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Minimally invasive papillary carcinoma of the extrahepatic bile ducts

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CASE REPORT

Minimally Invasive Papillary Carcinoma of The Extrahepatic Bile Ducts

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ABSTRACT

Invasive papillary carcinomas of the Extrahepatic Bile Ducts (EBD) are uncommon (4-5%). The course is less aggressive than conventional adenocarcinomas of the extrahepatic bile ducts. Non-invasive and minimally invasive papillary carcinomas are even rarer, behave as *in-situ* carcinomas and are associated with excellent long-term prognosis. A variety of lesions of the EBD that show papillary architecture should be distinguished from papillary carcinoma. Here, we report a case of papillary carcinoma of the common bile duct showing minimal invasion. Separation of invasive from non-invasive or minimally invasive papillary carcinoma is critical in estimating the patient outcome.

Key words: *Extrahepatic bile duct. Papillary carcinoma. Minimally invasive.*

INTRODUCTION

Carcinomas of the EBD are uncommon neoplasms that are morphologically heterogeneous, and associated with poor prognosis.[1] Invasive Papillary Carcinomas (PC) of the EBD represent 4-5% of all malignant epithelial tumours of this region, and appear to have a much less aggressive clinical course. Non-invasive and minimally invasive papillary carcinomas of EBD are even rarer, behave as carcinoma *in-situ*, and are associated with excellent long-term prognosis regardless of their cytological features, or their immunoreactivity for p53 and MIB 1.[2,3] Hence, separation of invasive from non-invasive or minimally invasive papillary carcinoma is critical in estimating the patient outcome.[1] We report a case of minimally invasive papillary carcinoma of the EBD in a 55-year-old gentleman.

These tumours should be distinguished from biliary papillomatosis, intraductal papillary mucinous carcinoma of the pancreas extending into the bile ducts, papillary adenoma and papillary hyperplasia.[2]

CASE REPORT

A 55-year-old previously healthy male presented with complaints of lethargy, weight loss, anorexia and epigastric pain for 2 months. On general physical examination, he was jaundiced and rest of the examination was unremarkable. Laboratory investigations revealed deranged liver function tests. The values were total bilirubin at 4.9 mg/dl, direct bilirubin at 2.7 mg/dl, indirect bilirubin at 2.2 mg/dl, gamma GT at 580 iu/L, SGPT at 180 iu/L and alkaline phosphatase at 471 iu/L.

Abdominal ultrasound revealed dilated common bile-duct (1.8 cm in diameter) and intrahepatic bile ducts. However, no definite obstructing mass was identified. Computed Tomography (CT) of the abdomen showed an enhancing irregular mass in the distal common bile duct, which measured 2.2 x 2.1 x 1.8 cm. It was causing proximal dilatation of intrahepatic duct, the cystic duct and the gallbladder. A possibility of cholangiocarcinoma was raised. Endoscopic Retrograde Cholangio-pancreatography (ERCP) and biopsy were recommended for further evaluation. However, as the CT clearly showed the mass in distal common bile duct, those were not performed and a Whipple's procedure, with an intraoperative frozen section was done.

Peroperatively, there was no ascites or evidence of peritoneal, pelvic or hepatic disease. A polypoidal tumour was seen localized to the distal Common Bile Duct (CBD) and cystic duct. Proximal CBD was tumour-free. Part of the tumour was sent for frozen section on which a diagnosis of a papillary neoplasm was given.

Pancreaticoduodenectomy was performed. The specimen was received in the section of histopathology coded as "Whipple's specimen with omentum". It comprised of the distal stomach, proximal small intestine, gallbladder with dilated common bile duct (CBD) and the head of pancreas. On opening the stomach and small intestine, the mucosa was unremarkable. The gallbladder was separated from the CBD, which measured 5 x 1.2 cm. On further sectioning the CBD, an exophytic, polypoidal, intraluminal whitish mass was identified obstructing the lumen (Figure 1). The lesion was 1.8 cm in the largest diameter

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extending upto the pancreatic duct. However, it was not grossly invading the wall. Multiple sections of the tumour along with the wall of the CBD were taken and submitted for microscopic evaluation. Nine lymph nodes were recovered from the specimen, all of which were submitted entirely.

A second container labeled as 'common hepatic artery lymph nodes' was also sent, from which four lymph nodes were recovered and all were submitted entirely for histopathological evaluation.

Histologic sections from the CBD lesion revealed a neoplasm exhibiting an exophytic proliferation of complex papillary structures into the lumen of the bile duct. Variably-sized, finger-like epithelial processes lined by pseudostratified columnar cells showing vesicular nuclei and prominent nucleoli were observed. Mitotic figures were appreciated (approximately 3-4/10 HPF).

A single focus of superficial invasion was seen in one section (Figure 2). No other focus of infiltration was seen in the entirely submitted specimen.

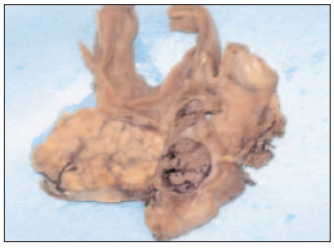

Figure 1: Exophytic, polypoidal, intraluminal whitish mass obstructing the lumen.

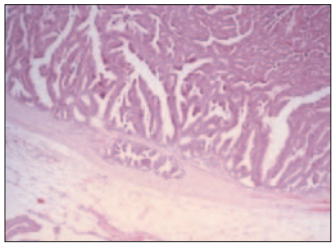

Figure 2: Intraluminal tumour with a single focus of invasion (H+E x 20).

A diagnosis of 'extra hepatic bile duct papillary carcinoma with minimal invasion' was given. The proximal gastric, distal duodenal and pancreatic resection margins were tumour-free. The omentum was not involved by the tumour. The 9 lymph nodes recovered from the main specimen as well as the 4 common hepatic artery lymph nodes were all tumour-free. The tumour was staged as Tis, No, Mx.

The patient was stable postoperatively. LFT's became normal. He experienced mild nausea and was tolerating liquids and soft food quite well. He was discharged on antibiotics and analgesics. Currently, he is doing well. Chemotherapy along with radiation is planned.

DISCUSSION

Despite their simple histological structure, the extra-hepatic bile ducts give rise to a group of morphologically heterogenous malignant epithelial neoplasms.

These tumours usually occur in older individuals with an average age of 68.4 years. Incidence is almost equal in either gender. Most patients present with obstructive jaundice, weight loss, elevated serum bilirubin, and right upper quadrant pain. Majority i.e. 49% of the cases occur in the upper third or hilar area, 25% in the middle third, and 19% in the lower third. Diffuse involvement occurs in 7% of the cases. Risk factors include primary sclerosing cholangitis, choledochal cyst, an anomalous pancreaticobiliary junction with reflux, cholelithiasis, gallbladder carcinoma, infection with liver flukes, and use of oral contraceptives.[3]

Most cancers of the EBD give rise to early symptoms because of obstruction. These tumours have a relatively poor prognosis. This is thought to be attributable in part to rapid infiltration of the tumour into the thin walls of the EBD and invasion into the periductal connective tissue, which is rich in vessels and nerves.[4]

Microscopically, the large majority of bile duct malignancies are well differentiated, mucin producing adenocarcinomas.[5]

Representing a small proportion (4-5%) of all malignant epithelial tumours of the EBD, that is 4-5%, papillary carcinomas tend to grow into the lumen, and only late in their course do they invade the ductal wall and periductal tissue. Because of this feature, they follow a protracted clinical course and appear to be associated with a better prognosis than conventional adenocarcinomas of EBD.[2]

Papillary carcinomas of the EBD can be classified as invasive and non-invasive. This separation is important because non-invasive and minimally invasive papillary carcinomas behave as *in-situ* carcinomas. Invasion of full thickness of the ductal wall and beyond appears to be the most significant prognostic factor.[1]

Saavedra *et al.* clearly demonstrated that the non-invasive and minimally invasive carcinoma of EBD, regardless of their cytological features, p53 and MIB 1 reactivity, are associated with an excellent long-term prognosis.[2] In this study, none of the patients developed recurrence or metastasis. The excellent prognosis of papillary carcinomas is in sharp contrast with the poor 5-year survival rate of the most common conventional adenocarcinomas of EBD and, therefore, warrants histological distinction.

The 5-year and 10-year relative survival rates for 71 patients with invasive papillary carcinoma, confined to the ductal wall, were found to be 28% and 21% in comparison to 18% and 12% for those with conventional adenocarcinoma respectively.[1]

The presence and location of the tumours are best shown by retrograde endoscopic cholangiography (ERCP), or percutaneous transhepatic cholangiography. Using the latter technique, the site of extrahepatic obstruction can be demonstrated in 95% of the cases.[6,7]

Surgical resection offers the only possibility of cure for

bile duct carcinoma. Proximal lesions are treated with resection (which may include hepatic lobectomy) and Roux-en-Y hepaticojejunostomy; distal lesions are treated by Whipple's procedure. A modest improvement in the results has been obtained with combined modality approach consisting of surgery, radiation therapy and chemotherapy. Location, histological grade, and histological type are the most important prognostic indicators.[8,9]

A variety of lesions of the EBD that show papillary architecture should be distinguished from papillary carcinoma, including papillomatosis, papillary or villous adenomas, primary papillary hyperplasia, and intraduct papillary mucinous neoplasms of the pancreas. Biliary papillomatosis is a multicentric disease that leads to multiple filling defects in several areas of the EBD, or the entire extrahepatic biliary tree. It is associated with a high rate of recurrence and poor prognosis. Malignant transformation occurs in 25% of the cases. In contrast, papillary carcinoma forms discrete, well-defined polypoidal lesion that obstructs the lumen of a single EBD. Papillary or villous adenomas show a less complex architecture, dysplastic changes are less pronounced. However, in adenomas, which show marked dysplasia, mitotic figures and some cribriforming are extremely difficult to differentiate from papillary carcinoma, especially in small biopsy sample. Primary biliary hyperplasia of the gallbladder may also involve the cystic duct, or CBD. However, there is no cytological atypia in these cases. Intraduct papillary mucinous carcinoma of pancreas may extend into the ampulla of Vater and CBD, simulating non-invasive papillary carcinoma. However, these tumours are usually multifocal, and produce abundant extracellular mucin, features that are lacking in these papillary carcinomas.[2]

Because the non-invasive and minimally invasive papillary carcinomas behave as non-metastasizing, or *in-situ* carcinomas, a conservative surgical approach such as segmental resection with frozen section of the surgical margins should be considered in select cases. Extension of the tumour into the surgical margins is a powerful adverse prognostic factor, and a predictor of local recurrence.[2]

It is important to separate invasive papillary carcinomas of the EBD from non-invasive and minimally invasive carcinomas as they behave as *in-situ* carcinomas and are associated with an excellent prognosis as compared to conventional adenocarcinomas of the EBD.

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