Well-Differentiated Neuroendocrine Carcinoma of the Extrahepatic Biliary Duct

Hande Köksal¹, N. Serdar Uğraş², Bülent Uysal¹, M. Cem Börüban³

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

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.
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.

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 percutaneous 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 monomorphic endocrine cells with mild or no atypia, in a nested, trabecular, or pseudoglandular pattern, restricted to mucosa or submucosa. As a rule, non-angio-invasive 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 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 angio-invasion 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 ac-
cording to the World Health Organization classification
for neuroendocrine tumors of the gastroenteropancre-
atic tract (6). The tumor cells had moderate atypia and
perineural invasion were noticed. This tumor was larger
than 2 cm in size. Immunohistochemical 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 tu-
more and the extent of the disease. En block resection
of the tumor and adjacent bile ducts, regional lymphad-
enectomy and Roux-en-Y hepaticojejunoanastomosis 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 hepaticojejunoanastomosis 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
2. Saavedra JA, Batich K, Hossain S, et al. Carcinoid tu-
mors and small-cell carcinomas of the gallbladder and ex-
trahepatic bile ducts: a comparative study based on 221
cases from Surveillance, Epidemiology, and End Results
3. Squillaci S, Marchione R, Piccolomini M et al. Well-
differentiated neuroendocrine carcinoma (malignant car-
cinoid) of the extrhepatic biliary tract: report of cases
and literature review. APMIS 2010; 118: 543-56.
5. Nesi G, Lombardi A, Batignani G, Ficari F, Rubio CA,
Tonelli F. Well-differentiated endocrine tumor of the dis-
tal common bile duct: a case study and literature review.
Virchows Arch 2006; 449: 104-11.
l G, Sobin LH, eds. Endocrine tumours of the gastrointes-