

Clinical Presentation and Frequency of Klatskin Tumor; A Single-center Retrospective Study

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Abstract

Klatskin tumor is an epithelial bile duct tumor that originates from the main hepatic duct or the right-left intrahepatic duct and appears proximal to the opening of the cystic duct. In this study, we examined the demographic characteristics, clinical, laboratory and radiological results at the time of first presentation of patients who were diagnosed with klatskin tumor in our clinic for a period of three years. For the study; 16 patients who were hospitalized at Internal Medicine Clinic between June 1, 2015-May 1, 2018 were diagnosed with Klatskin tumor were included retrospectively. Clinical, laboratory and radiological data of patients were analyzed. 16 patients in the study, 10 were male, 6 were female. Average age was 62.30 for males, 65.33 for females. The most common symptoms respectively jaundice, itching, abdominal pain, anorexia and weakness. Among the laboratory tests, the average of some values; AST:141.31 U/L, ALT:156.18 U /L, ALP:692.07 IU/L, GGT:622.14 U/L, T. Bilirubin:10.42 mg/dl, D. Bilirubin: 6.0 mg/dl, WBC:10.509 x10³u/L. diagnostic ERCPs of the patients were examined; Klatskin tumor was considered in 14 patients due to stenosis in the proximal part of the common bile duct. Clinical and laboratory findings in Klatskin tumors are not specific and the diagnosis is usually made in the late period because the clinical presentation of the disease is confused with many other diseases.

Key words: Klatskin Tumor, Cholangiocarcinoma, ERCP, Clinical Presentation.

Introduction

Cholangiocarcinomas (CC); are malignant tumors that make up 10-20% of all hepatobiliary malignancies and originate from bile duct epithelial cells (1). CC are classified according to their localization as intrahepatic, hilar and distal CC (2).

Klatskin tumor is a biliary tract tumor originating from the main hepatic duct or right-left intrahepatic duct and seen

proximal to the opening of the cystic duct. Klatskin tumor is the most common tumor in the biliary tract and accounts for 60% of all CC (3). The annual incidence of Klatskin tumor is not more than 1: 100,000, and it is a rare type of tumor (4). Among the etiological risk factors for the development of CC, Primary Sclerosing Cholangitis (PSC), some parasitic infections of the liver (*Clonorchis sinensis*

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and *Opisthorchis viverrini*) and hepatolithiasis are the best known. However, no etiological factor can be detected in the majority of patients (5).

Clinical manifestations in Klatskin tumors are usually those that develop due to obstruction in the bile ducts, such as jaundice and light-colored stools. In addition, symptoms compatible with malignancy such as loss of appetite, cachexia and fatigue may also be seen. Approximately 10% of the patients are accompanied by cholangitis at the time of diagnosis (7).

Among the laboratory findings of Klatskin tumor, there may be increases in carbohydrate antigen (CA-19-9) and Carcinoembryonic antigen (CEA) levels. However, they are not specific for diagnosis because they increase in many diseases other than Klatskin tumor. Again, among laboratory findings, there is an increase in cholestasis marker enzyme levels produced in the liver depending on the localization and size of the obstruction created by the tumor in the bile ducts (8).

From the radiological imaging methods of Klatskin tumors, Hepatobiliary ultrasonography (USG) the presence of dilatation in the intra and extrahepatic bile ducts and a mass or obstruction in the bile duct can be shown. Computed Tomography (CT), Magnetic Resonance Cholangiopancreatography (MRCP) and Endoscopic Retrograde Cholangiopancreatography (ERCP) are used in both diagnosis and staging (8, 9).

Surgical resection is the only curative treatment option for early stage tumors in Klatskin tumor. Therefore, early diagnosis of patients is extremely important for survival. The current approach in surgical treatment is radical surgical resection, which usually includes choledectomy,

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Materials and Methods

This study was started after the approval of the ethics committee with the date 18.02.2021 and reference number 2021/03-03. A total of 16 patients who applied to our Internal Medicine Clinic between 1 June 2015 and 1 May 2018 and were diagnosed with Klatskin tumor were included in the study. The study was conducted in a single center by retrospectively analyzing the patient data previously recorded with standard data collection forms. Patients with a diagnosis of malignancy other than Klatskin's tumor were excluded from the study due to the possibility of metastasis to the bile ducts. Age and gender of all patients, symptoms at first admission, laboratory tests of Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), Alkaline phosphatase (ALP), Gamma Glutamyl Transferase (GGT), Total Bilirubin, Direct Bilirubin and Leukocyte (WBC) parameters. and mean values were calculated and analyzed.

Again, among the radiological imaging methods performed at the first application of the patients, Hepatobiliary ultrasonography, all abdominal CTs and ERCP findings were examined. The results were statistically analyzed.

Statistical Analyses

Statistical package program SPSS 22 (Statistical Package for the Social Sciences, version 22, SSPS Inc, Chicago, IL, USA) was used for data analysis.

Results

Of the patients included in the study, 10 (62.5%) were male and 6 (37.5%) were female. The mean age of the male patients

was 62.30 (46-80), the mean age of the female patients was 65.33 (48-85) and the general average of age was 62.68.

When the symptoms of the patients during the first application were questioned, it was stated as; jaundice, itching, abdominal pain, loss of appetite and weakness.

Some laboratory tests of the patients in our study, which were checked at the time of the first application, were analyzed. Their mean values were respectively; AST: 141.31 U/L, ALT: 156.18 U/L, ALP: 692.07 IU/L, GGT: 622.14 U/L, T. Bilirubin: 10.42 mg/dl, D. Bilirubin: 6.0 mg/dl, WBC: 10509 x10³ u/L.

When the hepatobiliary USGs of the patients were examined during the first application, Intrahepatic bile ducts were seen to be dilated in 16 patients, In 10 patients, dilatation was detected in the proximal part of the common bile duct. A mass was detected at the level of the bifurcation of the main hepatic duct in 3 of these patients. An appearance compatible with liver metastasis was observed in 2 patients.

When the abdominal CT scans of the patients included in the study at their first application were examined, Dilatation of intrahepatic bile ducts was observed in 16 patients, Concomitant dilatation of the extrahepatic bile ducts was detected in 1 patient. A mass was detected at the level of the main hepatic duct bifurcation in 7 patients, mass lesions compatible with liver metastases were observed in 5 patients, and in 2 patients, a mass was detected in the uncinat process of the pancreas.

When the ERCPs of all patients in our study made during the first application were examined, in 14 patients, stenosis in the proximal part of the common bile duct and dilatation in the intrahepatic bile ducts

Clinical Presentation and Frequency of Klatskin Tumor were observed, and the preliminary diagnosis of Klatskin tumor was considered in these patients. Irregular filling defect in the common bile duct and dilatation of the intrahepatic bile ducts were detected in 1 patient. In 1 patient, dilated common bile duct was observed, irregular filling defect in the hilar region and dilatation in the intrahepatic bile ducts were detected.

Discussion

CC is a malignant tumor arising from epithelial cells of the bile ducts. They originate from different parts of the bile tree, so they are classified according to their localization. They are classified as intrahepatic, perihilar and distal cc according to their anatomical locations (2). The most common of these is hilar CC so Klatskin tumor with approximately 60% (11). The reason why Klatskin tumor is very rare is that it does not cause symptoms in the early stage and laboratory findings are nonspecific, so the diagnosis is usually made at an advanced stage. Therefore, in this study, we aimed to examine the clinical presentation of Klatskin tumor.

Klatskin tumor usually occurs in advanced ages, most of the patients are 60 years and older (12). In our study, the mean age of the patients was similarly 62.68 years. This disease is seen at similar rates in both sexes, but in some studies it is stated that it is more common in men (13, 14). Similarly, in our study, it was found that it was more common in males.

Clinically, Klatskin tumor is usually asymptomatic in its early stages, so patients are usually diagnosed late. The most common symptom is jaundice, which is seen in approximately 90% of patients (11). Other common symptoms except

jaundice are fatigue, weight loss, itching and abdominal pain (11, 16). Similar to the literature, the most common symptoms in our study were jaundice, itching, abdominal pain, loss of appetite and weakness respectively. In addition, cholangitis was considered in 3 patients due to the presence of icterus, leukocytosis and fever at the first admission. The rate of cholangitis in the patients in our study was determined as 18.75%. This rate was evaluated as slightly higher when compared with the literature data (7).

There are no specific laboratory tests used in the diagnosis of Klatskin tumor. Biochemically, in the diagnosis of the disease, there may be an increase in serum carbohydrate antigens CA-19-9 and CEA levels. In addition, increases in AST, ALT, ALP, GGT and Bilirubin values can be detected (17). In our study, the CEA and CA19-9 values at the first admission of the patients could not be reached, but significant increases in AST, ALT, ALP, GGT and bilirubin values measured at the diagnosis stage were found. The increases in these enzymes produced by the liver were significant because they showed the picture of cholestasis in the patients. The presence of cholestasis was not detected in only one patient at the first admission.

Hepatobiliary USG has a limited place in the diagnosis of Klatskin tumor in radiological imaging methods; therefore, it cannot be recommended for surveillance or diagnosis (18). In our study, all patients were evaluated with hepatobiliary USG at the time of first admission. Dilatation of the intrahepatic biliary tract was detected in 16 patients, concomitant dilatation of the common bile duct was observed in 10 patients, and a mass was detected at the level of the main hepatic duct bifurcation in 3 of these patients. In addition, lesion

Clinical Presentation and Frequency of Klatskin Tumor compatible with liver metastasis was observed in two patients. Our results, in parallel with the literature studies, support the low value of hepatobiliary USG in the diagnosis of Klatskin tumor.

Conventional CT has an accuracy rate of approximately 70% in the diagnosis of Klatskin tumors. Therefore, its use is limited in the diagnosis of Klatskin tumor, and its main purpose is to determine the extent of extrahepatic disease (19). In the analysis of the conventional CT findings of the patients in our study taken during the first application period, only 7 patients had a mass at the level of the bifurcation of the main hepatic duct. In addition, findings compatible with liver metastasis were observed in 5 patients, and a mass in the pancreatic uncinata process was observed in 2 patients. These results we obtained were correlated with the literature data stating that the accuracy rate of conventional CT in the diagnosis of Klatskin tumor is low.

ERCP can show direct mass and dilated bile ducts in the diagnosis of Klatskin tumor. At the same time, ERCP is the most valuable method for the diagnosis of Klatskin tumor because it allows the collection of brush swab samples from the bile ducts for cytological examination (20). In our study, as a result of the first ERCP procedures of the patients, stenosis in the proximal part of the common bile duct and dilatation in the intrahepatic bile ducts were detected in 14 patients. Irregular filling defect in the common bile duct in 1 patient, dilated common bile duct in 1 patient, irregular filling defect in the hilar region and dilatation in the intrahepatic bile ducts were detected in both patients.

When Klatskin tumors are detected at an early stage, surgical resection is the most effective treatment option for long-term

survival and cure (21). Orthotropic liver transplantation can be performed in diseases such as liver cirrhosis and primary sclerosing cholangitis which are not suitable for surgical resection (22). Chemotherapy and radiotherapy are used in the treatment of patients with advanced or inoperable Klatskin tumor, but their effects on survival alone are unfortunately limited when compared with complete surgical resection (23).

Conclusion

The incidence of Klatskin tumor has increased significantly in recent years. However, diagnosis is still delayed due to the non-specific clinical presentation. Early diagnosis is extremely important as the only cure is surgical treatment. For this reason, early diagnosis of patients by using imaging methods without wasting time in case of clinical suspicion will positively affect both the chance of cure and survival.

Limitations of the study

The limitations of our study and the small number of patients in our study are because of the fact that it was conducted in a single center, and the treatment options of the patients after the diagnosis and the duration of survival are not known. For these reasons, we believe that multicenter studies with larger patient series are needed to obtain more detailed information about Klatskin tumor.

Conflict of interest

The authors declare that they have no competing interests with regards to authorship and/or publication of this paper.

References

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1. Blechacz B, Gores GJ. Cholangiocarcinoma: advances in pathogenesis, diagnosis, and treatment. *Hepatology*. 2008;48(1):308-21.
2. Gatto M, Alvaro D. New insights on cholangiocarcinoma. *World J Gastrointest Oncol*. 2010;2(3):136-145.
3. Khan SA, Thomas HC, Davidson BR, et al. Cholangiocarcinoma. *Lancet* 2005;366(9493):1303-14.
4. Seehofer D, Kmhues C, Neuhaus P. Resection of Klatskin tumors. *Chirurg*. 2012;83(3):221-8.
5. Vauthey JN, Blumgart LH. Recent advances in the management of cholangiocarcinomas. *Semin Liver Dis*. 1994;14(2):109-14.
6. Jarnagin W, Winston C. Hilar cholangiocarcinoma: Diagnosis and staging. *HPB Oxford*. 2005;7(4):244-251.
7. Anderson CD, Pinson CW, Berlin J, et al. Diagnosis and treatment of cholangiocarcinoma. *Oncologist*. 2004;9(1):43-57.
8. Aloia TA, Charnsangavej C, Faria S, et al. High-resolution computed tomography accurately predicts resectability in hilar cholangiocarcinoma. *Am J Surg*. 2007;193:702-6.
9. Liu CL, Lo CM, Lai EC, et al. Endoscopic retrograde cholangiopancreatography and endoscopic endoprosthesis insertion in patients with Klatskin tumors. *Arch surg*. 1998;133(3):293-6.
10. Friman S. Cholangiocarcinoma-current treatment options. *Scand J Surg*. 2011;100(1):30-4.
11. DeOliveira ML, Cunningham SC, Cameron JL, et al. Cholangiocarcinoma: Thirty-one-year experience with 564 patients at a single institution. *Ann Surg*. 2007;245(5):755-62.
12. Everhart JE, Ruhl CE. Burden of digestive diseases in the United States Part III: Liver, biliary tract, and pancreas. *Gastroenterology*. 2009;136(4):1134-44.
13. Khan SA, Toledano MB, Taylor-Robinson SD. Epidemiology, risk factors, and pathogenesis of cholangiocarcinoma. *HPB (Oxford)*. 2008;10(2):77-82.
14. Tyson GL, Ilyas JA, Duan Z, et al. Secular Trends in the Incidence of Cholangiocarcinoma in the USA and the Impact of Misclassification. *Dig Dis Sci*. 2014;59(12):3103-3110.
15. Launois B, Reding R, Lebeau G, et al. Surgery for hilar cholangiocarcinoma: French experience in a collective survey of 552 extrahepatic bile duct cancers. *J Hepatobiliary Pancreat Surg*. 2000;7(2):128-34.
16. Zografos GN, Farfaras A, Zagouri F, et al. Cholangiocarcinoma: principles and current trends. *Hepatobiliary Pancreat Dis Int*. 2011;10(1):10-20.
17. Khan SA, Davidson BR, Goldin R, et al. Guidelines for the diagnosis and treatment of

cholangiocarcinoma: Consensus document. *Gut*. 2002;51(6):vi1-vi9.

18. Forsmark CE, Alessandro LD, Andrew XZ. "Consensus conference on hilar cholangiocarcinoma." *HPB: the official journal of the International Hepato Pancreato Biliary Association* 17.8 2015; 666.

19. Harewood GC, Baron TH, Stadheim LM, et al. Prospective, blinded evaluation of factors affecting the accuracy of biliary cytology interpretation. *Am J Gastroenterol*. 2004;99(8):1464-9.

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20. Weiss MJ, Cosgrove D, Herman JM, et al. Multimodal treatment strategies for advanced hilar cholangiocarcinoma. *Langenbecks Arch Surg*. 2014;399(6):679-92.

21. Petrowsky H, Hong JC. Current surgical management of hilar and intrahepatic cholangiocarcinoma: the role of resection and orthotopic liver transplantation. *Transplant Proc*. 2009;41(10):4023-35.

22. Nakeeb A, Pitt HA. Radiation therapy, chemotherapy and chemoradiation in hilar cholangiocarcinoma. *HPB (Oxford)*. 2005;7(4):278-82.