CASE REPORT

Peri-Ampullary Intraductal Tubulo-Papillary Neoplasm "Intraductal Tubulo-Papillary Neoplasm of Bile Duct (IPNB) at the Distal Common Bile Duct, Peri-Ampullary Tumor" A Case Report

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INTRODUCTION:

Intraductaltubulo- papillary neoplasm of bile duct (IPNB) is a less common variant of cholngiocarcinoma comparing it to more common types, sclerosing or nodular types. IPNB constitute about 12% of all cholangiocarcinoma[1]. IPNB characterized by a growth within the bile duct wall, showing papillary proliferatin of the lining epithelium having fibrovascular stalk protruding to the lumen of the bile duct. Tubular subtype, intraductal tubule-papillary neoplasm (ITPN) is even rarer variant of IPNB [1].

These biliary neoplasms have been drawn attention, they are characterized by excessive mucin production, and they show extensive papillary configuration into lumen of dilated bile duct and secrets excessive amounts of mucin. These neoplasms have various names such as mucin producing cholangiocarcinoma, mucin hyper secreting bile duct tumors and intraductal papillary mucinous tumors of bile duct. They may resemble intrapapillary mucinous neoplasms of pancrease, as both arise within a dilated duct system and demonstrate predominantly intraductal growth [2, 3].

Tumor location varies by a report. Some reports showed that the majority of IPNB was located at the intrahepatic bile duct, whereas the other showed that the most common location of IPNB was the hepatic hilum [1].

Sometimes multifocal, with or without macroscopically visible mucin secretion, and can be of any type of pathological transformation, from low-grade dysplasia to invasive carcinoma[4]. But few if any report about peri-ampullary IPNB as our case.

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IPNB also may affect pancreatic duct, which is uncommon, accounting for less than 1% of all pancreatic exocrine tumors and 3% of pancreatic intraductal neoplasms, most commonly located at the pancreatic head , and shows less aggressive behavior than other pancreatic malignancies[5].

KEYWORD: peri-ampullary intraductal neoplasm, intraductal papillary neoplasm of the bile duct, distal cholangiocarcinoma

This case presentation of rare invasive intraductal tubulo-papillary neoplasm IPNB of distal common bile duct that presented as peri-ampullary tumor

Case presentation

Fifty-three years old male patient presented with obstructive jaundice and itching to gastroenterology and hematology teaching hospital/ Baghdad (September 2018), investigations revealed severely elevated direct bilirubin and alkaline phosphatase that required early endoscopic retrograde cholangiography (ERCP) for palliation, which revealed that there is ampullary distortion and dilated commom bile duct (CBD) with distal filling defect suggesting common bile duct stone. Double bigtail stent deployed & biopsy taken from ampulla. Histopathology report revealed glandular distortion and villous configuration having low grade dysplasia.

Further assessment of the lesion was done by endoscopic ultrasound which revealed hyper echoic mass **11x15 mm at distal CBD** that causing CBD dilatation. Abdominal C.T. scan revealed no distant metastasis but ill-defined enhanced mass at peri-ampullary lesion 40x45 mm.

Whipple operation was planned, during exploration the lesion was found extend from distal CBD to the ampulla. (figure1).

Histopathology study revealed large dilated bile duct (cystically dilated) occupied by intra-ductal growth of tubule-papillary structures lined by columnar epithelium with eosinophilic cytoplasm showing variable degree of atypical changes, with invasion to duodenal wall, no invasion to pancrease, dysplasia in common bile duct resection margins (figures 2, 3, 4, 5) in keeping with tubule-papillary IPNB of distal common bile duct (pri-ampullary tumor).

All resection margins were tumor free (gastric, duodenum. Pancreatic (neck, and ancinate process) and common bile duct).

Nine lymph nodes were detected all were tumor free.

Pathological stage T3N0MX.

Patient develop low output pancreatic fistula that requires inpatient treatment for 2 weeks and discharge well after that.

DISCUSSION:

Intraductal papillary neoplasm of the bile duct (IPNB) is a variant of bile duct neoplasms; it is a rare variant, as the name indicates it has an intraductal growth pattern and better prognosis compared with common cholangiocarcinoma. IPNB has a papillary or villous growth within the bile duct lumen [6].

In 2010 this clinical entity IPNB was added to the world health organization WHO classification, which includes the intraductal papillary cholangiocarcinoma and its precursor lesions. (7)

Age incidence of IPNB is most commonly between 50 and 70 years, with different sex preponderances in different regions in the world such as: that male to female ratio is nearly 1:2 in Taiwan, 1:1 in japan, and 2:1 in Korea and western countries. [1, 8]

IPNB can be defined as a neoplasm that arises from biliary lining epithelium showing outgrowth exophytic nature as a papillary mass within the bile duct lumen exhibiting a prominent intraductal growth pattern, the level of this tumor can be anywhere in the biliary tree, weather in the intrahepatic or extrahepatic bile ducts. Theses tumors may be associated with overproduction of mucin and dilation of the bile duct.

Pathological features of these tumors showed microscopically fronds of papillary growth that have thin vascular cores. These papillary structures are lined by neoplastic epithelial cells showing varying degree of cytological and architectural atypia, the dysplasia ranged from low grade to borderline to high grade and lastly invasive carcinoma. [4]

These kinds of neoplasms can be considered as a pre-invasive (premalignant) lesions towards invasive cholangiocarcinoma. The WHO classification of these tumors is similar to that of intraductal papillary mucinous neoplasm of the pancreatic, where IPNB is classified into:

- Intraductal papillary neoplasm of the bile duct (IPNB) with "low grade dysplasia"
- IPNB "intermediate grade dysplasia": showing mild to moderate nuclear atypia, and nuclear pseudostratification limited to basal two third of the epithelium (borderline).
- "High grade" IPNB showing sever cytological atypia, loss of nuclear polarity or architectural cribriforming and papillary fusion. and lastly
- IPNB that is associated with stromal invasion: "invasive carcinoma". [9]

Grossly these tumors have variable morphological presentations: they could present as single or multiple exophytic polypoid masses protruded to the lumen of the dilated biliary system.

Another morphological pattern of gross presentation is visible granular or small papillary mucosal lesion. These masses can fill the lumen of the dilated ductal system by extending longitudinally with a cast like appearance. Another way of presentation is as a well-defined cystic lesion either as a septated cystic mass "multilocular", or "unilocular " cystic mass. These cysts contain thick mucinous fluid. While examining the inner wall of the cystic lesions, they are either smooth lining, or finely granular or containing nodules attached to the inner wall "papillary mural nodule". Sometimes it is difficult to demonstrate the anatomical relationship with the biliary ductal system. [10]

A combination of papillary and glandular architectural feature called "tubule-papillary" appearance, these cases lacks over secretion of mucin.

Generally extensive papillary structures having thin fibrovascular cores are the characteristic features, hence the name intraductal papillary neoplasm. [11]

Regarding microscopical findings in these lesions and according to conventional routine "hematoxylin and eosin" staining and immunohistochemical study with tumor markers of mucin core protein used, these neoplasm are classified into four types:

- First type: composed of columnar epithelial cells with round nuclei and pink cytoplasm, usually positive for MUC1, MUC5AC, MUC6 but negative for MUC2, they are called "the pancreaticobiliary type" which is the commonest type.
- Second type: when the neoplastic epithelial cells showed strong expression for MUC2, MUC5AC and CDX2 but not MUC1, this type is called "the intestinal type" which mimics intestinal villous tumor.
- Third type: composed of neoplastic epithelial cells with columnar features mimicking gastric foveae, they express MUC5AC but are negative for MUC1 and MUC2; they are called "the gastric type".
- Forth type: composed of neoplastic epithelial cells that have deep eosinophilic cytoplasm, express MUC5AC, MUC6, this type is called "the oncocytic type", it is rare. [12]

IPNB neoplasms are P53, CK7 and CK20 positive. Molecular cytogenetic description showed: K RAS actively mutation 29%, 18 q- in 31%, no loss of DPC4. [12]

Considering the staging of IPNB; it is dependent on "the degree of dysplasia and depth of invasion". AJCC stage T1 include: "IPNB with low to intermediate grade dysplasia", and "IPNB with high grade dysplasia". AJCC stage T2 include: "intraductal growth type cholangiocarcinoma". [12]

When stromal invasion develops in IPNB, the histologic types of the invasive carcinoma are either glandular adenocarcinoma "forming tubules and gland ", or mucin producing tumors, which are called "mucinous, colloid" carcinoma.[13]

Figure 1: the gross appearance of the tumor Shows dilated CBD with intraductal growth and stent inside

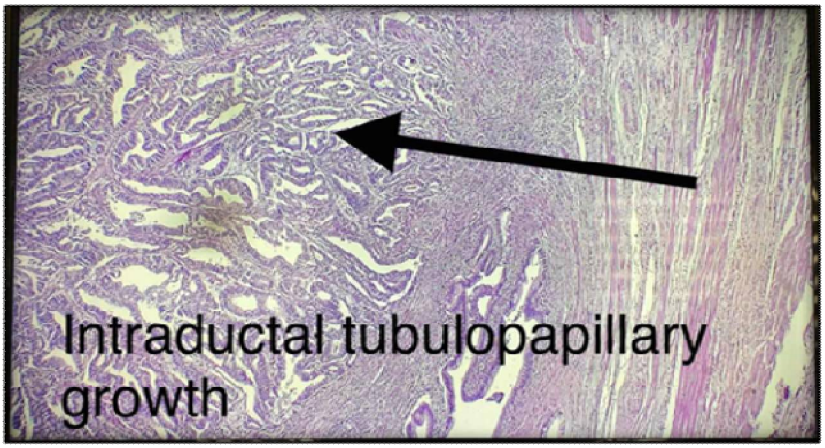

Figure 2: shows tubular pattern of intraductal papillary growth

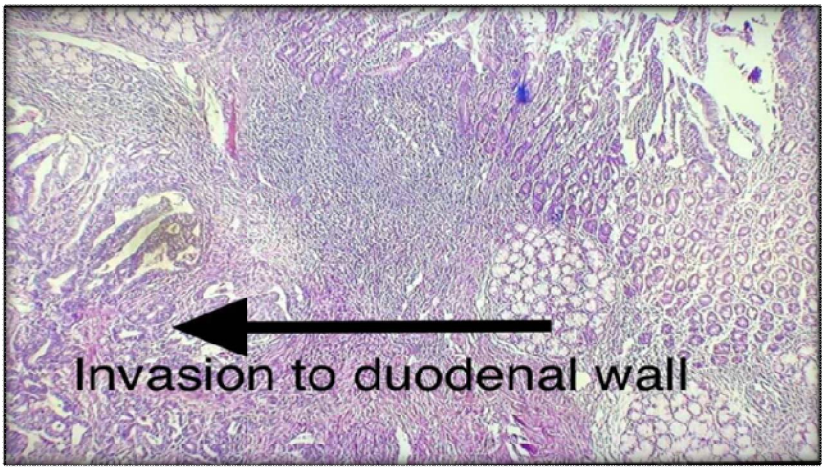

Figure 3: shows doudenal wall invasion by the tubule-papillary structures.

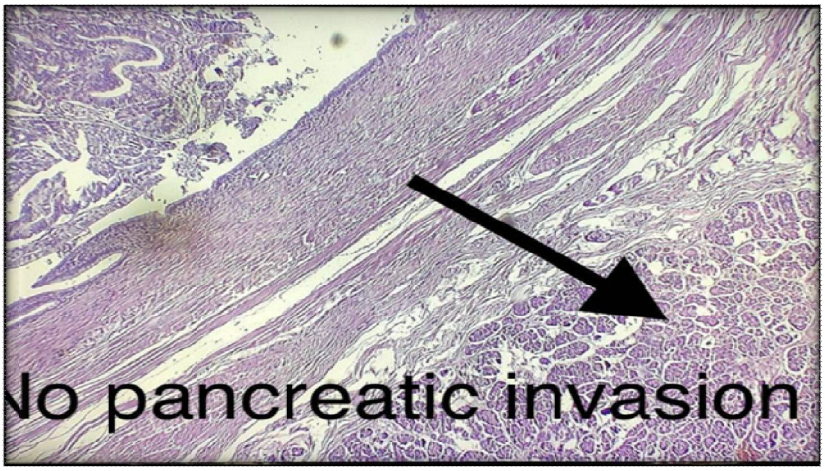

Figure 4: shows no pancreatic tissue without invasion

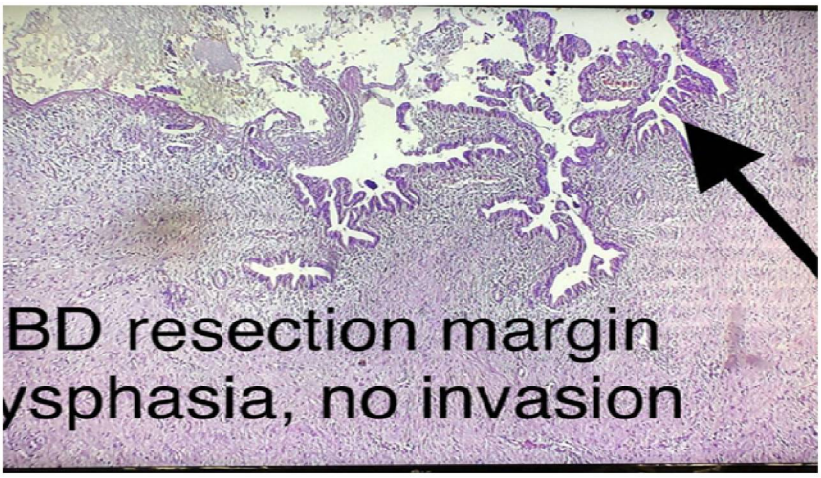

Figure 5: shows CBDresection margin with dysplasia but no invasion

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