CASE REPORT

Marked Distension of Main Pancreatic Duct by Intraductal Tubulopapillary Neoplasm Causing Global Pancreatic Atrophy

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ABSTRACT

Intraductal tubulopapillary neoplasm is a rare primary pancreatic tumor that accounts for less than 1% of all pancreatic tumors and 3% of all intraductal pancreatic neoplasms. Reports on intraductal tubulopapillary neoplasm have been rare, and most have described it in the classic macroscopic presentation. We describe a unique case of intraductal tubulopapillary neoplasm wherein the pancreatic duct has completely expanded to fill the borders of the pancreas without any noticeable remaining parenchyma. Global pancreatic parenchymal atrophy has occurred in this patient due to the marked distension of the intraductal tubulopapillary neoplasm. The extent of intraductal expansion makes recognition of commonly observed radiological signs difficult, as there is no clear demarcation between intraductal tumor growth and dilated duct without tumor growth. As more is understood about intraductal tubulopapillary neoplasms, it will be important to be able to recognize the classic and unique radiological presentations in order to provide prompt diagnosis and treatment for these patients.

INTRODUCTION

Intraductal tubulopapillary neoplasm (ITPN) is a rare primary pancreatic tumor that accounts for less than 1% of all pancreatic tumors and 3% of all intraductal pancreatic neoplasms [1]. Under the 2010 World Health Organization classification, ITPN is a distinct form of intraductal neoplasm, along with intraductal papillary mucinous neoplasm. Reports on ITPN have been rare, and most have described it in the classic macroscopic presentation. Here, we describe a unique case of ITPN wherein the classic imaging signs are not observed, and the pancreatic duct has completely expanded to fill the borders of the pancreas without any noticeable remaining parenchyma.

CASE REPORT

A 48 year-old male underwent abdominal CT to evaluate unintentional weight loss of 30 kilograms for the last eight months associated with intermittent steatorrhea. The patient otherwise had no significant past medical or surgical history. He denied alcohol or tobacco use and did not report any family history of malignancy.

Received October 01st, 2015 - Accepted November 15th, 2015
Keywords Atrophy; Pancreatic ducts; Neoplasm
Abbreviations ERCP endoscopic retrograde cholangiopancreatography; ITPN intraductal tubulopapillary neoplasm; MRCP magnetic resonance cholangiopancreatography
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On physical examination, his temperature was 98.8˚F, pulse 78, and blood pressure 139/89 mm/hg. Cardiac and pulmonary examinations were unremarkable. His abdomen was soft, nontender, and nondistended with positive bowel sounds and no organomegaly. There was no epigastric tenderness observed. Blood and laboratory studies were unremarkable, though the carcinoembryonic antigen (CEA) level was 431.

Biphasic contrast abdominal CT revealed a solid enhancing intraductal pancreatic mass markedly distending the main pancreatic duct and resulting in global atrophy of the pancreatic parenchyma **(Figures**

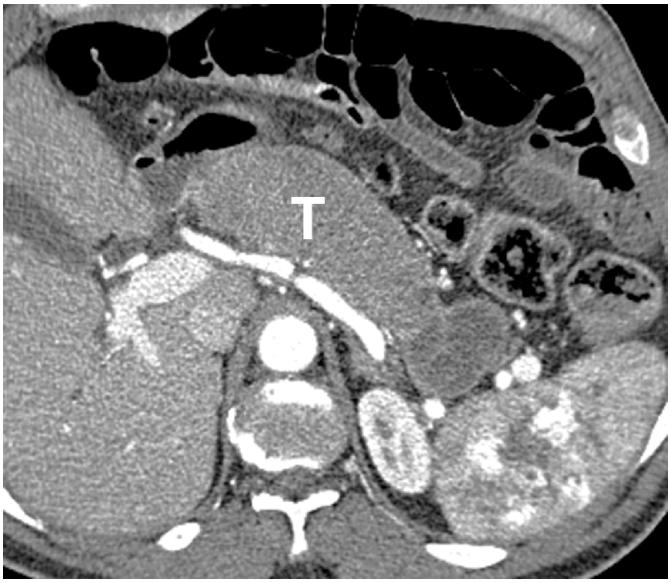

Figure 1. Arterial phase image of the body of the pancreas showing an enhancing solid tumor (T) markedly distending the main pancreatic duct. There is no visible normal pancreatic parenchyma.

1-3). Initial EUS-guided fine needle aspiration revealed normal duodenum and stomach, but abnormal pancreatic features like diffuse echogenicity and bulky parenchyma. The main pancreatic duct was not visualized at that time. Cytology then demonstrated sheets of ductal epithelial cells with architectural disarray, nuclear membrane irregularities and nuclear pleomorphism with scattered markedly enlarged nuclei, suggesting primary pancreatic adenocarcinoma. As a result, the initial concern was for an infiltrating malignancy involving the entire pancreas, and total pancreatectomy was pursued.

The patient then underwent total pancreatectomy, splenectomy, gastric antrectomy, and cholecystectomy. Surgical findings demonstrated no ascites and no carcinomatosis. The pancreas was very thick and abnormal, measuring 4-5 cm throughout the entire gland. The pancreatic tumor was adherent to the portal vein but did not demonstrate invasion. The pancreas was difficult to dissect because of the thickness of the mass within and also because of an inflammatory response around the pancreas. However, no metastases were noted and pancreatectomy was successful.

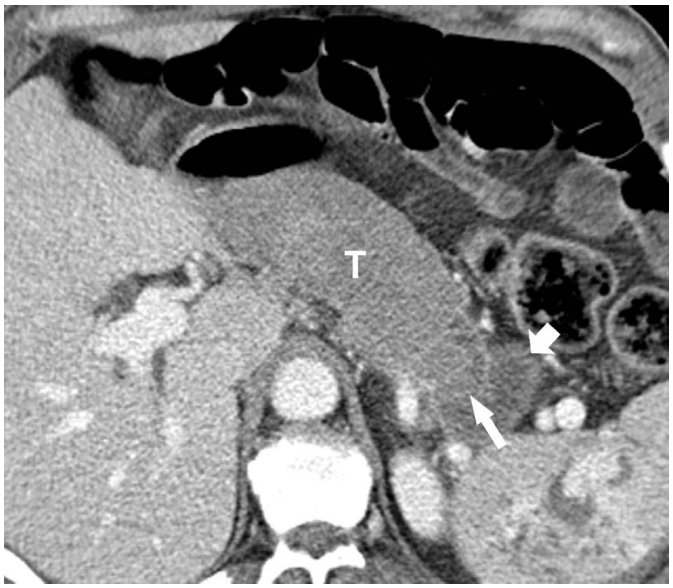

Figure 2. Venous phase image of the body and tail of the pancreas showing the enhancing tumor (T). Note the tumor protruding (long arrow) within a dilated portion of the pancreatic duct (short arrow).

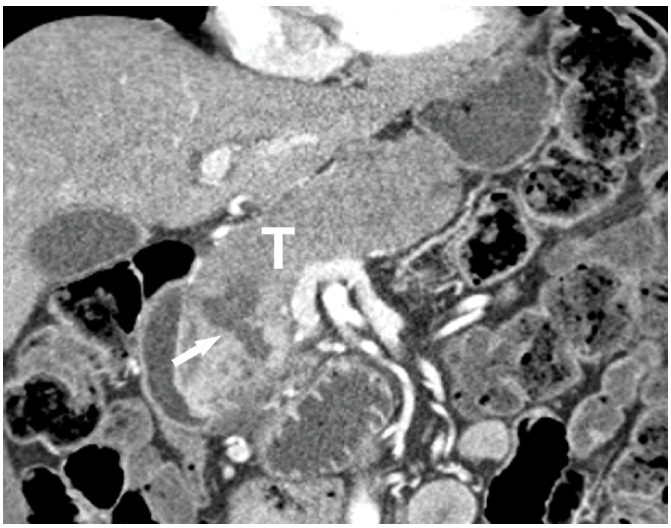

Figure 3. Coronal view of the pancreas showing the solid intraductal tumor (T) with an areas of central necrosis (arrow).

Grossly, the pancreas was serially sectioned to reveal a tan-white, well-circumscribed mass measuring 6.8 x 3.5 x 6.5 cm located in the head of the pancreas. The mass was located 0.2 cm from the uncinate margin and 0.6 cm from the posterior soft tissue edge. The tumor did not show gross invasion and the remainder of the pancreas was grossly involved by tumor.

Histological analysis revealed back-to-back tubular glands with focal papillary elements **(Figures 4, 5).** The glands were lined by low cuboidal cells characterized by medium sized uniform nuclei with small central nucleoli, with variable amounts of amphophilic cytoplasm. The tumor displayed high-grade cytoarchitectural features, with occasional cribriform arrangements noted. Luminal mucin was not readily identified. The lesion was surrounded by a thick fibrous wall and no invasion was identified. Mitotic figures were rare (0-1 per 10 high-powered fields). No pleomorphism, tumor cell necrosis, or abnormal division figures were found.

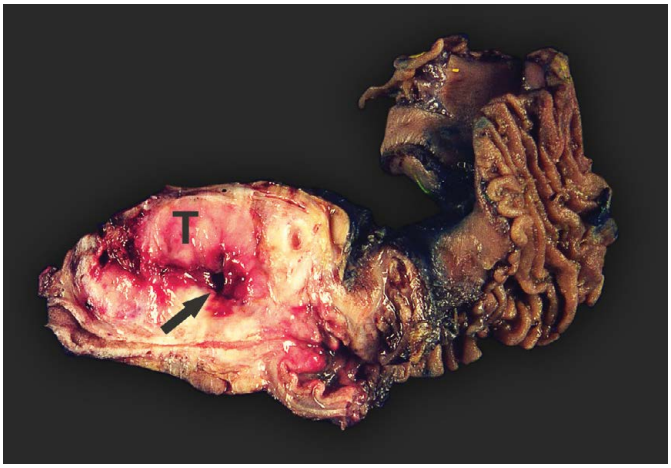

Figure 4. Gross pathology specimen of the head of the pancreas showing the intraductal tumor (T) with an area of necrosis (arrow).

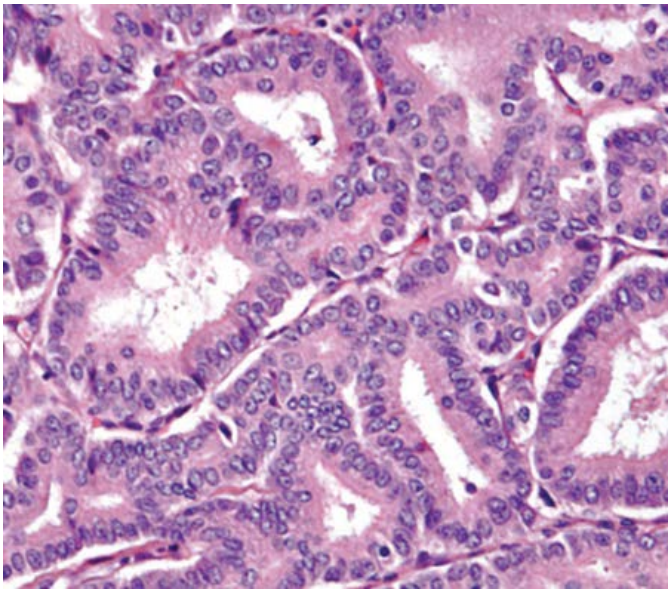

Figure 5. 100X magnified H&E stain of the pancreatic mass showing back–to-back glands with a tubular architecture.

Immunohistochemical staining was performed and the neoplastic cells failed to react against the neuroendocrine markers, synaptophysin or chromogranin. Further, the marker of acinar differentiation, chymotrypsin, was negative. Additional immunohistochemical and molecular analysis were not performed. Although necrosis was not prominent, the morphologic and immunohistochemical findings were felt to be consistent with an intraductal tubulopapillary neoplasm, given the lack of mucin, low cuboidal cellular morphology, and predominantly tubular architecture with extensive back-to-back gland formations.

The surrounding pancreatic tissue showed extensive atrophy with residual islands of bland appearing islet cells. The neoplasm measured 9.3cm in the greatest dimension with 25 uninvolved lymph nodes and negative margins. Since his surgery and starting pancrealipase, the patient is no longer losing weight and denies any diarrhea or steatorrhea.

DISCUSSION

ITPN is a rare primary pancreatic tumor that accounts for less than 1% of all pancreatic exocrine neoplasms and 3% of intraductal neoplasms of the pancreas [1, 2]. It is estimated that about 50% of ITPNs occur in the head of the pancreas, 35% grow diffusely, and 15% originate in the tail [3]. Under the World Health Organization (WHO) classification, ITPN has been designated as distinct from intraductal papillary mucinous neoplasm (IPMN) and pancreatic intraepithelial neoplasia (PanIN) [4]. IPMN and ITPN are macroscopically detectable neoplasms, while PanIN is defined microscopically.

However, because IPMNs and ITPNs both are initially recognized by the presence of dilated pancreatic ducts, it is important to understand the histopathological and radiological differences. Histologically, ITPN can be distinguished from the more common IPMN in a variety of ways. The most classic difference between the two entities is the abundance of mucin in IPMNs and the lack of mucin in ITPNs. In addition, tall columnar cells with visible cytoplasmic mucin and well-developed papillae are characteristic of IPMNs. On the other hand, cuboidal cells with minimal luminal mucin and necrotic foci are unique features of ITPNs [5].

Interestingly, despite such characteristic histopathological findings, ITPNs have been described with many subtle variations in the literature. For example, Jokoji et al. have described a case of ITPN with stromal osseous and cartilaginous metaplasia and Ahls et al. have described a case of ITPN with clear cell phenotype [3, 6]. In addition, ITPNs are not unique to the pancreas, as several reports of ITPNs occurring in the bile ducts have also been described [7-9].

Radiographically, most ITPNs are indistinguishable from IPMNs, as both neoplasms have intraductal growth, cystic dilatation, and both communicate with larger pancreatic ducts [2]. However, there are several histological distinctions between these two entities. Intraductal tubulopapillary neoplasms show the following pathological characteristics: (i) the appearance of a solid nodular tumor that obstructs the dilated ducts on macroscopic examination; (ii) absence of visible mucin secretion; (iii) tubulopapillary growth on histology; (iv) uniform high grade atypia throughout the neoplasm; (v) easily recognizable necrotic foci; (vi) ductal differentiation, as indicated by cytokeratin 7 and/or cytokeratin 19 expression; (vii) absence of acinar differentiation, as indicated by the negativity for trypsin; (viii) negativity of MUC2, MUC5AC, and fascin; and (ix) absence of mutations in KRAS and BRAF [1]. These findings suggest that ITPN is characterized by pancreatic duct differentiation as opposed to the gastroenteric differentiation of IPMN [10].

Previous studies have described several unique radiological features of ITPNs that may aid in identification and diagnosis. Classically, ITPNs are described as solid nodules obstructing dilated ducts without visible secreted mucin [1]. On CT imaging, intraductal tumor growth can be observed when the dilated pancreatic duct shows two different colors—lower density representing fluid without tumor growth, and a slightly higher density area indicating tumor growth intraductally. This has been described as a "2-tone duct sign" [5]. Other CT findings also include branch duct dilatation, hypoenhanced area of tumor necrosis, calcification, and infiltrative growth. Characteristic findings on magnetic resonance cholangiopancreatography (MRCP) and endoscopic retrograde cholangiopancreatography (ERCP) have also been described. A "cork-of wine bottle" sign, in which the tumor is surrounded by pancreatic fluid in the dilated duct, can also be observed with ITPNs [5].

We describe a unique case of ITPN wherein the pancreatic duct has completely expanded to fill the borders of the pancreas without any noticeable remaining parenchyma. Global pancreatic parenchymal atrophy has occurred in this patient due to the marked distension of the ITPN. The extent of intraductal expansion makes recognition of the 2-tone duct sign difficult, as there is no clear demarcation between intraductal tumor growth and dilated duct without tumor growth. As more is understood about ITPNs, it will be important to be able to recognize the classic and unique radiological presentations in order to provide prompt diagnosis and treatment for these patients.

Conflict of Interests

Authors declare no conflict of interests for this article.

References

1. Yamaguchi H, Shimizu M, Ban S, Koyama I, Hatori T, Fujita I, Yamamoto M, Kawamura S, et al. Intraductal tubulopapillary neoplasms of the pancreas distinct from pancreatic intraepithelial neoplasia and intraductal papillary mucinous neoplasms. Am J Surg Pathol 2009; 33:1164-1172. [PMID: 19440145]

2. Guan H, Gurda G, Lennon AM, Hruban RH, Erozan YS. Intraductal tubulopapillary neoplasm of the pancreas on fine needle aspiration: case report with differential diagnosis. Diagn Cytopathol 2014; 42:156-160. [PMID: 22807417]

3. Ahls MG, Niedergethmann M, Dinter D, Sauer C, Lüttges J, Post S, Marx A, Gaiser T. Case report: Intraductal tubulopapillary neoplasm of the pancreas with unique clear cell phenotype. Diagn Pathol 2014; 9:11. [PMID: 24443801]

4. Bosman FT, Carneiro F, Hruban RH, Theise ND. WHO classification of tumours of the digestive system. World Health Organization; 2010.

5. Motosugi U, Yamaguchi H, Furukawa T, Ichikawa T, Hatori T, Fujita I, Yamamoto M, Motoi F, et al. Imaging studies of intraductal tubulopapillary neoplasms of the pancreas: 2-tone duct sign and cork-of-wine-bottle sign as indicators of intraductal tumor growth. J Comput Assist Tomogr 2012; 36:710-717. [PMID: 23192209]

6. Jokoji R, Tsuji H, Tsujimoto M, Shinno N, Tori M. Intraductal tubulopapillary neoplasm of pancreas with stromal osseous and cartilaginous metaplasia; a case report. Pathol Int 2012; 62:339-343. [PMID: 22524663]

7. Katabi N, Torres J, Klimstra DS. Intraductal tubular neoplasms of the bile ducts. Am J Surg Pathol 2012; 36:1647-1655. [PMID: 23073323]

8. Park HJ, Jang KT, Heo JS, Choi YL, Han J, Kim SH. A potential case of intraductal tubulopapillary neoplasms of the bile duct. Pathol Int 2010; 60:630-635. [PMID: 20712650]

9. Zen Y, Amarapurkar AD, Portmann BC. Intraductal tubulopapillary neoplasm of the bile duct: potential origin from peribiliary cysts. Hum Pathol 2012; 43:440-445. [PMID: 21813159]

10. Tajiri T, Tate G, Inagaki T, Kunimura T, Inoue K, Mitsuya T, Yoshiba M, Morohoshi T. Intraductal tubular neoplasms of the pancreas: histogenesis and differentiation. Pancreas 2005; 30:115-121. [PMID: 15714133]