstones do not cause disease and do not need treatment. Gallstone disease is the main reason of hospitalization for surgical treatment. In the United States, every year more than 1 billion USD is spent for gall stone treatment, particularly for 500.000 cholecystectomy procedures which are performed every year. Risk of patients with gallstone to experience symptoms and complication is relatively small. However, after the stone started to cause specific biliary colic, risk of problems and complication increase gradually.[1]

Mirizzi syndrome is complication of gallstone disease which rarely happened. It usually occurs in 1% of all patients who suffer from cholelithiasis. This syndrome was firstly explained in 1948 with signature characteristics, which was the presence of gallstone impaction in cystic duct or in the neck of gallbladder, which then leads to mechanical obstruction in hepatic duct and cause inflammatory stricture in the biliary duct, thus further causes continuous obstructive jaundice.[2] Perioperative diagnosis in this condition is important. Intraoperative findings may resemble extrahepatic biliary malignancy, hence require further approach. Cholecystobiliary and cholecystoenteric fistulasdue to the gallstone impaction might cause postoperative complication which actually could be prevented by monitoring previous condition. Ultrasonography (USG) and computed tomography (CT) have currently been used as primary evaluation methods in obstructive jaundice. Similar condition also applied to endoscopic retrograde cholangiography (ERC).[2] Currently, minimally invasive therapy is important to treat gall stone. Doctor has to know various imaging modalities which have been developed. In this case report, we will discuss about the diagnostic approach and management of Mirizzi syndrome as one of the forms of obstructive jaundice caused by gall stone.

CASE ILLUSTRATION

A 58 year-old male patient came to Cipto Mangunkusumo Hospital with the complain of nausea and sometimes accompanied with vomiting 1-2 times per day for less than 100-200 mL in the form of food and yellowish liquid a month before hospital admission. Nausea and vomiting was described to be not meal time dependent. Patient denied the presence of stomachache. Pale colored stool and tea-like color urine were also being complained by the patients. Patient's eyes and skin also looked yellowish. Patient also complained of fever which present at nights, although the temperature was not too high. Patient also complained of itchiness in the entire body. Patient's body weight decreased 5 kg in the last month. Because of these complaints, patient visited Internal Medicine Outpatient Ward in Cipto Mangunkusumo Hospital and abdominal USG was performed, and it was concluded that there was stones in the gall bladder and duct. Patient was advised to undergo endoscopic retrograde cholangiopancreatography (ERCP).

Previously patient never experienced liver disease or jaundice. Patient also denied if he ever suffered from blood abnormalities or malignancy. Patient denied the presence of allergy. Patient did not suffer from diabetes mellitus and hypertension. None of the patient's family also ever suffered from malignancy, diabetes mellitus, or hypertension. Patient did not have smoking habit, alcohol consumption, or intravenous drug user, or blood transfusion history. In daily basis, patient was not exposed to radiation or chemical agent.

Physical examination of the patient at the time of admission, patient looked moderately ill, consciousness compos mentis, blood pressure 120/80 mmHg; heart rate 88 beats per minute (bpm), regular; respiratory rate 20 breaths per minute, regular, abdominothoracal respiratory pattern; axilla temperature 36.5^{o}C. Conjunctiva looked pale, icteric sclera, no palpebral edema. Skin looked icteric. Ears, nose, and throat were within normal limits. Jugular venous pressure 5-2 cmH_2O, lymph nodes not palpable. On the chest, no spider nevi was found. In both lungs, vesicular breath sound was found, without rhonchi or even wheezing. In heart examination, there was no cardiomegaly, normal first and second heart sound without the presence of murmur or gallop. Flat abdomen, with no presence of caput medusa, tender, no pain on palpation, timpani on percussion, negative shifting dullness, and normal positive bowel sound. On extremities, there was no edema or palmar erythema.

Laboratory results of the patient upon admission to the hospital include hemoglobin 13.5 g/dL, hematocrit 38.7%, leukocytes 9.170/uL, thrombocytes 393.000/uL. Mean corpuscular volume (MCV) 84.3 fL, mean corpuscular hemoglobin (MCH) 29.4 pg, mean corpuscular hemoglobin concentration (MCHC) 34.9 g/dL. In differential count examination basophil 0.7%, eosinophil 3.4%, neutrophil 71.7%, lymphocytes 16.2%, monocytes 8%. Aspartate transaminase (AST) 50 U/L, increased alanine transaminase (ALT) 103 U/L, increased total bilirubin 20.28 mg/dL, increased direct bilirubin 19.12 mg/dL, increased indirect bilirubin 1.16 mg/dL, ureum 24 mg/dL, creatinine 0.9 mg/dL, random blood glucose 111 mg/dL, sodium 135 mmol/L, potassium 3.81 mmol/L, and chloride 93.5 mmol/L. From peripheral blood smear, normocytic normochromic erythrocytes were found, impression of adequate leukocyte count, normal morphology, increased thrombocyte count, positive giant thrombocyte, positive clumping, and thrombocytosiswith leukocytes shift to the left. Reticulocyte level was not increased. Prothrombin time (PT) 11.3 with control 12.1, activated partial thromboplastin time (APTT) 38.5 with control 32.1,

uric acid 5.5 mg/dL, increased total cholesterol 344 mg/dL. Non-reactive anti hepatitis A virus (HAV) IgM, non-reactive HBsAg, non-reactive anti hepatitis C virus (HCV). In this patient, there was decreased level of total protein level as much as 6.3, with increased amylase 122 U/L and lipase 144 U/L. Normal C-reactive protein (CRP) 5.0 mg/L and CA 19 - 92.0 U/mL were also within normal limits.

From the results of abdominal USG (Figure 1), it was concluded that there was cholelithiasis, distal choledocholithiasis of the common bile duct (CBD) with dilatation of intrahepatic gall duct and CBD.

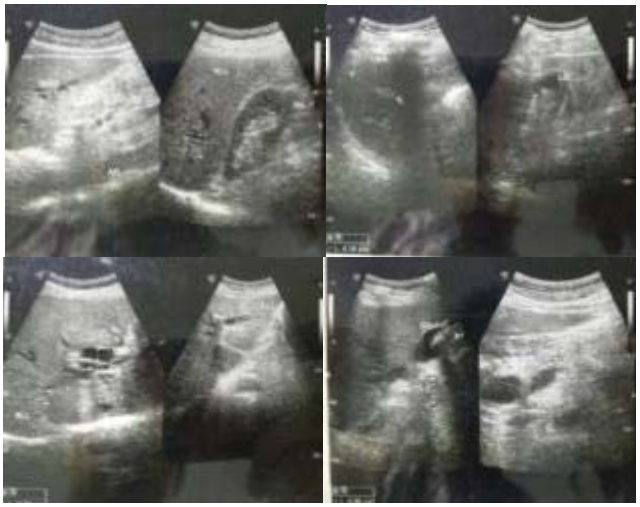

Figure 1. Abdominal ultrasonography revealed hyperechoic lesion in the gall bladder with the diameter of 0,96 cm with acoustic shadow. In intrahepatic gall duct, dilatation was present. The common bile duct was dilated, with hyperechoic lesion with the diameter of 1.16 cm with acoustic shadow

During hospitalization, patient was given low fat, soft diet 1700 kcal. Because the patient's intake was not adequate, he was also given additional parental nutrition Triofusin E 1000 per 12 hours and Asering 500 cc per 12 hours. Empiric antibiotic was administered intravenous Cefoperazone Sulbactam 1 g three times daily for 7 days. Other supportive therapies include intravenous Omeprazole 40 mg twice daily, oral Domperidon 10 mg three times per day, oral Curcuma 200 mg three times daily, oral ursodeoxycholate acid 250 mg three times daily, oral Simvastatin 20 mg once daily, and oral Cetirizine 10 mg once daily. ERCP which was performed a month later revealed dilated common bile duct and left and right hepatic duct. There was small image of stone in CBD and a quite large shadow of stone in further evaluation was suspected to be located in the cystic duct. Gallbladder was visualized accompanied with image of stone within it and appearance of dilated cystic duct which gave impression of suppressing CBD. Sphingterotomy

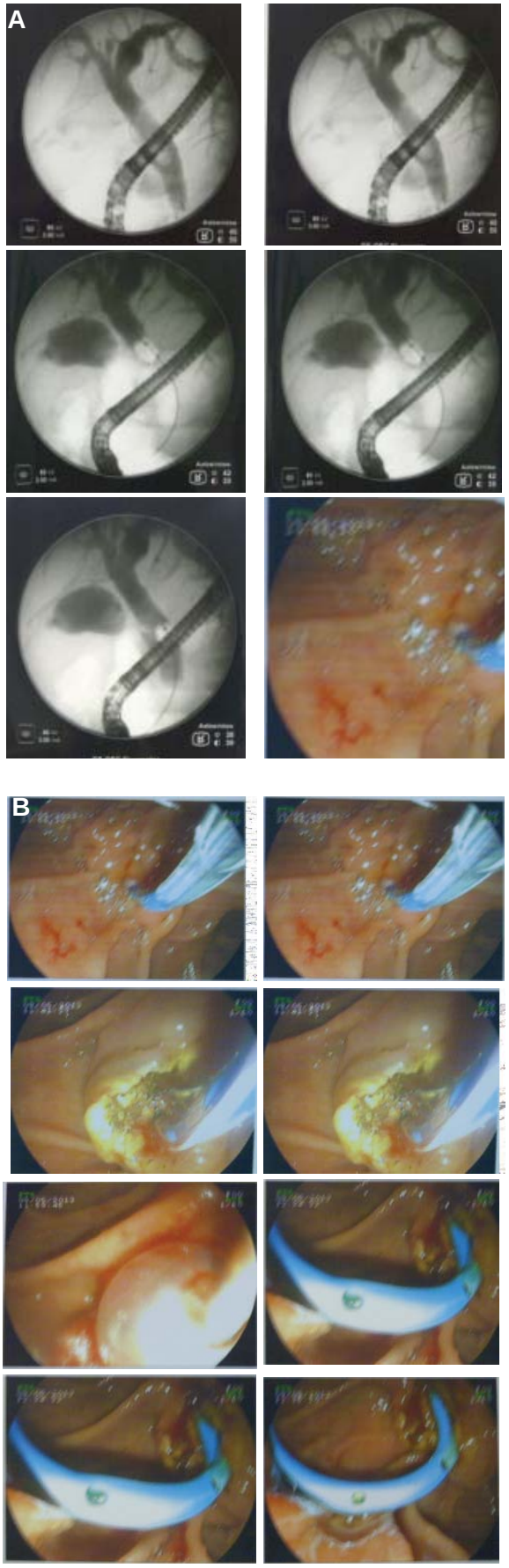

Figure 2. Endoscopic retrograde cholangiography exhibited dilated common bile duct and left and right hepatic duct (A and B)

was performed and continued with ductal clearance using balloon and basket. Only several small stones came out from the CBD. To the patient, stenting were performed using 10 fr 7 cm double pigtail stents. Post stenting, bile oozed. Therefore, it could be concluded that there was obstructive jaundice: suspect of Mirizzi syndrome, distal CBD stone, and cholelithiasis.

DISCUSSION

From USG results in this patient, there was hyperechoic lesion appearance with diameter of 0.96 cm with acoustic shadow in the gall bladder, dilatation of the intrahepatic bile duct, and dilated duct and hyperechoic lesion with diameter of 1.16 cm with acoustic shadow in CBD. Later, in ERCP results, there was dilated common bile duct and right and left hepatic duct. There was also small image of stone in CBD with a quite big acoustic shadow, which in further evaluation, it was suspected to be in the cystic duct. Gall bladder was visualized accompanied with image of stone within it and appearance of dilated cystic duct which gave impression of suppressing CBD. This was in line with the literature on the classification of Mirizzi syndrome, which placed the patient in type I Mirrizi Syndrome, which was external compression of the bile duct due to the bile stone which adhere to the infundibulum of the gall bladder of cyst duct.[2,3,4]

First mechanism explained that bile stone which adhere and its secondary inflammation process may close cyst duct, the adhered bile stone will struggle to enter into the bile duct and will lead to stress ulcer which will finally scrape the wall of the gall bladder and wall of the bile duct and formed fistula between lumens.[2,3,4]

Mirizzi syndrome usually occurred at the average age of 53-70 years old, with most patients were female, approximately 70% of all cases. However, this syndrome might happen in any age and in all patients with bile stone. Chronic bile stone diseases, with the average of 29.6 years, have been reported as patients with Mirizzi syndrome. Mirizzi syndrome often present in acute form, however it can also be seen in chronic form. Although the clinical symptoms of Mirizzi syndrome is unspecific, the most common form of the symptoms were obstructive jaundice (60-100%), accompanied with upper and right upper quadrant abdominal pain (50-100%), and fever in patients which were known or suspected to suffer from bile stone disease. Previous jaundice history might be present. Frequently, patients with Mirizzi syndrome came with acute cholecystitis, acute cholangitis, or acute pancreatitis.[2-6]

Recently, Mirizzi syndrome with bile stone ileus require special attention from surgeons. In this patient, although there was no specific pain in upper right quadrant of the abdomen, but there was nausea and vomiting, accompanied with not too high fever for the last month. He also realized the presence of obstructive jaundice, including yellowish eyes and skin, skin itchiness, also tea-like color urine and pale stool. The most general results of laboratory examination was the presence of hyperbilirubinemia in patient. Other abnormalities were increased level of aminotransaminase enzymes and presence of leukocytosis, also often found acute cholecystitis, cholangitis, or pancreatitis. Lately, drastic increase of tumor marker (CA 19-9) was consistently found in patients with type II or higher type of Mirizzi syndrome. Consequently, CA19-9 has to be interpreted with caution in patients with suspect of biliary malignancy, because if Mirizzi syndrome is not eliminated, patient might be diagnosed to suffer from gall bladder cancer. In this patient, there was corresponding abnormalities in the laboratory results including increased of AST, ALT, total bilirubin, direct bilirubin, indirect bilirubin, amylase, and lipase.

The differential diagnosis of Mirizzi syndrome was other obstructive jaundice, including gall bladder cancer, cholangiocarcinoma, pancreatic cancer, metastatic disease, and others.[3,5,6] In this patient, gall bladder cancer, cholangiocarcinoma, and primary sclerosis cholangitis can be excluded because from the abdominal USG and ERCP, there was no mass in the wall of gall bladder, the result of CA19-9 was not increased, and there was no stricture in the intra or even extrahepatic duct. Similarly, pancreatic cancer can also be excluded because from the abdominal USG and ERCP, there was no mass in the pancreas and there was no increase in the CA 19-9 level.

Stiff gall bladder accompanied with thickening or gall bladder with very thin wall accompanied with single large gall stone or even multiple small gall stones which adhered to the infundibulum may be seen. Dilated hepatic duct in the extrahepatic and intrahepatic above the obstruction site, and CBD will have normal size below the site of obstruction. Diagnostic accuracy reported through USG in Mirizzi syndrome was 29% with sensitivity of 8.3% to 27%.[4] In this patient, the results of the USG were the presence of acoustic shadow which showed stone in gall bladder and in CBD, there was dilatation of the intrahepatic duct and above the site of CBD obstruction.

More than 50% patients with Mirizzi syndrome were diagnosed during surgery. The surgical characteristics include the narrowing of the gall bladder with changes or dilatation of the gall bladder with wall thickening and big stone, or multiple stones, impaction in the neck of gall bladder or infundibulum, Calot's Triangle closure, and dense adhesion from subhepatic space. Intraoperative cholangiography was difficult to perform and persistent dissection in Calot's Triangle area may cause wound in the gall bladder. Intraoperative ultrasonography is reported to be useful in identifying anatomy of biliary duct and help to accurate dissection from biliary duct in the site of inflammation.[3,7]

Management of Mirizzi syndrome is important for surgeons because presurgical diagnosis is not always possible, and because this surgical management is associated with increased significant risk from bile duct injury. Additionally, severe inflammatory process with thick, hard, dense adhesion and associated with tissue swelling. The presence of cholecystobiliary fistula increases the risk of biliary duct injury. During surgery, operating Calot's Triangle may cause bile duct injury or excessive bleeding, also the appearance of other morbidities, such as: sepsis, bile duct stricture, and secondary biliary cirrhosis. Surgical management of Mirizzi syndrome does not use the exact standard and has to be tailored individually, depending on the simplicity of the case and proficiency of the surgeons' team. However, several guidelines may be pulled out and have been used for the last few years.[8-10]

Abdominal CT might identify gall bladder and measure wall thickness, and size of dilated duct. But, the presence of inflammation around the duct may be misinterpreted with the appearance of cancer. Radiology imaging from CT is not specific. The main use of CT is to exclude the possibility of malignancy in the area of portal hepatic or in the liver.[3] In this patient abdominal CT was not performed, because initially the presence of Mirizzi syndrome was not suspected in the previous physical examination and supporting examination. In the previous USG, only the appearance of stone in CBD was seen, therefore ERCP was performed to evacuate the stone. After ERCP was conducted, eventually the feature of Mirizzi syndrome was evident.

Similar to abdominal CT, to this patient magnetic resonance cholangiopancreatography (MRCP) was not performed, other than initially the presence of Mirizzi syndrome was not suspected, MRCP examination also has lower diagnostic accuracy compared to ERCP.

In addition to diagnostic tool, ERCP also allow sphingterectomy to be performed for stone extraction and facilitate other intervention such as: stenting or placing nasobiliary tube or other procedures. Candidates for surgery who are financially disadvantaged, might have interesting option with the use of ERCP to alleviate bile duct obstruction due to Mirizzi syndrome. Patient with cholangitis might benefit from pre-surgery biliary drainage as temporary procedure before definitive surgery. Generally, endoscopy management, bile drainage, stone evacuation, and stenting. Standard stone evacuation technique was usually performed, including balloon facility, mechanic lithotripsy, and electrohydraulic litotripsi. However, the morbidity and mortality of ERCP have been known, also risk has to be weighed to the benefit in patients suspected to suffer from Mirizzi syndrome.[3]

In this patient, ERCP with sphingterectomy continued with ductal clearance using balloon and basket were performed. Only several small stones came out from the CBD, later patient was stented using double pigtail stent 10 fr 7 cm. After stenting, bile oozed. However, not all stones could be evacuated due to impaction and were very risky, therefore it was decided to perform cholecystectomy. Due to evacuation of bile stone in the cyst duct was not possible with ERCP, patient was further being consulted for the consideration of elective cholecystectomy. Finally, to the patient, elective cholecystectomy was performed after eleven days of hospitalization.

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Correspondence
Dadang Makmun
Division of Gastroenterology
Department of Internal Medicine
Dr. Cipto Mangunkusumo General National Hospital
Jl. Diponegoro No.71 Jakarta Indonesia
Phone: +62-21-3153957 Facsimile: +62-21-3142454
E-mail: hdmakmun@yahoo.com