Case Report : Choledocholithiasis as Risk Factor for Klatskin Tumor: A Rare Cholangiocarcinoma

by Edward Kurnia Setiawan Limijadi

Submission date: 07-Apr-2023 03:36PM (UTC+0700)
Submission ID: 2058271451
File name: CASE REPORT CHOLEDOCHOLITHIASIS AS RISK FACTOR FOR KLATSKIN.pdf (549.36K)
Word count: 2904
Character count: 15593

JURNAL KEDOKTERAN DIPONEGORO
(*DIPONEGORO MEDICAL JOURNAL*)
Online http://ejournal3.undip.ac.id/index.php/medico
E-ISSN : 2540-8844
DOI :
JKD (DMJ), Volume 12, Number 1, January 2023 :

CASE REPORT : CHOLEDOCHOLITHIASIS AS RISK FACTOR FOR KLATSKIN TUMOR: A RARE CHOLANGIOCARCINOMA

Edward Kurnia Setiawan Limijadi [1]*, Esa Loyallita Lestari[1]
[1]Departement Clinical of Pathology, Faculty of Medicine, Universitas Diponegoro, Semarang, Indonesia
*Corresponding Author : Email: edwardksl@fk.undip.ac.id

ABSTRACT

Background: Klatskin tumor is a rare liver cancer that involves the bile ducts. Its incidence begins to increase over time and is usually only diagnosed in patients who are already at an advanced stage. The annual incidence of klatskin tumors is not more than 1:100,000. Klatskin tumor is suspected based on signs of biliary obstruction, ultrasonography showing a stricture or bile mass, cholangiography with ERCP and MRCP, abnormal liver function tests, and elevated tumor marker CA 19-9. **Case Report**: A 65-year-old man presented to the hospital with complaints of yellowing of the eyes and body that began one month ago, as well as a lump in the right upper abdomen that had grown larger over the previous five months. Physical examination revealed yellow eyes, and a palpable lump in the upper quadrant of the patient's abdomen. The patient defecates looked like putty and urinates looked like tea. The diagnosis leaded to a klatskin tumor because the results of MRCP showed a mass in the hilar region of the liver that extended to the proximal common bile duct, which described the appearance of a klatskin tumor. There were an increasing CA 19-9 level and liver function tests. **Conclusion**: Patient has been diagnosed with klatskin tumors, has choledocholithiasis risk factor, supported by appropriate MRCP images and increasing CA 19-9 level

Keywords: *Cholangiocarcinoma, CA 19-9, Klatskin Tumors, MRCP*

INTRODUCTION

Klatskin tumor, or perihilar cholangiocarcinoma (CCA), is a bile duct tumor involving the bifurcation of the common hepatic duct but may arise from the intrahepatic (IHCCA) or extrahepatic (EHCCA) portion of the biliary tree. Klatskin tumor discovered by Gerald Klatskin in 1965, describes a tumor arising in the main bile duct, hence the name Klatskin tumor which is a special form of CCA characterized by the perihilar location of the liver processes which includes a rare condition of liver cancer involving the bile ducts[1]. Southest Asia is the region with the highest incidence of klatskin tumor cases globally and the disease is rare in the United States[2]. Factors explaining the occurrence of racial predisposition for Asians are due to the high rates of hepatolithiasis and liver fluke infection in Asia[3].

The cause of Klaskin tumors is still unclear but several causative risk factors have been identified. The infection appears to be closely associated with cholangiocarcinoma development in Asian countries[2]. Liver flukes, including Clonorchis trematode and Thai liver flukes, can chronically infect the bile ducts and lead to the development of cholangiocarcinoma[4]. Other risk factors associated with Klatskin tumors include alcoholism, hepatitis B and hepatitis C viruses, chronic pancreatitis, primary sclerosing cholangitis, choledochal cysts, liver fluke infections (Clonorchis sinensis and Opisthorchis viverrini), and cholelithiasis (intrahepatic bile duct stones)[5]. Klatskin tumors mostly are sporadic without clear predisposing factors[6].

Therefore, this case report discusses the Klatskin tumor, which has an ad malam prognosis, with surgical therapy as a curative measure. To the researcher's knowledge, there have only been two cases of Klatskin tumor published in Indonesia, where this case report was written in Indonesia for the third time after the case report in Palembang in 2018.

CASE PRESENTATION

A 65 years old man, came to the emergency room of RSUP Dr. Kariadi hospital with symptoms such as jaundice in body and eyes. Other symptoms that found in patient is a lump in the upper right abdomen for the past five months, initially small and gradually getting bigger. Defecation had a putty-colored stool with normal consistency, not liquid, urinating had a tea-colored color, and intermittent right upper abdominal pain. There were no symptoms like fever, nausea, or vomiting, and there was no history of alcohol consumption, smoking, or hepato-toxic drugs.

Patient in composmentis consciousness, blood pressure was 100/60 mmHg, pulse rate of

JURNAL KEDOKTERAN DIPONEGORO
(*DIPONEGORO MEDICAL JOURNAL*)
Online http://ejournal3.undip.ac.id/index.php/medico
E-ISSN : 2540-8844
DOI :
JKD (DMJ), Volume 12, Number 1, January 2023 :

89x/minute, respiratory rate of 20x/minute, and temperature of 36.5oC (axillary temperature). The patient's weight was 42 kilograms, and his height was 160 centimeters. Physical examination showed icteric skin with pale palpebral conjunctiva and icteric sclera in both eyes. In addition, on abdominal examination, a mass was palpable in the upper quadrant region, approximately 3x4 cm in size, lumpy, mobile, and well-defined. The laboratory test results are listed in Table 1.

The laboratory examination results showed normochromic normocytic anemia, mild thrombocytosis, and no eosinophilia on the peripheral blood leukocyte count, but there were prolonged coagulation studies, impaired liver function, and a CA19-9 level more than normal (normal value <37 U/mL). Meanwhile, hepatitis B and hepatitis C serological tests were negative.

Ultrasound examination of the abdomen revealed a solid mass in the right hypochondriacal region, leading to a widening of the common bile duct (CBD), suggesting that a mass of the head of the pancreas did not show any other abnormalities. Magnetic resonance cholangiopancreatography (MRCP) examination of the abdomen with contrast showed widening of the right hepatic duct (± 9.6 mm in diameter), left hepatic duct (± 11.6 mm in diameter), cystic duct (± 8.6 mm in diameter), and hydrops of vesica fellea et causa mass in the hilar region of the liver extending to the proximal CBD (size ± AP 2.89 x LL 1.5 x CC 1.9 cm). Abdominal MRCP examination also showed a predisposition to hilar cholangiocarcinoma (Klatskin tumor).

During the treatment period, the patient was programmed to undergo Endoscopic Retrograde Cholangiopancreatography (ERCP), there was stenosis in proximal CBD, according to Klatskin tumor and choledocholithiasis (secondary). A sphincterotomy was performed, and in the proximal CBD, a brush biopsy was performed, a stent was placed, and bile flowed smoothly.

A biopsy was performed during ERCP, and the results did not show malignant cells in the patient's preparations sent to the anatomical pathology laboratory. The patient received therapy with cefotaxime, ursodeoxycholic acid (UDCA), atorvastatin, and fenofibrate.

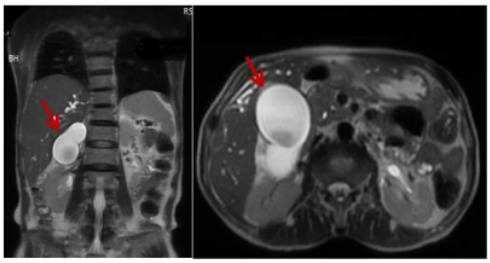

Figure 1. Abdominal MRCP shows clatskin tumor (red arrows)

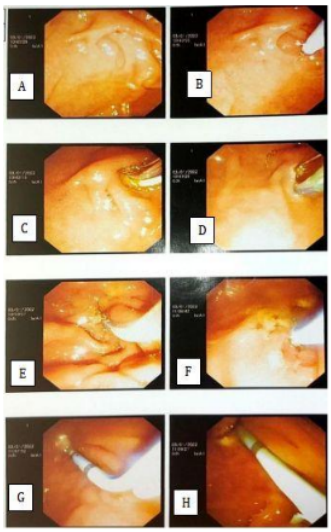

Figure 2. ERCP showed clatskin tumor. Description: (picture A shows a normal ampulla, still bile coming out, picture B cannulate the common bile duct and aspirated, picture C shows a greenish-yellow discharge, picture D shows narrowing of the common bile duct proximal and hilum, picture E shows widening of the common bile duct middle and distal, as well as right and left intrahepatal ducts, image F shows multiple filling defects in the middle 1/3 common bile duct, image G performed a sphincterotomy and a brush biopsy was performed on the proximal common bile duct, image H is a stent braided, the bile flows smoothly.)

JURNAL KEDOKTERAN DIPONEGORO
(*DIPONEGORO MEDICAL JOURNAL*)
Online http://ejournal3.undip.ac.id/index.php/medico
E-ISSN : 2540-8844
DOI :
JKD (DMJ), Volume 12, Number 1, January 2023 :

Table 1. Blood Profile Analysis

Parameter	Normal Value	Units	Day of Treatment			
			1	4	10	17
Hemoglobin	13,2-17,3	gr/dL	8,9		9,7	9,5
Hematrocit	32-62	%	27,2		29,6	28,5
Eritrocytes	4,4-5,9	$X10^{6}/\mu L$	2,86		3,17	3,08
MCH	27-32	pg	31,1		30,6	30,8
MCV	76-96	fL	95,1		93,4	92,5
MCHC	29-36	g/dL	32,7		32,8	33,3
Leucocytes	3,8-10,6	$X10^{3}/\mu L$	9,5		10,4	10,5
Trombocyte	150-400	$X10^{3}/\mu L$	544		540	561
RDW	11,6-14,8	%	18,4		18,7	17
MPV	4,0-11,0	fL	10		10,1	9,8
Protrombin Time (PT)	11-14,5	second	18,8		20,7	15,4
Activated Partial Thromboplastin Time (APTT)	24,0-36,0	second	35,3		32,9	34,3
SGOT	15-34	U/L	71		94	102
SGPT	15-60	U/L	45		49	41
GGT	5-85	U/L	206			354
Billirubin total	0,0-1,0	mg/dL	14,98	11,9	9,9	7,18
Billirubin direct	0,0-0,3	mg/dL	8,81	8,5	7,1	3,05
Billirubin Indirect	0,1-0,5	mg/dL	6,17	3,5	2,8	4,13
Total Protein	6,4-8,2	g/dL	5,4			5,2
Albumin	3,4-5,0	g/dL	2,9	2,7		2,6
Cholesterol Total	< 200	mg/dL	398			
Triglycerides	< 150	mg/dL	531			
HDL	40-60	mg/dL	11			
LDL	0-100	mg/dL	236			
Alkaline Phospatase (ALP)	50-136	U/L	541		354	
Lactate Dehydrogenase (LDH)	120-246	U/L	328			
CA 19-9	< 37,0	U/mL		130,41		

DISCUSSION

Choledocholithiasis is most often caused by cholesterol stones formed due to increased cholesterol and decreased bile acid production so that it can lead to infection and then hyperplasia and cell proliferation into malignant transformation, one of which is a Klatskin tumor[7].

Klatskin tumor diagnosed based on ultrasonography showing a stricture or bile mass and cholangiography with ERCP and MRCP, signs of biliary obstruction, abnormalities liver function tests, and elevated carcinoembryonic antigen (CEA) and carbohydrate antigen (CA) 19-9 that include as tumor markers [8-9]. Bile duct malignancies condition in patient usually led to increase in serum tumor marker concentrations of CA 19-9.

Serum tumor marker concentrations of CA 19-9 normally will also elevate in cholangitis and cholestasis condition. CA 19-9 serum has a sensitivity up to 50-60% for detecting cholangiocarcinoma in primary sclerosing cholangitis condition. Although CA19 has good sensitivity, the increase in value is not specific for only one disease. Elevated CA 19-9 level can occur in pancreatic carcinoma, cholangiocarcinoma, gastric malignancies or severe liver disorders condition with unclear cause. In addition, combined examination using CA 19-9 and CEA did not increase sensitivity[9]. In this case, there was a significant increase in the CA 19-9 value of 130.41 U/mL in this patient.

In clinical practice, liver function considered asa an important factor in the prognosis of various types of cancer, such as liver, gallbladder, and colorectal cancer. The markers of liver function include albumin, globulin, total protein, ALP, SGPT, SGOT, GGT, LDH, total bilirubin, and direct bilirubin, which are indices that can reflect liver damage. In the study of Zhang et al (2017)., an association between elevated ALP and GGT was found in patients with a poorer prognosis, which may indicate cholestatic dysfunction among patients

JURNAL KEDOKTERAN DIPONEGORO
(*DIPONEGORO MEDICAL JOURNAL*)
Online http://ejournal3.undip.ac.id/index.php/medico
E-ISSN : 2540-8844
DOI :
JKD (DMJ), Volume 12, Number 1, January 2023 :

with Klatskin tumors. However, there is no significant correlation between SGPT and SGOT on the survival rate of patients with Klatskin tumors[10]. It is consistent with the results in this case, where there was an increase in ALP, GGT, LDH, total bilirubin, direct bilirubin, and a decrease in total protein and hypo albumin.

Liver with impaired synthesis function that characterized by impaired hemostasis, where there was an increase in PT (Prothrombin Time) of 18.8 seconds and APTT (Activated Partial Thromboplastin Time) of 35.3 seconds. Impaired synthesis function in liver can lead to hemostasis disorder that were caused by reduced synthesis of coagulation factors.

Impaired hemostasis in patients with the hepatobiliary condition can cause various changes in coagulation pathways that increased fibrin and fibrinolysis formation simultaneously. It also caused coagulation decreased, thus requiring interventional treatment when bleeding occurs. Here, hepatocytes are the major site of synthesis of all the coagulation factor proteins, except for the von Willebrand factor and factor VII C. These proteins depend on vitamin K, namely factors II, VII, IX, and X, as well as factors V, VIII, XI, and XII, fibrinogen and factor XIII. Not ony intrahepatic cholestasis but also extra hepatic cholestasis can cause Vitamin K deficiency. Prenteral supplementation that contains of vitamin K for patient with Cholestasis condition can rapidly correct PT to normal values within 24-48 hours and it also can be used as a consideration in determining the diagnosis. If the coagulopathy is caused by liver disease, PT can be increased but cannot reach normal levels[9].

Result of patient hematological examination showed that patient has chronic anemia, which usually categorized as mild or moderate normochromic normocytic anemia[11]. Thrombocytosis was also found in patients whose platelet value was always more than 500 x $10^3/\mu$L, which can be caused by anemia that stimulates the bone marrow to produce more erythroid progenitors and increases the production and/or release of platelets[12].

Endoscopic retrograde cholangiopancreatography (ERCP), Magnetic resonance cholangiopancreatography (MRCP), or percutaneous transhepatic cholangiogram (PTC) are some method that can be used to perform Cholangiography. MRCP method considered to have an advantage for being non-invasive, and possible to obtain additional information about intra and extrahepatic anatomic structures. ERCP and PTC also have the advantage such as allowing bile duct sampling for diagnostic analysis, being able to evaluate the presence of biliary obstruction by insertion of a stent. In addition, choosing imaging modality to perform Cholangiography also depends on the location of tumor. Sometimes, Klatskin tumors can only be managed by placing a percutaneous stent[12].

Anatomic pathology (PA) examination did not reveal any malignant tumors. It might be due to the possibility that the sample examined is not representative. In addition, a negative result of tumor cells on PA examination does not rule out the possibility of malignancy because there is still a possibility that the tumor will not be detected[9]. In this case, the patient was discharged from the hospital after the patient's general condition improved, and the patient was scheduled for outpatient treatment.

Klatskin tumor also has a poor prognosis with a possible five-year survival rate of 10%, and most patients die within the first year. Surgery is the only curative measure. However, the percentage is quite small for tumors with the potential to be successfully treated with surgery, which is between 5-20%[13].

CONCLUSION

Klatskin tumor in this patient was diagnosed by finding jaundice on physical examination, pale stools, and dark urine. Laboratory examination revealed high levels of CA 19-9 and increased transaminase enzyme. In addition, a definite diagnosis of the Klatskin tumor in the patient was obtained from the MRCP results.

ACKNOWLEDGMENTS

We thank the patient and all the staff who helped and took care of the patient in RSUP Dr. Kariadi for their support.

JURNAL KEDOKTERAN DIPONEGORO
(*DIPONEGORO MEDICAL JOURNAL*)
Online http://ejournal3.undip.ac.id/index.php/medico
E-ISSN : 2540-8844
DOI :
JKD (DMJ), Volume 12, Number 1, January 2023 :

AUTHOR CONTRIBUTIONS

Edward Kurnia Setiawan Limijadi and Esa Loyallita Lestari contributed equally to this work. All authors read and approved the final manuscript.

FUNDING

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

DECLARATIONS

Ethics approval and consent to participate
This study has been performed according to the Declaration of Helsinki.

CONSENT FOR PUBLICATION

Written informed consent was obtained from the patient's legal guardian for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

COMPETING INTERESTS

The authors declare that they have no competing interests.

REFERENCES

1. Sharma P, Yadav S. Demographics, tumor characteristics, treatment, and survival of patients with Klatskin tumors. Annals of gastroenterology. 2018;31(2): p.231.
2. Shin HR, Oh JK, Masuyer E, Curado MP, Bouvard V, Fang YY, et al. Epidemiology of Cholangiocarcinoma: an Update Focusing on Risk Factors. Cancer Science, 2010;101(3):579-585.
3. Zhang X, Liu H. Klatskin Tumor: A Population-Based Study of Incidence And Survival. Medical science monitor: international medical journal of experimental and clinical research [MSM]. 2019;25:4503.
4. Shaib YH, El-Serag HB, Nooka AK, Thomas M, Brown TD, Patt YZ, et al. Risk factors for intrahepatic and extrahepatic cholangiocarcinoma: a hospital-based case–control study. Official journal of the American College of Gastroenterology [ACG], 2007;102(5): pp.1016-1021.
5. Mansour JC, Aloia TA, Crane CH, Heimbach JK, Nagino, M, Vauthey, JN. Hilar cholangiocarcinoma: expert consensus statement. Hpb, 2015;17(8): pp.691-699.
6. Friedman LS. Martin P. Hepatic Tumor in Handbook of Liver Disease E-Book. Elsevier Health Sciences. 2018.
7. McNicoll CF, Pastorino A, Farooq U, St Hill CR. Choledocholithiasis. In StatPearls [Internet]. StatPearls Publishing. 2021.
8. Adiyanti, SS, Sosrosumihardjo R. The Role of Various Laboratory Parameters and Imaging Associated with Obstructive Jaundice in Cholangiocarcinoma. The Indonesian Journal of Gastroenterology, Hepatology, and Digestive Endoscopy [JGHE], 2014;15(1): pp.57-62.
9. Zhang C, Wang H, Ning Z, Xu L, Zhuang L, Wang P, et al. Serum liver enzymes serve as prognostic factors in patients with intrahepatic cholangiocarcinoma. OncoTargets and therapy. 2017;10:p.1441.
10. Weiss G, Goodnough LT. Anemia of chronic disease. New England Journal of Medicine [NEJM]. 2005; 352(10): pp.1011-1023..
11. Trombositoz, Y. Spurious thrombocytosis in the setting of hemolytic anemia and microcytosis secondary to extensive burn injury. Turk J Hematology, 2018;35: p.205.
12. Blechacz, BR. Gores GJ. Cholangiocarcinoma. Clinics in liver disease. 2008;12(1):pp.131-150.
13. Van Beers BE. Diagnosis of cholangiocarcinoma. HPB. 2008;10(2): pp.87-93.

Case Report : Choledocholithiasis as Risk Factor for Klatskin Tumor: A Rare Cholangiocarcinoma

ORIGINALITY REPORT

16%	13%	10%	5%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	jmedicalcasereports.biomedcentral.com Internet Source	4%
2	healthjade.net Internet Source	3%
3	www.hematronix.com Internet Source	1%
4	mafiadoc.com Internet Source	1%
5	annalsgastro.gr Internet Source	1%
6	"APASL Seoul 2008 Meeting", Hepatology International, 2008 Publication	1%
7	M.W van Lacum, R.A.P.A Hessels, G.D Kremer, C.A.J.J Jaspers. "A splenic cyst and a high serum CA 19-9: a case report", European Journal of Internal Medicine, 2000 Publication	1%

8	www.advanceforlpns.com Internet Source	1 %
9	www.amjcaserep.com Internet Source	1 %
10	"Advanced ERCP for Complicated and Refractory Biliary and Pancreatic Diseases", Springer Science and Business Media LLC, 2020 Publication	<1 %
11	"IgG4-Related Sclerosing Cholangitis", Springer Science and Business Media LLC, 2019 Publication	<1 %
12	Sunyoung Ahn, Jungyong Park, Young Ran Kim, Jeong-Ho Kim, Hyon-Suk Kim. "Stability of lyophilized pooled sera as quality control materials for tumor marker assays in external quality assessment", Clinica Chimica Acta, 2017 Publication	<1 %
13	peraturan.bpk.go.id Internet Source	<1 %
14	worldwidescience.org Internet Source	<1 %
15	bmccancer.biomedcentral.com Internet Source	<1 %

16	M. Hejna. "The clinical role of somatostatin analogues as antineoplastic agents: much ado about nothing?", Annals of Oncology, 05/01/2002 Publication	<1 %
17	ar.scribd.com Internet Source	<1 %
18	bmcsurg.biomedcentral.com Internet Source	<1 %
19	openaccess.marmara.edu.tr Internet Source	<1 %
20	www.ncbi.nlm.nih.gov Internet Source	<1 %

Exclude quotes	Off	Exclude matches	Off
Exclude bibliography	On		

Case Report : Choledocholithiasis as Risk Factor for Klatskin Tumor: A Rare Cholangiocarcinoma

GRADEMARK REPORT

FINAL GRADE

/0

GENERAL COMMENTS

Instructor

PAGE 1

PAGE 2

PAGE 3

PAGE 4

PAGE 5