Eur J Gen Med 2015; 12(1): 157-159
DOI : 10.15197/sabad.1.12.31

Case Report

Well-Differentiated Neuroendocrine Carcinoma of the Extrahepatic Biliary Duct

Hande Köksal[1], N. Serdar Uğraş[2], Bülent Uysal[1], M. Cem Börüban[3]

ABSTRACT

Extrahepatic bile duct tumors are uncommon, with the majority being adenocarcinomas. Primary neuroendocrine tumors of the extrahepatic bile ducts are extremely rare. Herein, we report a case of the extrahepatic biliary duct primary well-differentiated neuroendocrine carcinoma in a 45-year-old woman.

Key words: *Biliary ducts, neuroendocrine tumor, treatment*

Ekstrahepatik Safra Yollarının İyi Diferansiye Nöroendokrin Karsinoması

ÖZET

Önemli bir kısmını adenokarsinomların oluşturduğu ekstrahepatik safra yolları tümörleri nadirdir. Primer ekstrahepatik safra yollarının priemr nöroendokrin tümörleri oldukça nadirdir. Burada, ekstrahepatik safra yollarının iyi diferansiye primer nöroendokrin tümörlü 45 yaşında bir kadın hasta sunulmaktadır.

Anahtar kelimeler: *Safra yolları, nöroendokrin tümör, tedavi*

INTRODUCTION

Neuroendocrine tumors (NETs) arise from neuroendocrine cell type widely distributed in the body. NETs are seen in the small intestine, appendix, rectum, lung, pancreas and rarely, in the ovaries, testes, liver, bile ducts and other localizations (1, 2). NETs of the extrahepatic biliary ducts have extremely rare occurrence (1-3). NETs of the gastroenteropancreatic tract are categorized by the World Health Organization into 3 groups: Well-differentiated neuroendocrine tumors (carcinoid tumors), well-differentiated neuroendocrine carcinoma-low grade malignant (malignant carcinoid tumors) and poorly differentiated neuroendocrine carcinomas-high grade malignant (1). Herein, we present a case of a well-differentiated neuroendocrine carcinoma (NEC) located on the extrahepatic biliary duct.

CASE

A 45-year-old female patient was admitted with complaints of intermittent nausea and right upper quadrant pain for two years. She had no history of jaundice, fever, and vomiting. Physical examination revealed a mild tenderness in the right hypocondrium on deep palpation and umbilical hernia. Complete blood count and biochemistry analyses were normal except mild high AST (81 U/L, N: 8-33). Abdominal US showed multiple biliary stones in gallbladder. The operation began with laparoscopic approach, but after exploration laparotomy was performed and revealed multiple stones in the gallbladder and an intramural tumor located on the junction of cystic duct and common hepatic duct. After cholecystectomy, excision of common hepatic duct and choledochus, and Roux-en-Y hepaticojejunostomy were performed.

[1]Konya Numune Hospital, Department of General Surgery, Konya, [2]Selçuk University, Selçuklu Faculty of Medicine, Department of Pathology, Konya, [3]Selçuk University, Meram Faculty of Medicine, Department of Oncology, Konya, Turkey

Received: 07.03.2014, Accepted: 05.08.2014

Correspondence: *Hande Köksal*
Konya Numune Hospital Department of General Surgery Konya, TURKEY
Tel: 2354500
E-mail: drhandeniz@yahoo.com

No palpable regional lymph node was determined. She had an uneventful postoperative course. Histologically, the tumor was composed of endocrine cells showing moderate atypia and growing in the form of solid nests, trabeculae and pseudoglandular pattern. Perineural invasion was seen. This tumor was 2.1 cm. Immunohistochemical analysis showed neoplastic cells diffusely positive for chromogranin A and synaptophysin. The final pathological diagnosis was well-differentiated NEC of the extrahepatic bile ducts. The patient is well with no evidence of disease 8 months after surgery.

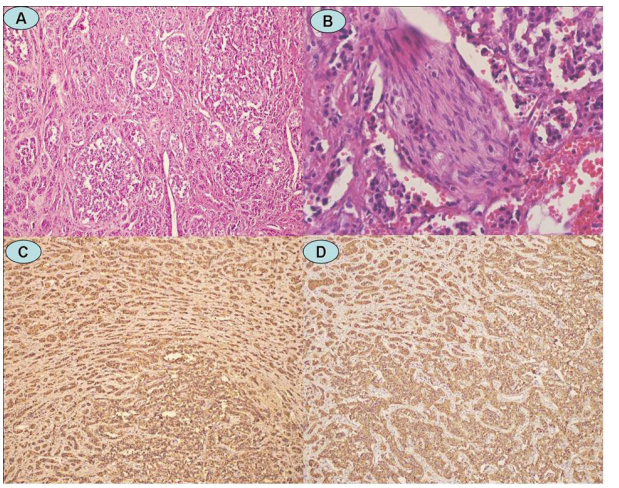

***Figure 1**. A: The tumor is composed of endocrine cells showing moderate atypia and growing in the form of solid nests, trabeculae and pseudoglandular pattern.B) Perineural invasion is seen (H&Ex400). C) Neoplastic cells are diffusely positive for chromogranin A (x100). D) Neoplastic cells are diffusely positive for synaptophysin (x100)*

DISCUSSION

Extrahepatic biliary duct tumors are uncommon, with the majority being adenocarcinomas, mostly of the well-differentiated type. NET of the extrahepatic biliary ducts, described firstly by Davies in 1959, is extremely rare (4, 5). NETs of the extrahepatic biliary ducts occur more frequently in women and the mean patient age is in 2 and 3 decades. The most frequent site for NET of the extrahepatic is the proximal/middle tract of common bile ducts (3, 5).

The major presenting symptoms are jaundice, biliary colic, abdominal or back pain and weight loss. In some patients, the tumor can be found incidentally (3, 5). In our patient, the presenting symptoms are intermittent nausea and the right upper quadrant pain for two years.

Brush cytology can be used for preoperative diagnosis of NETs of the extrahepatic, but the incidence of false negative results may be high due to the submucosal location of the neoplasm. Most NETs of the extrahepatic bile ducts are found incidentally during biliary tract operations performed for other indications. Some imaging studies including abdominal ultrasonography, computed tomography, endoscopic retrograde cholangiopancreatography, echoendoscopy and percutaneus transhepatic cholangiography are helpful methods, but the final diagnosis is usually made postoperatively after pathologic examination (5). The tumor was determined during operation for cholelithiasis in our patient.

Microscopically, NETs of the extrahepatic biliary ducts exhibit combined patterns with trabecular anastomosing structure, solid nests and occasional tubule formation. Tumor cells show positive staining for chromogranin, synaptophysin, NSE, and several hormones including gastrin and somatostatin (5). NETs of the gastroenteropancreatic tract are categorized by the World Health Organization into 3 groups: (a) Well-differentiated neuroendocrine tumors (carcinoid tumors) are composed of monomorphous endocrine cells with mild or no atypia, in a nested, trabecular, or pseudoglandular pattern, restricted to mucosa or submucosa. As a rule, non-angioinvasive tumors not larger than 1 cm and with 2 or less mitoses per 10 high-power fields are benign; (b) Well-differentiated neuroendocrine carcinoma-low grade malignant (malignant carcinoid tumors) are composed of endocrine cells showing moderate atypia and growing in the form solid nests, trabeculae or larger, less well-defined aggregates, which deeply invade the gut wall (muscularis propria or beyond) or show metastases to regional lymph nodes or liver. These, as a rule, are larger than1 cm, with a moderately elevated mitotic index (>2 mitoses/10 high-power fields) or proliferation index (>2% Ki-67-positive cells); (c) Poorly differentiated neuroendocrine carcinomas-high grade malignant are composed of highly atypical small to intermediate-sized tumor cells growing in the form of larger, ill-defined aggregates, often with necrosis and prominent angioinvasion and/or perineural invasion. The tumor usually shows a very high mitotic rate (≥10 mitoses/10 high-power fields) and a high proliferation index (>15% Ki-67-

positive cells), p53 immunostaining, and both local and distant metastases (1).

In our case, the final pathological diagnosis was well-differentiated NEC of the extrahepatic bile duct according to the World Health Organization classification for neuroendocrine tumors of the gastroenteropancreatic tract (6). The tumor cells had moderate atypia and perineural invasion were noticed. This tumor was larger than 2 cm in size. Immunhistochemical analysis showed neoplastic cells diffusely positive for chromogranin A and synaptophysin.

Surgical resection is the mainstay of treatment. Treatment approach depends on the location of the tumor and the extent of the disease. En block resection of the tumor and adjacent bile ducts, regional lymphadenectomy and Roux-en-Y hepatiocojejunostomy can be performed in patients with hepatic, cystic and proximal common bile duct neoplasms (5). In our patient, after cholocystectomy, excision of common hepatic duct and choledochus, and Roux-en-Y hepaticojejunostomy were performed. No palpable regional lymph node was seen. In conclusion, NETs of the extrahepatic biliary ducts are rare and its preoperative diagnosis is difficult. Surgical resection is the mainstay of treatment.

REFERENCES

1. *Noronha YS, Raza AS. Well-differentiated neuroendocrine (carcinoid) tumors of the extrahepatic biliary ducts. Arch Pathol Lab Med 2010; 134: 1075-9.*
2. *Saavedra JA, Batich K, Hossain S, et al. Carccinoid tumors and small-cell carcinomas of the gallbladder and extrahepatic bile ducts: a comparative study based on 221 cases from Surveillance, Epidemiology, and End Results Program. Ann Diagn Pathol 2009; 13: 378-83.*
3. *Squillaci S, Marchione R, Piccolomini M et al. Well-differentiated neuroendocrine carcinoma (malignant carcinoid) of the extrhepatic biliary tract: report of cases and literature rewiev. APMIS 2010; 118: 543-56.*
4. *Davies AJ. Carcinoid tumors (argentaffinomato). Ann R Coll Surg Engl 1959; 25: 277-80.*
5. *Nesi G, Lombardi A, Batignani G, Ficari F, Rubio CA, Tonelli F. Well-differentiated endocrine tumor of the distal common bile duct: a case study and literature review. Virchows Arch 2006; 449: 104-11.*
6. *Solcia E, Capella C, Klopeel G, et al. In: Solcia E, Kloppel G, Sobin LH, eds. Endocrine tumours of the gastrointestinal tract. In: Histological Typing of Endocrine Tumours. 2nd ed. Berlin, Germany: Springer-Verlag; 2000: 61-8.*