

Case Report

Intraductal Oncocytic Papillary Neoplasm of the Pancreas

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Abstract

Intraductal oncocytic papillary neoplasm (IOPN) is a rare subset of intraductal papillary mucinous neoplasm (IPMN). Herein, we report a case of IOPN in a 77 year-old woman with history of colonic adenocarcinoma and bilateral primary renal tumors, and we present a review of related literature. A computed tomography (CT) for follow-up of the renal tumors showed dilation of the pancreatic duct with abnormal soft tissue. The patient underwent fine needle aspiration and subsequent Whipple resection. Histologically, the tumor was entirely confined within the pancreatic duct, predominantly solid, and markedly pleomorphic with medullary-like features. The final diagnosis was IOPN. IOPN, first described in 1996, is recognized in pancreas and biliary tract. This neoplasm is typically composed of complex papillary structures and frequently associated with high-grade dysplasia. Due to the rarity of the tumor, its management and survival outcome are not well understood. The present case illustrates an IOPN composed entirely of high-grade neoplastic cells (intraductal oncocytic carcinoma) in a patient with history of clear cell renal cell carcinoma (clear cell RCC) and oncocytoma.

ABBREVIATIONS

IOPN, IPMN, IDN, ITPN, WHO, RCC, CT

CASE REPORT

Our patient is a 77 year old Caucasian woman with a history of resected colonic adenocarcinoma at the age of 71, resected clear cell RCC of the right kidney at age 72 and an aspirated and subsequently ablated bland oncocytic neoplasm of left kidney at age 76. A contrast enhanced CT scan of the abdomen performed in follow-up surveillance demonstrated dilation of the pancreatic duct and ampulla with abnormal soft tissue attenuation. There was no evidence of liver, lymph node or lung metastasis by imaging. The pancreatic tumor was confined within the duct, and the patient underwent a pancreaticoduodenectomy. Grossly, the tumor was tan-white and friable, encompassing 2.5 cm of the pancreatic duct. Tumor extended into the major papilla; the duodenum was otherwise unremarkable (Figure 1, arrow at ampulla). There was no sign of invasive disease. The entire pancreas and ampulla were submitted for histologic evaluation. On microscopy, the tumor was highly cellular with pleomorphic, high-grade nuclei, prominent nucleoli and had medullary features with abundant eosinophilic cytoplasm and intra-tumoral lymphocytes. It was predominantly solid with occasional complex papillary foci (H&E- Figure 2 and inset). Pancreatic tumor by morphology was distinctly different from the patient's colonic and renal tumors. To entirely exclude a possibility of metastatic disease, comparative immunostaining was performed which proved the pancreatic tumor as an independent primary.



Figure 1 Gross picture, IOPN involving pancreatic duct with extension to the ampulla (arrow pointing to the ampulla).

Tumor was positive with CK7 (OV-TL 12/30; Thermo Scientific) and mitochondrial antibody (113-1; Biogenex) but was negative for CDX-2 (CDX2-88; Biogenex), CK20 (Ks 20.8; Thermo Scientific), alpha-1-antitrypsin (Polyclonal; Thermo Scientific), estrogen receptor (ER1D5; Dako), RCC (PN; Thermo Scientific), CD10 (56C6; Thermo Scientific), PAX-8 (MRQ-50; Ventana) and S-100 (4C4.9; Thermo Scientific). Further work up for mismatch repair evaluation by immunoperoxidase staining was negative for protein loss in both the pancreatic IOPN as well as the prior colonic adenocarcinoma. Clinical and imaging surveillance six

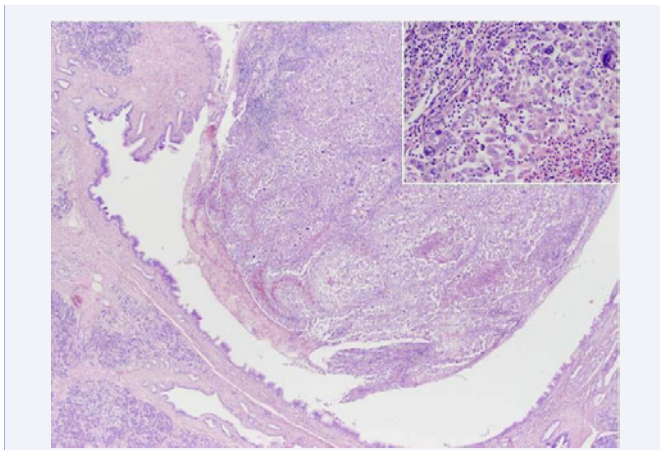


Figure 2 H&E- Predominantly solid neoplasm with papillary foci, confined within the pancreatic duct. Tumor is composed of high grade neoplastic cells with eosinophilic cytoplasm and prominent nuclei; note the abundant interspersed inflammatory cells (40x and inset 400x).

months after pancreatic tumor resection remains negative for evidence of disease progression in our patient.

DISCUSSION

IPMNs constitute common cystic entities of the pancreas and a precursor for invasive ductal adenocarcinoma [1]. Although intraductal neoplasms (IDNs) have been long recognized, the most recent WHO defines new categories. According to the 2010 WHO classification of tumors of the digestive tract, IDNs are classified into intraductal papillary mucinous neoplasms (IPMNs) and intraductal tubulopapillary neoplasms (ITPNs). In recent years, there has been an increase in our knowledge of these tumors [2-4].

Pancreatic IDNs are defined as epithelial neoplasms arising and proliferating within the pancreatic duct, often associated with ductal dilation. IPMNs often show epithelia with differentiated papillary features and mucin secretion. They can arise from the main pancreatic duct or the branch duct [2,5].

The predominant architecture, histomorphology and/or subtyping of mucin expression allow for classification of IPMNs into 4 different categories: gastric, intestinal, pancreaticobiliary and oncocytic. IPMNs are associated with, in variable degrees, epithelial dysplasia or carcinoma. This is reflected in the 2010 WHO classification as IPMN with low-intermediate grade dysplasia, with high grade dysplasia and IPMN with an invasive component [1,2,5-7]. According to the literature, high-grade dysplasia or carcinoma is more frequently observed in pancreaticobiliary or oncocytic type, followed by intestinal and less frequently gastric type [8]. In IPMNs, both growth pattern (main duct versus branch duct) and histologic subtypes have prognostic relevance. The 5-year survival of the pancreaticobiliary type is significantly worse than the intestinal type. Both high-grade dysplasia and aggressive behavior have been also reported in IOPN. Yet due to the rarity and limited clinical experience, behavioral difference between IOPN and other subtypes of IPMN is not clearly elucidated [2,6,8-10].

IOPN was first described in 1996 by Adsay *et al.* and since then has been recognized in the pancreas as well as the biliary tree [11-13]. Histologically, it is an eosinophilic neoplasm with complex arborizing papillae or cribriform foci. The papillae are lined by several layers of cuboidal to columnar cells. A constant finding is presence of abundant granular, eosinophilic cytoplasm due to the accumulation of mitochondria. Other cell types including goblet cells may be occasionally interspersed. Most IOPNs have adequate cytoarchitectural atypia to be classified as high-grade dysplasia/ carcinoma in situ and invasive carcinoma can arise in their association [10,13-14]. In the original case series, nine of the eleven IOPNs were entirely intraductal. One case demonstrated focal microinvasion, while another had widespread invasion [11]. While IOPN can be associated with an invasive component, extension of the intraductal neoplasm into small or larger ducts may mimic true invasion; familiarity with this process is critical to avoid misdiagnosis.

Diagnosis of IOPN is morphology based; however, immunostaining may play a role in exclusion of metastasis, particularly in patients with multiple primary tumors. MUC6, CK7, HepPar1 and anti-mitochondrial staining is a feature of many IOPNs, and MUC1, MUC5AC, CEA, and CA19-9 staining have been variably identified. MUC 2 staining is usually weak or focal, if any. PAS and PAS-D stains show cytoplasmic positivity. These tumors are generally negative for CK20 and CDX2 [10,12,15].

Although both IOPN and pancreaticobiliary IPMN are associated with high grade dysplasia/ carcinoma, in contrast to pancreaticobiliary subtype, IOPN uncommonly harbors the KRAS mutation [14,16]. KRAS mutations were identified in only 17% of pancreatic IOPN while 58% of the pancreatobiliary subtype [16]. Schlitter *et al.* reports lack of KRAS mutations in all IOPNs of the bile duct in their series [17].

Clinic-radiologic features of IOPN are similar to other types of IPMN and thus making pre-operative diagnosis difficult [18]. It is possible that early detection and surgical treatment can lead to a cure, yet no conclusion about the efficacy of surveillance and long term follow-up can be drawn [5]. Considering the risk of multifocality, necessity for lifelong surveillance has been considered for IOPN cases with partial resection [10]. Features including size, mural nodules, and mass effect (obstructive symptoms), as worrisome predictors of progression in IPMNs, [19,20] may have potential in decision making regarding follow up in IOPN. However, the specific data, as relates to IOPN, is lacking.

Subtype differentiation can lead to improvement in clinical management of patients with IPMN [21]; once invasive carcinoma develops, prognosis is generally poor for any IPMN, even an otherwise-indolent subtype such as gastric [22]. Thus en-block tissue evaluation is critical not only for accuracy of diagnosis but assessment of clinical outcome. As there is a strong consensus for resection of IPMNs with invasive components, an IOPN with any invasion should be treated the same as an invasive adenocarcinoma [6]. In the presented case, an entirely high-grade histologic spectrum of IOPN (intraductal oncocytic carcinoma) with medullary features and its association with bilateral renal neoplasm are noteworthy. To the best of our knowledge, association of IOPN with clear cell or oncocytic renal tumors

has not been reported. Whether this represents a spectrum of a syndromic process is not known.

REFERENCES

- Schlitter AM, Esposito I. [Pathology and classification of intraductal papillary mucinous neoplasms of the pancreas]. *Chirurg*. 2012; 83: 110-115.
- Yamaguchi H, Kuboki Y, Hatori T, Yamamoto M, Shimizu K, Shiratori K, et al. The discrete nature and distinguishing molecular features of pancreatic intraductal tubulopapillary neoplasms and intraductal papillary mucinous neoplasms of the gastric type, pyloric gland variant. *J Pathol*. 2013; 231: 335-341.
- Cooper CL, O'Toole SA, Kench JG. Classification, morphology and molecular pathology of premalignant lesions of the pancreas. *Pathology*. 2013; 45: 286-304.
- Lüttges J. [What's new? The 2010 WHO classification for tumours of the pancreas]. *Pathologe*. 2011; 32 Suppl 2: 332-336.
- Grützmann R, Post S, Saeger HD, Niedergethmann M. Intraductal papillary mucinous neoplasia (IPMN) of the pancreas: its diagnosis, treatment, and prognosis. *Dtsch Arztebl Int*. 2011; 108: 788-794.
- Distler M, Welsch T, Aust D2, Weitz J, Grützmann R1. [Intraductal papillary mucinous neoplasm of the pancreas (IPMN)--standards and new aspects]. *Zentralbl Chir*. 2014; 139: 308-317.
- Kang MJ, Lee KB, Jang JY, Kwon W, Park JW, Chang YR. Disease spectrum of intraductal papillary mucinous neoplasm with an associated invasive carcinoma invasive IPMN versus pancreatic ductal adenocarcinoma-associated IPMN. *Pancreas*. 2013; 42: 1267-1274.
- Hara T, Ikebe D, Odaka A, Sudo K, Nakamura K, Yamamoto H, et al. Preoperative histological subtype classification of intraductal papillary mucinous neoplasms (IPMN) by pancreatic juice cytology with MUC stain. *Ann Surg*. 2013; 257: 1103-1111.
- Liszka L, Pajak J, Zielińska-Pajak E, Krzych L, Gołka D, Mrowiec S, et al. Intraductal oncocytic papillary neoplasms of the pancreas and bile ducts: a description of five new cases and review based on a systematic survey of the literature. *J Hepatobiliary Pancreat Sci*. 2010; 17: 246-261.
- Wohlauer MV, McManus M, Fukami N, Gajdos C. Intraductal oncocytic papillary neoplasm of the pancreas: report of a case requiring completion pancreatectomy. *JOP*. 2013; 14: 77-80.
- Adsay NV, Adair CF, Heffess CS, Klimstra DS. Intraductal oncocytic papillary neoplasms of the pancreas. *Am J Surg Pathol*. 1996; 20: 980-994.
- Jurczyk MF, Zhu B, Villa C, DeFrias D, Lin X. Cytomorphology of intraductal oncocytic papillary neoplasm of the liver. *Diagn Cytopathol*. 2014; 42: 895-898.
- Kato Y, Konishi M, Kinoshita T, Takahashi S, Gotohda N, Kinoshita T. Intraductal oncocytic papillary neoplasm of the extrahepatic bile duct: report of a case. *Surg Today*. 2012; 42: 1240-1243.
- Patel SA, Adams R, Goldstein M, Moskaluk CA. Genetic analysis of invasive carcinoma arising in intraductal oncocytic papillary neoplasm of the pancreas. *Am J Surg Pathol*. 2002; 26: 1071-1077.
- Tanaka M, Fukushima N, Noda N, Shibahara J, Kokudo N, Fukayama M. Intraductal oncocytic papillary neoplasm of the bile duct: clinicopathologic and immunohistochemical characteristics of 6 cases. *Hum Pathol*. 2009; 40: 1543-1552.
- Xiao HD, Yamaguchi H, Dias-Santagata D, Kuboki Y, Akhavanfar S, Hatori T. Molecular characteristics and biological behaviours of the oncocytic and pancreatobiliary subtypes of intraductal papillary mucinous neoplasms. *J Pathol*. 2011; 224: 508-516.
- Schlitter AM, Born D2, Bettstetter M3, Specht K, Kim-Fuchs C4, Riener M05. Intraductal papillary neoplasms of the bile duct: stepwise progression to carcinoma involves common molecular pathways. *Mod Pathol*. 2014; 27: 73-86.
- Kato T, Ikari S, Hirata K, Machida T, Nakamura H, Meguro T. FDG-PET Findings of Intraductal Oncocytic Papillary Neoplasms of the Pancreas: Two Case Reports. *Case Rep Gastroenterol*. 2012; 6: 415-424.
- Buxbaum JL, Jhala NC, Christein JD, Eloubeidi MA. Oncocytic intraductal papillary mucinous neoplasm with carcinomatous degeneration. *Gastrointest Endosc*. 2012; 75: 898-899.
- Ogura T, Masuda D, Kurisu Y, Edogawa S, Imoto A, Hayashi M. Potential predictors of disease progression for main-duct intraductal papillary mucinous neoplasms of the pancreas. *J Gastroenterol Hepatol*. 2013; 28: 1782-1786.
- Distler M, Kersting S, Niedergethmann M, Aust DE, Franz M, Rückert F. Pathohistological subtype predicts survival in patients with intraductal papillary mucinous neoplasm (IPMN) of the pancreas. *Ann Surg*. 2013; 258: 324-330.
- Yamada S, Fujii T, Shimoyama Y, Kanda M, Nakayama G, Sugimoto H. Clinical implication of morphological subtypes in management of intraductal papillary mucinous neoplasm. *Ann Surg Oncol*. 2014; 21: 2444-2452.

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