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Case Report

Pancreatic intraductal tubular adenoma in a coexistent intraductal papillary mucinous neoplasm masquerading radiologically as a mural nodule

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Abstract: Intraductal tubular adenoma (ITA) of the pancreas is a rare lesion. Some cases have been described in association with an intraductal papillary mucinous neoplasm (IPMN)-gastric type, while others have occurred in isolation. A 73-year old man had an incidentally detected cystic mass in the pancreas, the radiological features of which were suggestive of an IPMN with a mural nodule. In view of this worrying radiological feature, a distal pancreatectomy was performed. Histological evaluation of the pancreas revealed a gastric-type IPMN. Within a dilated pancreatic branch duct, a polypoid mass was noted. The polyp was lined by gastric (pyloric) epithelium and contained several glands lined by similar epithelium, in keeping with an ITA. In addition, there was evidence of torsion of the ITA with stromal mixed inflammation, hemosiderin deposits, foamy macrophages and osteoclastic giant cells. ITA has been noted to coexist with IPMN, however, the case presented herein showed radiological features mimicking a mural nodule thus raising the clinico-radiological suspicion of malignancy arising in an IPMN.

Keywords: Intraductal tubular adenoma, intraductal papillary mucinous neoplasm, pancreas

Introduction

Intraductal lesions of the main pancreatic duct and their immediate branches are uncommon although increasingly recognized. Three distinct intraduct lesions are encountered: intraductal papillary mucinous neoplasm (IPMN), intraductal tubular adenoma (ITA) and intraductal carcinoma. Rarely, intraductal forms of other pancreatic tumors may be encountered.

ITA pyloric-type is a rare entity with the first case being described in 1999 [1]. Subsequently, other cases have been documented [2-8]. It is morphologically similar to the tubular/papillary adenoma that occurs in the gallbladder [9]. It is characterized by an intraductal location (often filling the duct lumen), polypoid configuration and by the closely packed tubular or glandular structures that are highly reminiscent of pyloric glands. ITAs differ from adenomas of the colorectum in that the epithelium from which it arises is pancreatico-biliary with gastric-type metaplasia rather than intestinal-type metaplasia. As such, the morphology and dysplastic change seen in ITA is somewhat different from usual tubular adenomas of the colorectum.

IPMN is now a well-recognized clinical, radiological and pathological entity. IPMNs may be composed of different types of epithelium: gastric or pyloric type, intestinal, pancreaticobiliary, oncocytic or combinations of these epithelia. Recently, it has been proposed that IPMN be graded as low- or high-grade lesions [10].

Low-grade IPMN (previously classified as IPMN-adenoma) are typically lined by gastric type epithelium and these have to be distinguished from an ITA.

It has been suggested that ITA is a discrete lesion, separate to and distinct from IPMN, however, there have been several cases where the two lesions have coexisted and, in all cases reported thus far, there has been a great deal of morphologic overlap noted between the two entities. One of the reasons advanced for sepa-

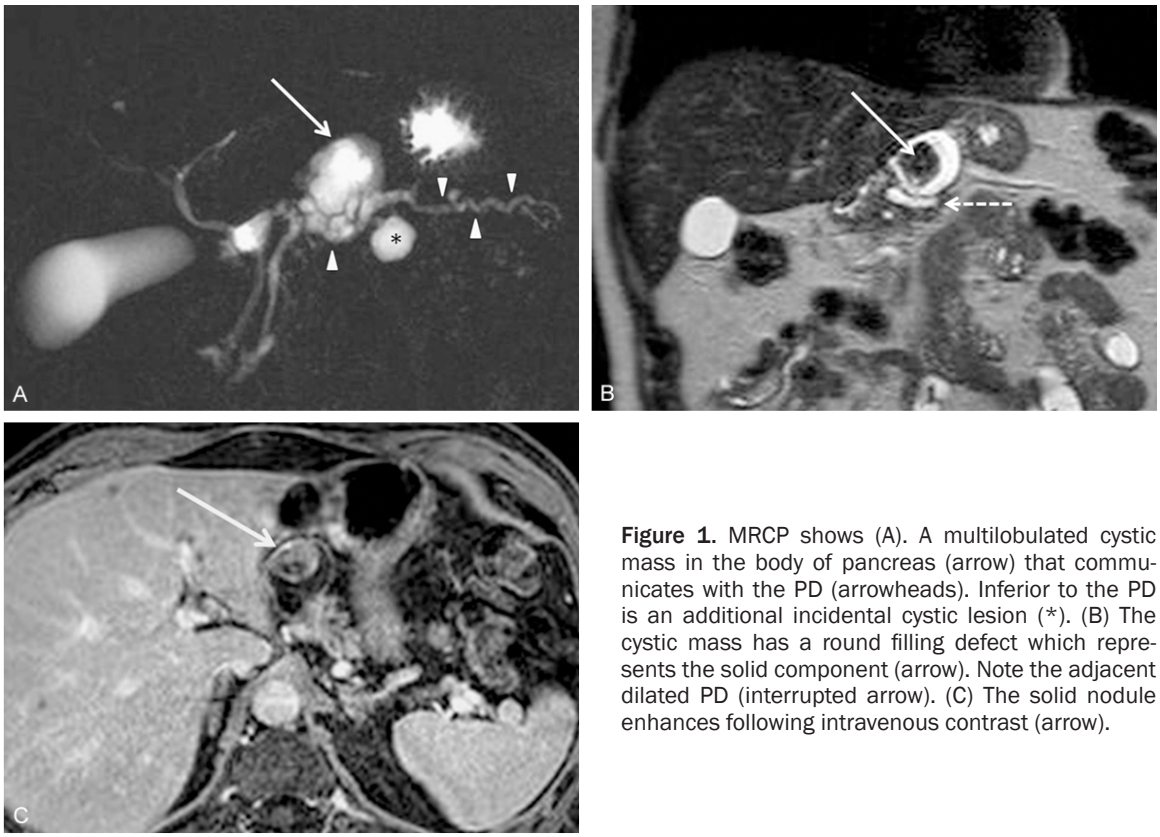

Figure 1. MRCP shows (A). A multilobulated cystic mass in the body of pancreas (arrow) that communicates with the PD (arrowheads). Inferior to the PD is an additional incidental cystic lesion (*). (B) The cystic mass has a round filling defect which represents the solid component (arrow). Note the adjacent dilated PD (interrupted arrow). (C) The solid nodule enhances following intravenous contrast (arrow).

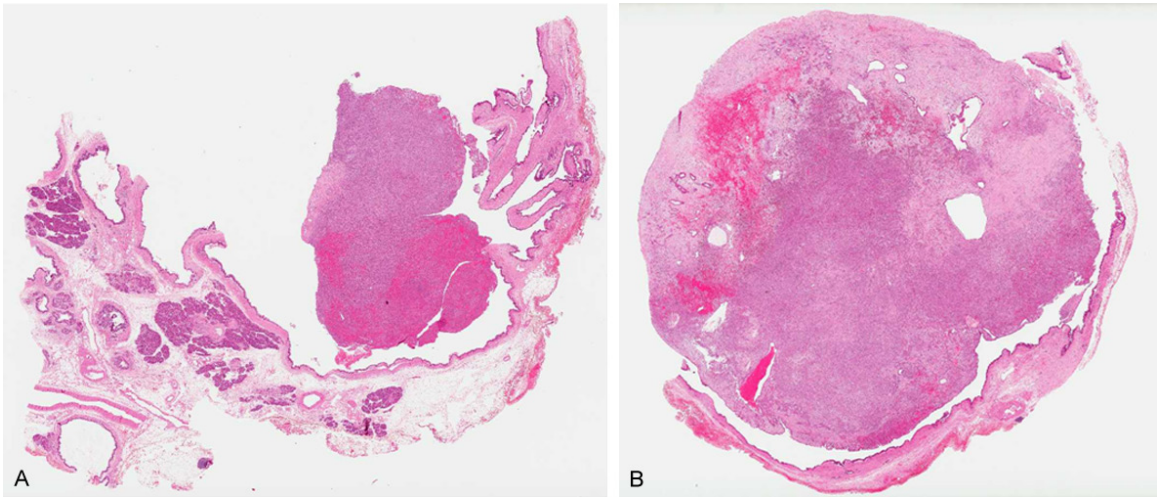

Figure 2. A low power scanning image showing dilated pancreatic branch ducts containing a gastric type IPMN (A). A dilated branch pancreatic duct contains an intraductal polypoid mass (B) (H&E X 20).

rating the two entities has been based on their behaviors: ITA being an indolent lesion while IPMN has an association with dysplasia and hence, potentially invasive lesions. This is especially true of the intestinal and pancreaticobiliary subtypes of IPMN; however, the gastric-type IPMN is usually a low-grade, lesion with a good prognosis.

In this paper we wish to highlight a case of coexistent ITA and IPMN, the former appearing radiologically as a “mural nodule”, thus raising

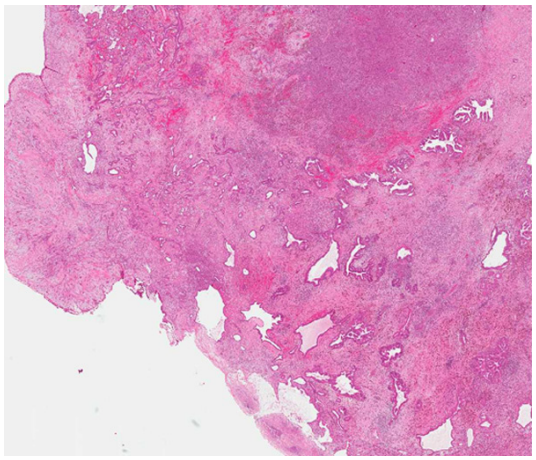

Figure 3. The surface of the polyp showed intact pyloric-type epithelium which was focally ulcerated. Within the polyp, glandular structures were present (H&E X 30).

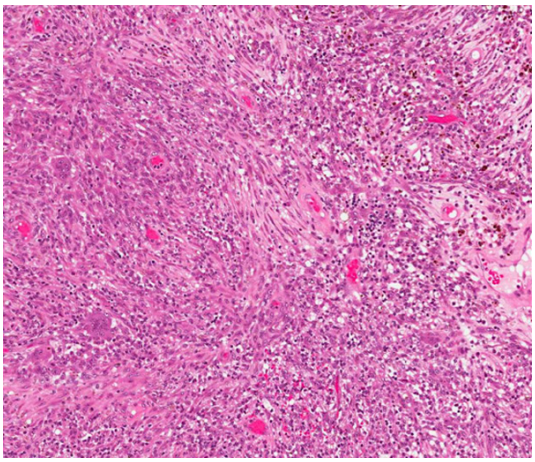

Figure 5. The stroma of the polyp showed a fibro-inflammatory background with granulation tissue, mixed inflammation, Hemosiderin and osteoclastic-type giant cells (H&E X 200).

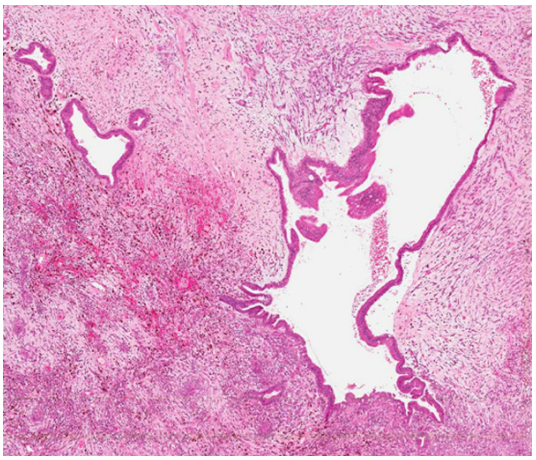

Figure 4. The glands forming the polyp were lined by a similar lining to that of dilated branch pancreatic duct. Occasional glands were dilated (H&E X 200).

the suspicion of carcinoma within the context of an IPMN.

Case report

A 73-year old male presented with a rectal mass that was proven to be a rectal adenocarcinoma after biopsy. In the course of his pre-operative work-up, MRI showed a cystic lesion in his pancreas. He was successfully treated for his rectal cancer and was asymptomatic from his pancreatic lesion.

Radiological evaluation

An MR cholangiopancreatogram (MRCP) revealed a 3.2 x 2.8 x 3.1 cm multilobulated cystic mass in the body of pancreas that contained a 2 cm enhancing rounded solid component. Inferiorly, the cystic mass appeared connected to the pancreatic duct (PD), which was focally dilated (**Figure 1A-C**). The radiologic appearances were in keeping with IPMN with a high risk of malignancy because of the solid enhancing nodule.

In view of the solid focus and worrisome radiological appearances, a distal pancreatectomy with preservation of the spleen was undertaken.

Pathology

The portion of pancreas contained a multicystic lesion measuring 3.7 x 3.7 x 3.5 cm. Within the cavity of the largest cystic space was a solid, yellow, hemorrhagic nodule measuring 2.2 cm in maximal diameter. The remainder of the pancreas was within normal limits.

Microscopic examination showed the presence of an IPMN of gastric type involving the pancreatic branch ducts (**Figure 2A**). The lining mucosa was bland and resembled gastric pyloric epithelium. Within the most dilated pancreatic duct was an intraductal, polypoid lesion (**Figure 2B**). A point of attachment to the dilated duct was noted and the polypoid lesion was lined by epithelial lining that was similar to that lining the dilated pancreatic duct, ie., gastric pyloric epithelium. There was focal ulceration with denudation of the lining of the surface of the polypoid mass (**Figure 3**). Within the substance

of polyp were occasional benign glandular structures (some of which were dilated) lined by regenerating gastric-type epithelium (**Figure 4**). These glands were embedded within a fibroinflammatory stroma composed of mixed inflammation, numerous foamy and hemosiderin-laden macrophages, frank hemorrhage, reactive osteoclast-type giant cells and florid reparative granulation tissue (**Figure 5**). In addition, morules of metaplastic squamous mucosa were also noted. No evidence of cytologic atypia or obvious malignancy was present. The remainder of the pancreas was within normal limits. The intraductal polypoid mass was construed as the mural nodule noted radiologically. The microscopic appearance was in keeping with that of an ITA that had undergone torsion with resultant hemorrhage and inflammation, arising in a duct showing a gastric-type IPMN. The patient remains well 5 years after the operation.

Discussion

Some confusion may arise between an ITA and IPMN-gastric type because of their intraductal location and also because both lesions are lined by gastric (pyloric-type) epithelium. This confusion is further heightened by the coexistence of the two entities in at least 50% of cases of ITA [6, 11].

The IPMN-gastric type typically involves branch pancreatic ducts and is composed of gastric (pyloric)-type epithelium with only low-grade atypia most frequently. This lesion does not produce a localized mass or polyp but rather is a diffuse process involving the entire circumference of several, usually pancreatic branch ducts.

With more sophisticated imaging techniques, small cystic lesions in the pancreas are being detected more often. ERCP was considered the imaging modality of choice for the diagnosis of IPMN. A bulging papilla with mucin pouring out of the ampulla at the time of the procedure is pathognomonic of IPMN although it is only seen in about 20% of patients with IPMN. Furthermore, the entire pancreatic duct may not be visualized with this modality as viscous mucin may prevent adequate inflow of contrast. As these tumors are often discovered incidentally, ultrasound (transabdominal or endoscopic) and CT are often the initial modalities with which IPMNs are diagnosed or suspected. It can be difficult however to differentiate an IPMN from other cystic pancreatic lesions. MRCP is now regarded the initial modality of choice, which shows dilatation of the main PD in main-duct type IPMNs or grapelike clusters of cysts in branch-duct type IPMNs. In the latter type, the tumor may appear unilocular or multilocular and there is often associated main PD dilatation. Independently, predictive signs of malignancy in IPMN include dilated main pancreatic duct (>1 cm), lesion >3 cm, the presence of mural nodules, thick septa or thick walls and peripancreatic haziness [12, 13]. Mural nodules in IPMN are typically echogenic on ultrasound, hyperdense on CT and hypointense relative to the surrounding fluid on MR imaging. Although mucin globules tend to be in a dependant position and nodules are usually attached to the IPMN wall, distinction between mural nodules and mucin globs can be difficult on imaging unless there is enhancement of the nodules following contrast administration [14].

The resemblance of an ITA to a mural nodule has been documented previously: the case reported by Nagaike and colleagues was described as a “main-duct intraductal papillary mucinous adenoma of the pancreas with a large mural nodule” [7]. However, on careful inspection of the illustrations and reading the microscopic description, the lesion described would appear to be an ITA, pyloric gland-type rather than an IPMN. Although not commented on specifically, the lining mucosa and papillary structures illustrated in the main pancreatic duct appear to be the same as the tubular/glandular structures of the intraluminal mass, suggesting that this lesion is an ITA arising within the context of an IPMN (in other words, an ITA and a coexistent gastric-type IPMN, type B) [7, 11].

The use of the term “mural nodule” in the context of IPMN raises concerns of carcinoma in situ or possible invasive carcinoma arising from the IPMN. This mandates sampling of the entire IPMN as high-grade and/or invasive areas may be extremely localized to a focal area in the specimen. In general, IPMN involves the entire circumference of the involved ducts and hence is a “diffuse” lesion, in contrast to an ITA which, by definition, grows into the lumen as a polyp.

Fifty-percent of the cases of ITA reported in the literature [11] and, the case documented herein, describe the coexistence of ITA and IPMN

within the same duct or in separate ducts that are close by. When the two entities coexist, the ITA may represent an intraluminal extension of the IPMN, hence presenting as an intraductal polypoid mass-like lesion. In those cases of ITA not associated with an IPMN, it is possible that they arose from a small focus of gastric/pyloric metaplasia and grow into the lumen with no radial extension along the circumference of the duct.

This case highlights several features. From a radiological point of view it shows that an ITA may mimic a mural nodule in the setting of a coexistent IPMN. The presence of a mural nodule raises connotations of a more aggressive lesion associated with IPMN; thus, awareness and careful attention to the imaging will prevent a misdiagnosis. In addition, this case is another example of the coexistence of ITA and IPMN. Approximately 50% of the cases of ITA described in the literature have been associated with an IPMN and specifically the gastric-type. This suggests a pathogenetic relationship between the two lesions. Finally, the histological features of this case are in keeping with torsion and subsequent secondary changes leading to an exuberant fibroinflammatory response, a feature not previously described in ITA. In addition, the radiologic presentation as a mural nodule is rare and, to the best of our knowledge, not described previously in this clinical context.

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