Case Report

Intraductal papillary neoplasm of bile ducts: report of a case and literature review

Nuray Colapkulu*, Gurhan Bas, Fatih Buyuker, Damla Beyazadam, Ibrahim A. Ozemir, Orhan Alimoglu

Department of General Surgery, Istanbul Medeniyet University, Faculty of Medicine, Goztepe Training and Research Hospital, Istanbul, Turkey

Received: 24 April 2019
Accepted: 01 June 2019

*Correspondence:
Dr. Nuray Colapkulu,
E-mail: nuraycolapkulu@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

A 67 year old male with right upper quadrant abdominal pain diagnosed with intraductal papillary neoplasm of bile ducts (IPNB) by endoscopic biopsy. The patient was treated surgically and disease free on first year follow-up. Intraductal papillary neoplasm of bile duct (IPNB) is a rare entity with malignant counterparts and recently classified by The World Health Organization. The aim of this study is to present a case of IPNB and review the literature. Pubmed/MEDLINE was searched and articles were extracted. Twenty four case reports and 17 retrospective case series were evaluated. From 41 studies, 824 cases were included. There was slight male predominancy among patients and almost all cases were from eastern countries. Even though the etiology remains unclear, hepatolithiasis was the most common potential etiological association. Most cases were treated with surgical intervention. More than half of the 577 resected specimens had invasive component. Incidence rate of histopathological subtypes were as followed: Intestinal (35%), pancreaticobiliary (32%), gastric (19%) and oncocytic (12%). Intraductal papillary neoplasm of bile duct has an increased malignancy rates at postoperative pathological diagnosis, consequently early surgical management is important.

Keywords: Biliary, Biliary tumours, IPNB, Mucinous adenocarcinoma

INTRODUCTION

Intraductal papillary neopasm of the bile ducts (IPNB) is a rare tumor and has classified as one of the mucin-producing tumours of biliary tree by The World Health Organization (WHO). IPNB cases are generally reported from eastern countries where hepatolithiasis and clonorchiasis are commonly seen. Despite this knowledge, sporadic cases from western countries, without these forementioned predisposition factors, are increasingly being reported. Hepatolithiasis, clonorchiasis and primary sclerosing cholangitis are among the risk factors for developing IPNB.

The clinical manifestations of IPNB are right upper quadrant pain, jaundice or cholangitis. Computed tomography (CT) and magnetic resonance imaging (MRI) are the most commonly used diagnostic studies. Although they are insufficient to make a specific diagnosis, secondary findings caused by obstruction could be revealed by those methods. IPNB cases show wide range of histological characteristic and pathological features. It can be classified as non-invasive and invasive diseases, and those two categories vary between low grade dysplasia and carcinoma. Phenotypes of IPNB are pancreaticobiliary, gastric, intestinal and oncocytic, similar to intraductal papillary mucinous neoplasm of pancreas (IPMN-P). For years IPNB has been considered as biliary IPMN-P with pancreatic counterparts but some studies reported IPNB is a more aggressive tumor than IPMN-P.
We herein report a case of IPNB and also conduct a literature review to have a better understanding about histopathological features, clinical approaches and prognosis of IPNB.

**CASE REPORT**

A 67 year old male presented to our hospital with right upper quadrant abdominal pain without any other complaints. Patient had history for cancer of descending colon and underwent surgery for left hemicolectomy five years ago and received 8 cycles of chemotherapy treatment and has been disease free since then. He also has high blood pressure and type II diabetes.

![Figure 1: Axial T1W pre-contrast image. Lesion (23x19 mm) in CHD leading dilatation of intrahepatic bile ducts with high signal due to mucin content.](image1)

PET/SCAN revealed a mass in CHD with a maximum standardized uptake value (SUV max) of 11.9 (Figure 2). The patient underwent Endoscopic Retrograde Cholangiopancreatogram (ERCP) and CHD was dilated and irregular. Also membranous-like tissues were seen and a biopsy was obtained. Pathologic evaluation have been identified as intraductal papillary mucinous neoplasm of bile duct. He underwent surgery for segmental resection of common hepatic and bile duct with cholecystectomy and hepaticojejunostomy. The location of the tumor was junction of the CHD and CBD (Figure 3). Microscopic examination of the biliary mass was consistent with biliary intraductal papillary neoplasm. The specimen showed gastric differentiation and low-intermediate grade dysplasia. There was no evidence of infiltrative features. By immuno-histochemistry, the tumor was positive for mucin core protein 6 (MUC 6) and CK7 (cytokeratin); negative for DPC 4, CK 20 and CDX2. Genetic analysis was positive for G12 R mutation at KRAS gene. The resection margin was negative for tumor. The patient was discharged on eighth day after surgery and did not receive any further treatment. His one year follow up were completed with no sign of recurrence. His scans are clear and Ca 19.9 dropped to normal levels.

![Figure 3: Location of the tumour.](image2)

**Preferred reporting items for systematic review and meta-analyses (PRISMA) guidelines were used to build the conduct of this study.**

1. Pubmed/MEDLINE were searched on January 29, 2017 by one author to distinguish the studies according to their relevancies without using a time interval. “Intraductal papillary mucinous neoplasm AND bile ducts” and “intraductal papillary mucinous neoplasm AND biliary” were used as phrases to implement a more specific search. Studies, that were...
documented as biliary mucinous neoplasms or adenocarcinoma, were included. Studies without pathology report that demonstrates IPNB or diagnosed by imaging only and duplicate studies were excluded. After the elimination of duplicate studies, 395 articles out of 531 were extracted from database system and evaluated. Articles that met the inclusion criteria were examined in full text.

**DISCUSSION**

Article selection after examining the studies is demonstrated in PRISMA study flow (Figure 4). There was also significant number of patients without any symptoms (10%). Possible etiological factors were identified in 231 patients from 12 studies and hepatolithiasis (80%) were the most frequent reported condition. Colonorchis sinensis (7%) and schistosomiasis (2%) are two infections mostly reported from eastern countries where it is endemic. Viral hepatitis were present in 18 (%8) individual. Tumor markers were evaluated in 75 patients from 9 studies and the percentage elevated CA 19-9 and CEA levels were 49% and 51%, respectively. ERCP, CT and MRI are the most frequent diagnostic imaging methods. Intraductal mass accompanied by bile duct dilatation on on cross-sectional imaging and mucin presence are the two most common findings. Most cases were managed surgically and the type of surgery varied according to location of the tumor.

![Figure 4: Study flow.](image)

| Table 1: Demographic and clinical features. |
|---------------------------------------------|
| **Sex** | **Total patients** |
| Male | 463 (56) |
| Female | 323 (39) |
| N/A | 38 (4) |

| **Nationality** | **Total patients** |
|-----------------|-------------------|
| Asian | 799 (97) |
| Non-Asian | 25 (3) |

| **Presentation** | **Total patients** |
|------------------|-------------------|
| Abdominal pain (RUQ) | 168 (39) |
| Jaundice | 106 (24) |
| Cholangitis | 58 (13) |
| No symptoms | 47 (10) |
| Weight loss | 23 (5) |
| Fever | 18 (4) |
| Pruritus | 4 (0.9) |
| Dark colored urine | 3 (0.6) |
| Acholic stool | 2 (0.5) |

| **Possible etiological association** | **Total patients** |
|-------------------------------------|-------------------|
| Hepatolithiasis | 187 (80) |
| Colonorchis sinensis | 17 (7) |
| Viral infection (HBV/HCV/HBV+HCV) | 18 (8/3/2) |
| Schistosomiasis | 9 (2) |

| **Tumor markers** | **Total patients** |
|------------------|-------------------|
| Elevated CA 19.9 | 37 (49) |
| Elevated CEA | 38 (51) |

Continued.
| Diagnostic imaging          | No. of patients (%) | Total patients | References          |
|----------------------------|--------------------|----------------|---------------------|
| ERCP                       | 136 (33)           | 409            | 8,4,16,14,12,7,21,22,23,24,25,26,19,27,28,29,30,31,32,33,34,35,36,37,45,46,48,49,50 |
| CT                         | 118 (28)           |                |                     |
| MRI                        | 110 (26)           |                |                     |
| USG                        | 44 (10)            |                |                     |
| EUS                        | 1 (0.2)            |                |                     |

| Imaging findings           | No. of patients (%) | Total patients | References          |
|----------------------------|--------------------|----------------|---------------------|
| Intraductal mass           | 125 (42)           |                |                     |
| Mucin presence at ERCP     | 88 (30)            | 292            | 4,16,14,12,7,21,34,37,45,46,48,50 |
| Bile duct dilation         | 42 (14)            |                |                     |
| Other                      | 37 (13)            |                |                     |

| Treatment                  | No. of patients (%) | Total patients | References          |
|----------------------------|--------------------|----------------|---------------------|
| Hepatectomy                | 394 (74)           |                |                     |
| Extrahepatic bile duct excision | 98 (18)     |                |                     |
| Pancreatoduodenectomy      | 25 (4)             | 527            | 4,5,16,14,7,21,22,23,24,25,26,27,28,29,30,31,32,33,35,36,39,44,48,50,51 |
| Palliative intervention    | 5 (0.9)            |                |                     |
| Liver transplantation      | 3 (0.5)            |                |                     |
| Chemotherapy               | 2 (0.3)            |                |                     |

**Table 2: Histopathologic and immunohistochemistry features.**

| Tumor location           | No. of patients (%) | Total patients | References          |
|--------------------------|--------------------|----------------|---------------------|
| Intrahepatic             | 357 (68)           | 520            | 8,9,4,5,14,7,32,41,43,45,51 |
| Extrahepatic             | 139 (26)           |                |                     |
| Intra and extrahepatic   | 24 (4)             |                |                     |

| Tumor grade              | No. of patients (%) | Total patients | References          |
|--------------------------|--------------------|----------------|---------------------|
| Adenocarcinoma           | 321 (55)           |                |                     |
| Dysplasia                | 246 (42)           |                |                     |
| Low-Moderate             | 83 (14)            |                |                     |
| High                     | 86 (15)            |                |                     |
| N/A                      | 77 (13)            |                |                     |
| Carcinoma in situ        | 26 (4)             |                |                     |
| Adenoma                  | 4 (0.6)            |                |                     |

| Intraluminal mucin presence | No. of patients (%) | Total patients | References          |
|-----------------------------|--------------------|----------------|---------------------|
| 219 (100)                   |                    | 219            | 5,12,7,21,22,24,25,26,19,27,28,29,30,31,32,33,34,35,36,37,39,40,43,49,50,51 |

| Histologic subtype         | No. of patients (%) | Total patients | References          |
|---------------------------|--------------------|----------------|---------------------|
| Intestinal                | 202 (35)           | 574            | 8,5,16,12,22,26,34,37,38,39,40,43,44,45,46,47,48,51 |
| Pancreatobiliary           | 189 (32)           |                |                     |
| Gastric                   | 111 (19)           |                |                     |
| Oncocytic                 | 72 (12)            |                |                     |

| Tumor antigens            | No. of patients (%) | Total patients | References          |
|---------------------------|--------------------|----------------|---------------------|
| MUC1 (+/-)                | 101/7 (93/7)       | 108            |                     |
| MUC2 (+/-)                | 69/7 (90/10)       | 76             |                     |
| MUC5Ac (+/-)              | 113/1 (99/1)       | 114            |                     |
| MUC6 (+/-)                | 48/0 (100/0)       | 48             |                     |
| CDX2 (+/-)                | 35/5 (87/13)       | 40             |                     |
| CK1 (+/-)                 | 1/0 (100/0)        | 1              |                     |
| CK7 (+/-)                 | 65/11 (85/15)      | 76             |                     |
| CK20 (+/-)                | 27/6 (81/19)       | 33             |                     |

Histopathological features are revealed in Table 2. Tumor location in the biliary tree was identified in 520 patients and intrahepatic type was the most common (68%). Tumor grade was reported in 577 patients and 55% of the cases comprise invasive component. Histological subtype was documented in 574 cases from 18 studies. Rate of
incidence according to histopathological subtypes were as followed: intestinal (35%), pancreaticobiliary (32%), gastric (19%) and oncocytic (12%). Tumor antigens were assessed in 496 specimens from 18 studies and the results are revealed in Table 2.

Patients with IPNB are usually in the sixth decade of life and male predominance has been noticed among studies.\textsuperscript{2,3,11} Most common clinical symptom is right upper quadrant pain (35-88%) and second most common symptom is obstructive jaundice (20-36%).\textsuperscript{2,7} Some patients may present with acute cholangitis (5-59%).\textsuperscript{2}

IPNB lesions are soft, friable and mucin hypersecreting tumor and arises from both extra and intrahepatic bile duct. There are also tubular components with or without connective tissue.\textsuperscript{12} IPNBs are accepted as preinvasive intraepithelial neoplasm for tubular or mucinous adenocarcinoma.\textsuperscript{12} They have tendency to grow in intrahepatic bile ducts more commonly than intrahepatic bile ducts with the ratio of 2:1.\textsuperscript{11} Some authors suggested that biliary and pancreatic intraductal papillary neoplasms develop through the similar pathogenetic factors since they both are originated from the ventral endoderm of the foregut.\textsuperscript{12,15} But, since the IPNB shows association with invasive disease more frequently than IPMN-P, there are probably different oncological pathways between those two conditions. Intrahepatic IPNBs are more similar to IPMN than the extrahepatic type histopathologically.\textsuperscript{12} In a study published by Wang et al with 19 cases, 10 out of 19 tumor showed mucin secretion [14]. The frequency of phenotypes in IPNBs are pancreaticobiliary (45%), gastric (25%), intestinal (20%) and oncocytic (10%), respectively.\textsuperscript{3,12} Immunohistochemical study of specimens indicates that IPNB cells contain a biliary phenotype. Subtyping of IPNBs with immunostain is important to predict the prognosis of patients. MUC1/2/5AC/6, CK7 and CK20 are most frequently used markers. MUC 1 expression is usually associated with invasive lesions and especially tubular adenocarcinoma when MUC2 over expression is related to mucinous adenocarcinoma with MUC1 negativity.\textsuperscript{2,8} Rocha et al. showed in their study that MUC1 expression is more likely to related with pancreaticobiliary type and they also associated this anomaly with poor prognosis.\textsuperscript{5}

Molecular pathogenesis of IPNB is still unclear but some studies showed KRAS activation and p53 mutation.\textsuperscript{4,15,16}

In our case there was also G12 positivity at KRAS gene.

Gordon Weeks et al published a systematic review involving 57 studies which showed 43% invasive component of 476 IPNB cases.\textsuperscript{6} Again in two series with 19 and 32 cases showed almost 50% malignancy with IPNB.\textsuperscript{11} Zen et al indicates in their study that IPNB is a more aggressive tumor than IPMN-P and the prognosis of patients with invasive IPNB is poorer than IPMN-P.\textsuperscript{5}

Focal dilatation of extra or intrahepatic biliary tree, intraductal masses and growth pattern through the interior wall are considered as a warning to suspect from IPNB. Ultrasound and CT/MRI are useful imaging methods for detecting IPNB but extra attention should be paid for the patients without a visible tumor.\textsuperscript{6} Clinically and radiologically, it is difficult to diagnose IPNB. Even though some patients had no detected intraductal masses, after resection they had been diagnosed with benign or malignant IPNB.\textsuperscript{4} In a study, Egri et al investigated five different cases based on their imaging features. In those cases ERCP showed filling defect and ductal dilatation and MRI show solid components of the masses.\textsuperscript{3} Hong et al. examined MRI findings of 38 patients in their study and found that some patients manifests a thread sign (intraductal linear or curvilinear hypointense striations) on MRI which is an indicator of intraductal mucin bundles and highly specific finding for IPNB.\textsuperscript{17} The results of F-18 FDG PET/CT scan findings are limited in literature. Contrary to carcinomas with an high activity of glucose metabolism, malignant IPNBs with small mural nodule with excessive amount of mucin may present with false negativity since mucin is insufficient with glucose intake.\textsuperscript{18} Since endoscopic biopsy is a poor diagnostic test, early surgical management of IPNB is highly important to gain a better prognosis. Gomez et al reported a case of IPNB treated with chemotherapy with excellent results.\textsuperscript{19}

Clinical suspicion supported by radiological and laboratory findings are very important for early treatment of this disease. Given the poor diagnostic features of ERCP with IPNB, it is useful to decompress the biliary tract with patients that present with obstructive jaundice.\textsuperscript{6} Mucin secretion especially seen on ERCP is a possible indicator for IPNB. Paik et al investigated 25 patient who underwent surgery for biliary tumors and diagnosed with IPNB. After the pathological examination of the resection specimen, 19 cases had invasive disease when eight of them had benign features.\textsuperscript{8} In the study of Rocha et al. with 39 cases; R0 resection, presence, depth (≥5 mm, <5 mm) and percentage (≥10%, <10%) of invasive component were associated with survival. MUC1 expression and CEA positivity are also associated with poor prognosis.\textsuperscript{5,6} According to comparative study by Wang et al., there are similarities and differences between IPNB and IPMN-P. They speculate that being originated from the same embryological structure constitutes their similarities, whereas phenotypic subtypes (pancreaticobiliary, gastric, intestinal and oncocytic) designates their differences.\textsuperscript{7}

Patients with a prediagnosis of IPNB should be considered as a candidate for resection, because even if the lesion is thought to be premalignant or benign it is hard to make a definite pathological diagnosis preoperatively due to incompetency of biopsy to show the degree of cytologic atypia.\textsuperscript{20} In our case preoperative reported pathology was intraductal papillary mucinous neoplasm without showing any sign of dysplasia. But after resection, final pathological diagnosis was consisted with intraductal papillary neoplasm accompanied by low grade dysplasia.
CONCLUSION

In summary, we conclude that IPNB has wide spectrum of pathological findings. Since the pathological features and phenotypes play an important role on prognosis, making an accurate diagnosis determines course of the disease. Resection with adequate oncological margins should be performed due to high malignancy rates and its positive effect on survival.

ACKNOWLEDGEMENTS

Authors would like to express their very sincere appreciation to Prof. Dr. Orhan Alimgolu for his valuable and constructive suggestions during the planning and development of this work. His willingness to give his time so generously has been very much appreciated.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Nakanuma Y, Curado MP, Franceschi S. editors. WHO Classification of tumors of the digestive system, 4th Ed. Lyon: WHO. 2010: 217-224.
2. Wan XS, Xu YN, Qian JY, Yang XH, Wang AQ, He L, et al. Intraductal papillary neoplasm of the bile duct. World J Gastroenterol. 2013;19(46):8595-604.
3. Egri C, Yap WW, Scudamore CH, Webber D, Harris A. Intraductal papillary neoplasm of the bile duct: Multimodality imaging appearances and pathological correlation. Can Assoc Radiol J. 2017;68(1):77-83.
4. Paik KY, Heo JS, Choi SH, Choi DW. Intraductal papillary neoplasm of the bile ducts: the clinical features and surgical outcome of 25 cases. J Surg Oncol. 2008;97(6):508-12.
5. Rocha FG, Lee H, Katabi N, DeMatteo RP, Fong Y, D’Angelica MI, et al. Intraductal papillary neoplasm of the bile duct: a biliary equivalent to intraductal papillary mucinous neoplasm of the pancreas? Hepatology. 2012;56(4):1352-60.
6. Gordon-Weeks AN, Jones K, Harriss E, Smith A, Silva M. Systematic Review and Meta-analysis of Current Experience in Treating IPNB: Clinical and Pathological Correlates. Ann Surg. 2016;263(4):656-63.
7. Wang M, Deng BY, Wen TF, Peng W, Li C, Trishul NM. An observational and comparative study on intraductal papillary mucinous neoplasm of the biliary tract and the pancreas from a Chinese cohort. Clin Res Hepatol Gastroenterol. 2016;40(2):161-8.
8. Jung G, Park KM, Lee SS, Yu E, Hong SM, Kim J. Long-term clinical outcome of the surgically resected intraductal papillary neoplasm of the bile duct. J Hepatol. 2012;57(4):787-9.
9. Zen Y, Jang KT, Ahn S, Kim DH, Choi DW, Choi SH, et al. Intraductal papillary neoplasms and mucinous cystic neoplasms of the hepatobiliary system: demographic differences between Asian and Western populations, and comparison with pancreatic counterparts. Histopathology. 2014;65(2):164-73.
10. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Internal Med. 2009;151(4):264-9.
11. Klöppel G, Adsay V, Konukiewitz B, Kleeff J, Schlüter AM, Esposito I. Precancerous lesions of the biliary tree. Best Pract Res Clin Gastroenterol. 2013;27(2):285-97.
12. Nakanuma Y, Sudo Y. Biliary tumors with pancreatic counterparts. Semin Diagn Pathol. 2017;34(2):167-75.
13. Nakanuma Y. A novel approach to biliary tract pathology based on similarities to pancreatic counterparts: is the biliary tract an incomplete pancreas? Pathol Int. 2010;60(6):419-29.
14. Wang X, Cai YQ, Chen YH, Liu XB. Biliary tract intraductal papillary mucinous neoplasm: report of 19 cases. World J Gastroenterol. 2015;21(14):4261-7.
15. O’Dell MR, Huang JL, Whitney-Miller CL, et al. Kras(G12D) and p53 mutation cause primary intrahepatic cholangiocarcinoma. Cancer Res 2012;72(6):1557-67.
16. Dute K, Ohtsuka T, Fujimoto T, et al. GNAS and KRAS mutational analyses of intraductal papillary neoplasms of the pancreas and bile duct developing in the same individual: A case report. Pancreatology 2015;15(6):713-6.
17. Hong GS, Byun JH, Kim JH, et al. Thread sign in biliary intraductal papillary mucinous neoplasm: a novel specific finding for MRI. Eur Radiol. 2016;26(9):3112-20.
18. Takamani K, Yamada T, Tsuda M, et al. Intraductal papillary mucinous neoplasm of the bile ducts: multimodality assessment with pathologic correlation. Abdom Imaging. 2011;36(4):447-56.
19. Gomez MA, Riveros J, Regino W. A case report of biliary tract intraductal papillary mucinous neoplasm. Revista Colombiana de Gastroenterologia. 2015;30(3):347-50.
20. Ohtsuka M, Shimizu H, Kato A, Yoshitomi H, Furukawa K, Tsuyuguchi T, et al. Intraductal papillary neoplasms of the bile duct. Int J Hepatol. 2014;2014:4590-1.
21. Choudhary A, Barakat MT, Leal JN, Louie CY, Visser BC, Banerjee S. Green Sludge: Intraductal papillary mucinous neoplasm of the bile duct presenting with intermittent biliary obstruction due to abundant mucus. Dig Dis Sci. 2017;62(8):1897-900.
22. Tan Y, Milikowski C, Toribio Y, Singer A, Rojas CP, Garcia-Buitrago MT. Intraductal papillary neoplasm of the bile ducts: A case report and
literature review. World J Gastroenterol. 2015;21(43):12498-504.
23. Luvira V, Pugkhem A, Tipwaratorn T, Chamgramol Y, Pairojkul C, Bhudhisawadsi V. Simultaneous extensive intrahepatic papillary neoplasm of the bile duct and pancreas: A very rare entity. Case Rep Surg. 2016;2016:1518707.
24. Peeters K, Delvaux P, Huysentruyt F. Intraductal papillary neoplasm of the bile duct: a case report. Acta Chir Belg. 2017;117(4):260-3.
25. Parekh R, Krol G, Piraka C, Batra S. A rare case of intraductal papillary mucinous neoplasm of the biliary duct in a patient with prostate adenocarcinoma. Case Rep Gastroenterol. 2016;10(3):743-8.
26. Tajima S, Ohata A, Koda K, Maruyama Y. Intraductal papillary neoplasm of the bile duct, gastric type, arising in the intrapancreatic common bile duct could progress to colloid carcinoma: report of a case. Int J Clin Exp Pathol. 2013;8(5):5848-55.
27. Subhash R, Valiyaveettil IA, Natesh B, Raji L. Biliary tract intraductal papillary mucinous neoplasm: a brief report and review of literature. Indian J Pathol Microbiol. 2014;57(4):588-90.
28. Yun S, Choi D. Ruptured intrahepatic biliary intraductal papillary mucinous neoplasm in a Jehovah’s Witness patient. Int Surg. 2014;99(5):590-4.
29. Kawaguchi Y, Kawashima Y, Maruno A, et al. An intraductal papillary neoplasm of the bile duct at the duodenal papilla. Case Rep Oncol. 2014;7(2):417-21.
30. Budzynska A, Hartleb M, Nowakowska-Dulawa E, Krol R, Remiszewski P, Mazurkiewicz M. Simultaneous liver mucinous cystic and intraductal papillary mucinous neoplasms of the bile duct: a case report. World J Gastroenterol. 2014;20(14):4102-5.
31. Kim BS, Joo SH, Lim SJ, Joo KR. Intrahepatic biliary intraductal papillary mucinous neoplasm with gallbladder agenesis: case report. Surg Laparosc Endosc Percutan Tech. 2013;23(2):61-4.
32. Yoon M. Intrahepatic and extrahaepatic intraductal papillary neoplasms of bile duct. Korean J HepatoBiliary Pancreat Surg. 2013;17(1):48-52.
33. Sohn WJ, Jo S. A huge intraductal papillary mucinous carcinoma of the bile duct treated by right trisectionectomy with caudate lobectomy. World J Surg Oncol. 2009;7(1):93.
34. Yaman B, Nart D, Yilmaz F, Coker A, Zeytunlu M, Kilic M. Biliary intraductal papillary mucinous neoplasia: three case reports. Virchows Arch 2009;454(5):589-94.
35. Carrafiello G, Bertolotti E, Sessa F, Cafaro T, Dionigi G, Genovese E, et al. Intraductal papillary mucinous tumor of bile ducts radiologic and pathologic features: a case report. Cases J. 2008;1(1):319.
36. Sudo T, Murakami Y, Uemura K, Morifuji M, Hayashidani Y, Takesue Y, et al. Successful preoperative diagnosis and complete resection of biliary intraductal papillary-mucinous neoplasm of the liver. J Gastrointest Surg. 2005;9(6):860-2.
37. Tajiri T, Tate G, Matsumoto K, Hoshino H, Iwamura T, Kodaira Y, et al. Diagnostic challenge: intraductal neoplasms of the pancreatobiliary system. Pathol Res Pract. 2012;208(11):691-6.
38. Ohtsubo I, Ajiki T, Hori Y, Murakami S, Shimizu K, Itoh T, et al. Distinctive expression of CD133 between intraductal papillary neoplasms of the bile duct and bile duct adenocarcinomas. Hepatol Res. 2012;42(6):574-82.
39. Kubota K, Nakanuma Y, Kondo F, Hachiya H, Miyazaki M, Nagino M, et al. Clinicopathological features and prognosis of mucin-producing bile duct tumor and mucinous cystic tumor of the liver: a multi-institutional study based on the Japan Biliary Association. J Hepatobiliary Pancreat Sci 2014;21(3):176-85.
40. Sasaki M, Matsubara T, Nitta T, Sato Y, Nakanuma Y. GNAS and KRAS mutations are common in intraductal papillary neoplasms of the bile duct. PLoS One. 2013;8(12):e81706.
41. Zen Y, Pedica F, Patcha VR, Capelli P, Zamboni G, Casaril A, et al. Mucinous cystic neoplasms of the liver: a clinicopathological study and comparison with intraductal papillary neoplasms of the bile duct. Mod Pathol. 2011;24(8):1079-89.
42. Matsubara T, Sato Y, Sasaki M, Harada K, Nomoto K, Tsuneyama K, et al. Immunohistochemical characteristics and malignant progression of hepatic cystic neoplasms in comparison with pancreatic counterparts. Hum Pathol. 2012;43(12):2177-86.
43. Tsai JH, Yuan RH, Chen YL, Liu JY, Jeng YM. GNAS Is frequently mutated in a specific subgroup of intraductal papillary neoplasms of the bile duct. Am J Surg Pathol. 2013;37(12):1862-70.
44. Kloek JJ, van der Gaag NA, Erdogan D, Rauws EA, Busch OR, Gouma DJ, et al. A comparative study of intraductal papillary neoplasia of the biliary tract and pancreas. Hum Pathol. 2011;42(6):824-32.
45. Choi SC, Lee JK, Jung JH, Lee JS, Lee KH, Lee KT, et al. The clinicopathological features of biliary intraductal papillary neoplasms according to the location of tumors. J Gastroenterol Hepatol 2010;25(4):725-30.
46. Li T, Ji Y, Zhi XT, Wang L, Yang XR, Shi GM, et al. A comparison of hepatic mucinous cystic neoplasms with biliary intraductal papillary neoplasms. Clin Gastroenterol Hepatol 2009;7(5):586-93.
47. Ohtsuka M, Kimura F, Shimizu H, Yoshidome H, Kato A, Yoshitomi H, et al. Similarities and differences between intraductal papillary tumors of the bile duct with and without macroscopically visible mucin secretion. Am J Surg Pathol. 2011;35(4):512-21.
48. Jhuang JY, Hsieh MS. Pseudomyxoma peritonei (mucinous carcinoma peritonei) preceded by
intraductal papillary neoplasm of the bile duct. Hum Pathol. 2012;43(7):1148-52.

49. Ruiz A, Vedel B, Fabre C, Derycke T, Zurlinden O, Merzeau C. Intraductal papillary mucinous neoplasm of the bile ducts (IPMN-B). Clin Res Hepatol Gastroenterol. 2016;40(4):370-2.

50. Somogyi L, Dimashkieh H, Weber FL Jr, Buell J. Biliary intraductal papillary mucinous tumor: diagnosis and localization by endoscopic retrograde cholangioscopy. Gastrointest Endosc 2003;57(4):620-2.

51. Kim KM, Lee IK, Shin JU, Lee KH, Lee KT, Sung JY, et al. Clinicopathologic features of intraductal papillary neoplasm of the bile duct according to histologic subtype. Am J Gastroenterol 2012;107(1):118-25.

Cite this article as: Colapkulu N, Bas G, Buyuker F, Beyazadam D, Ozemir IA, Alimoglu O. Intraductal papillary neoplasm of bile ducts: report of a case and literature review. Int Surg J 2019;6:2579-86.