

CASE REPORT

Intraductal Papillary Mucinous Neoplasm With Extensive Mural Osseous Metaplasia and Calcification

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ABSTRACT

Context This case highlights the unusual radiological findings of an intraductal papillary mucinous neoplasm presenting as a radiologically opacified lesion. This correlated histologically with extensive ossification and calcification of the wall of the cyst. Additionally, an accompanying intraductal tubular adenoma masqueraded as a mural nodule. **Case report** A seventy-year old man presented with vague epigastric pain and a CT-scan revealed a cystic pancreatic lesion with egg-shell opacification of the cyst wall. Pathological examination confirmed an intraductal papillary mucinous neoplasm of gastric type, low-grade dysplasia and an accompanying intraductal tubular adenoma in the distal pancreas. There was extensive osseous metaplasia and dystrophic calcification within the wall of the intraductal papillary mucinous neoplasm which accounted for the opacification noted radiologically. Based on these radiologic findings, the patient underwent a distal pancreatectomy and splenectomy. **Conclusions** extensive osseous metaplasia is exceedingly rare in intraductal papillary mucinous neoplasm, especially sufficient to result in a radiological opacification of the cyst and the presence of a concomitant intraductal tubular adenoma in a gastric type intraductal papillary mucinous neoplasm can masquerade radiologically as a mural nodule.

INTRODUCTION

Intraductal papillary mucinous neoplasms (IPMN) are detected with increasing frequency as more patients are subjected to ever improving imaging modalities. IPMN typically are cystic lesions that are connected to pancreatic ductal system and have well-characterized histological features and sub-types. IPMNs are important to recognize both radiologically and pathologically as they are a precursor lesion to pancreatic adenocarcinoma, usually the mucinous variant although conventional ductal cancer is also encountered with IPMN. The radiologic examination of these lesions, especially in a sequential fashion, is an important facet of the management of early lesions. Progression is monitored and increase in size, complexity of the cystic lesion, mural nodule formation, mural thickening, main duct involvement and extension into surrounding pancreatic parenchyma are all pointers towards more aggressive behaviour, ie., development of invasive carcinoma.

The presence of radiologically detected mural opacification in IPMN is thought to occur in approximately 10-25% of IPMN. This usually occurs in larger lesions and when combined with other radiological features may well be taken as a sign of malignancy within an IPMN [1, 2, 3, 4, 5]. It is also important to separate pancreatic parenchymal calcification away from the IPMN which is a form of dystrophic calcification related to chronic pancreatitis and/or fat necrosis.

Osseous metaplasia within the wall of an IPMN is exceedingly rare and has not been well-documented in the English language literature, to the best of our knowledge. Mural osseous metaplasia in a high-grade gastric type IPMN with an associated tubular adenocarcinoma has been described in the Japanese literature [6]. We present a gastric-type IPMN which has three notable features that warrant documentation. Firstly, the radiological features of the IPMN were unusual and were that of an egg-shell opacification in parts of the mass. Secondly, histopathologically there was extensive complete osseous metaplasia (with bone and marrow fat with hematopoietic elements) in the cyst wall immediately subjacent to the lining epithelium, and thirdly, the luminal enhancing nodule was due to the presence of an intraductal tubular adenoma accompanying the IPMN.

CASE REPORT

A seventy-year old man presented with abdominal discomfort and pain over period of 18 months prior to seeking medical attention. This was not accompanied by any other signs or symptoms such as weight loss, anorexia

Received December 12th, 2017 - Accepted January 26th, 2018
Keywords Adenocarcinoma; Carcinoma; Pancreas
Abbreviations IPMN intraductal papillary mucinous neoplasm;
MRI magnetic resonance imaging
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or jaundice. The patient was a lifelong non-smoker with no admitted history of alcohol consumption, and there were no other relevant clinical findings. His amylase level was 348U; calcium, random blood glucose (5.3 mmol/L), carcino-embryonic antigen (0.9 ng/ml), CA19-9 (10 U/ml) and CA125 (3 U/ml) levels were all normal.

As part of the clinical work up, the patient underwent a CT scan (with and without contrast medium) of the abdomen demonstrating a lobulated, exophytic cystic lesion in the tail of the pancreas. The lesion had internal septations and one of the cystic components had thin mural, so-called eggshell calcification (**Figure 1a-c**). Additionally, there was a vascularized, enhancing 2.3 cm nodule within the cyst which suggested the possibility of malignant transformation (**Figure 1d-e**). A MRI was also performed which was of limited quality. The MRI scan confirmed the

cystic nature of the mass with thin internal septations, and a normal pancreatic duct without communication with the mass. However, the enhancement of the solid papillary nodule was poorly appreciated on the MRI due to adjacent artifacts. Endoscopic ultrasound was not performed pre-operatively. A distal pancreatectomy and splenectomy was performed in view of the clinical and radiological suspicion of malignancy.

The specimen consisted of a portion of pancreas measuring 7.2×3.6×2.6 cm containing a cystic lesion measuring 2.0×2.0×1.8 cm (**Figure 2**). The lumen of the cyst contained a papillary, friable lesion measuring 1.8 cm in maximal diameter. Parts of the lesion had detached and were noted within the luminal debris. The cyst wall was noted to be thick, pale and measured 0.1 cm in thickness. The cyst and intraluminal lesion were sampled in total. The attached spleen was unremarkable.

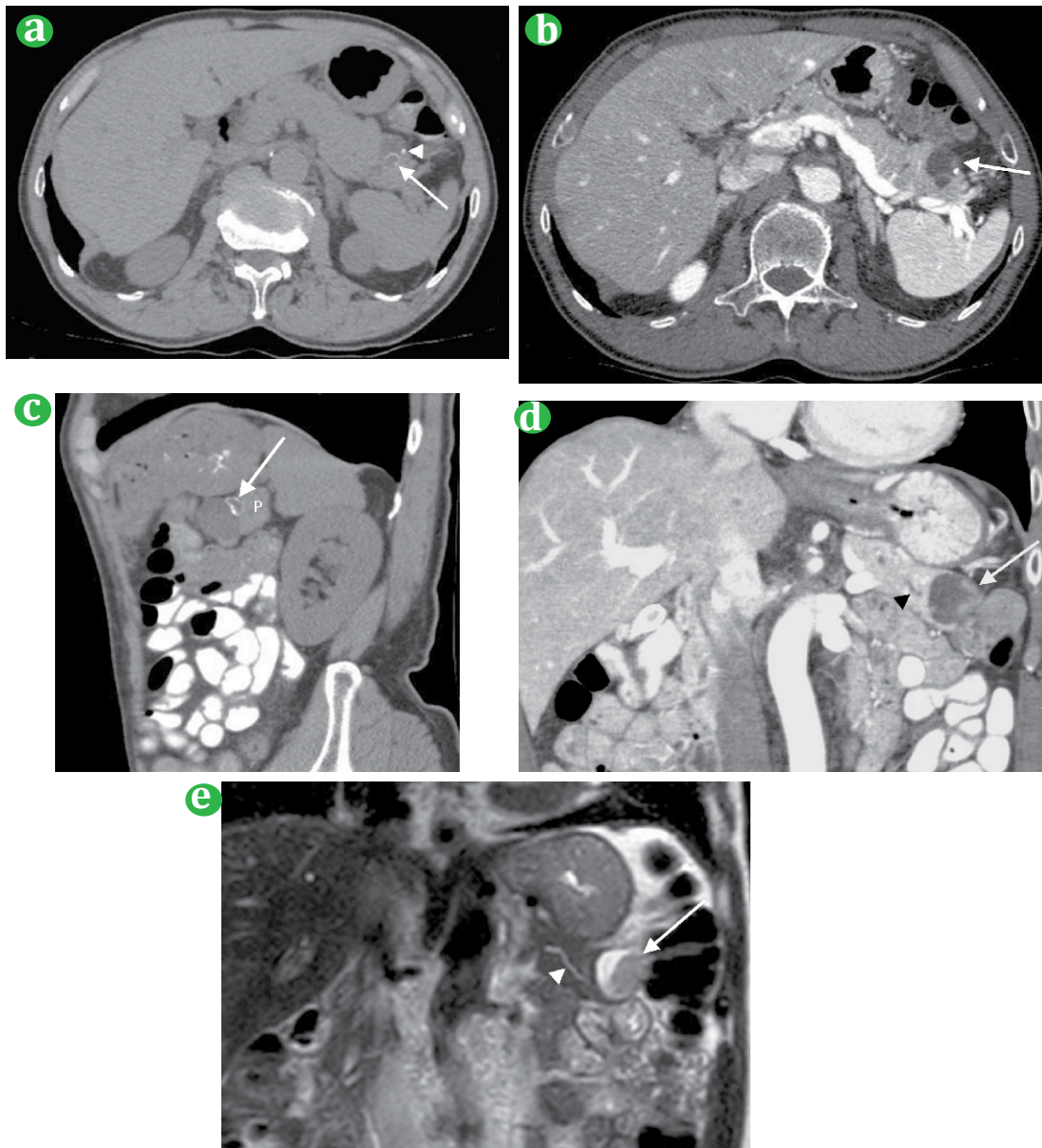


Figure 1. (a). Axial unenhanced CT scan shows the fluid density cystic lesion in the pancreatic tail with an area of egg-shell calcification (arrow). There is a separate focus of calcification (arrowhead) which corresponded to the dystrophic calcification within the tubule-papillary adenoma. (b). Axial contrast enhanced image at the same level depicts the enhancing adenoma (arrow). (c). Sagittal unenhanced image provides better detail of the eggshell calcification (arrow) within the lesion arising exophytically off the tail of the pancreas (P). (d). Coronal enhanced CT scan shows optimally the enhancing adenoma (arrow) and a normal pancreatic duct (arrowhead). (e). Coronal T2 Weighted MRI demonstrates the cystic nature of the mass with solid components (arrow) and a normal pancreatic duct downstream (arrowhead).

Histological evaluation of the cyst showed it to be septate and lined by gastric foveolar and pyloric type mucosa (**Figure 3a**). The epithelium was flat with small papillary infoldings and tufts into the lumen. There was mild pleomorphism, stratification and hyperchromasia of nuclei, very rare mitoses and abundant apical cytoplasmic mucin (**Figure 3b**). The cytologic findings amounted to low-grade dysplasia. No evidence of high-grade dysplasia or invasive cancer was seen and the entire specimen was examined microscopically. In focal areas the mucosa was either stripped or attenuated. The intraluminal mass seen both radiologically and on gross examination of the specimen was a tubulo-papillary lesion lined by similar gastric-type epithelium as the

main cystic structure and attached to the cyst wall. The epithelium was MUC5AC positive but MUC1 and 2 negative.

A striking histological feature was the widespread presence of osseous metaplasia and calcification within the wall of the main cyst and in a septum (**Figure 4a**). The metaplastic bone was located in the fibrous tissue part of the cyst wall, immediately subjacent to the lining epithelium (**Figure 4b**). Focally, the bone protruded into the lumen of the cyst causing slight attenuation of the overlying epithelium (**Figure 4b**).

In parts, the osseous metaplasia was accompanied by dystrophic calcification and marked hyalinization of the wall. There was no ossification or calcification noted within



Figure 2. The distal pancreatectomy specimen displaying the cystic structure that communicated with the main pancreatic duct, an intraluminal component (arrow) and the very distinct thick cyst wall.

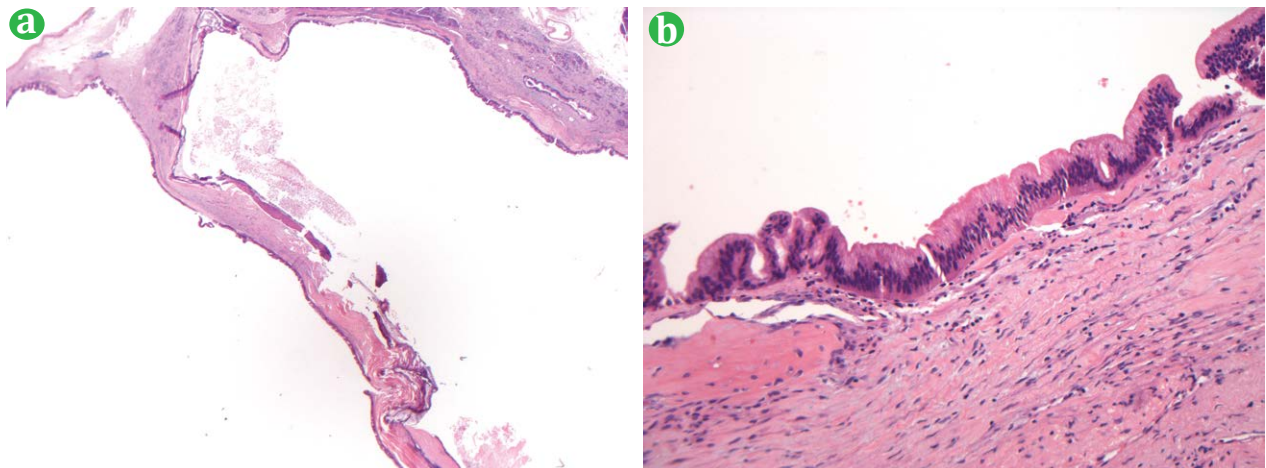


Figure 3. (a). A low power image of the cyst showing the intraluminal tubulo-papillary adenoma and a septum. The cyst lining was gastric pyloric and foveolar in type with basal nuclei and abundant cytoplasmic mucin. **(b).** The epithelial dysplasia in this lesion was low-grade.

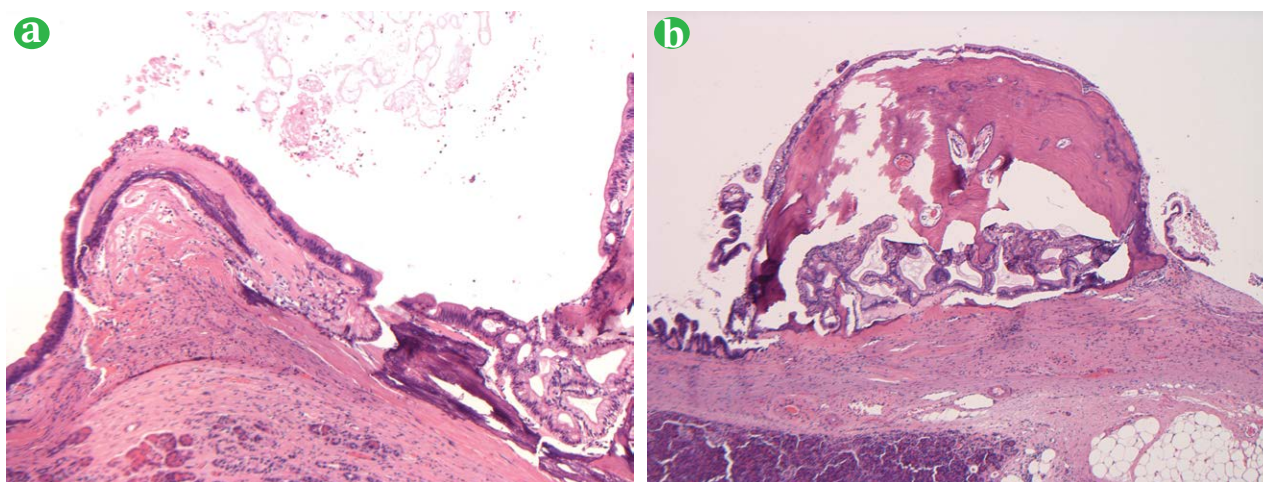


Figure 4. (a). The cyst wall and a microscopically noted septum showed mainly osseous metaplasia and some calcification. **(b).** The osseous metaplasia was immediately beneath the lining epithelium and focally protruded into the cyst lumen.

the luminal contents of the cyst or infarcted/ulcerated parts of the intraductal tubulo-papillary adenoma.

The osseous metaplasia and accompanying dystrophic calcification were regarded as secondary features and a result of longstanding, low-grade chronic inflammation.

DISCUSSION

As mentioned earlier, prominent osseous metaplasia is a distinctly rare occurrence in IPMN with a single report occurring in the Japanese literature [6]. In the case presented herein, the bone formation was detected radiologically and was in excess of the accompanying calcification. While osseous metaplasia has not been documented in IPMN, the presence of calcification has and its significance evaluated in several publications [1, 2, 3, 4, 5].

Calcification has been noted to occur in 2 locations in IPMN, the wall of the cyst, and within the lumen. Calcification within pancreatic parenchyma in the vicinity of the cyst is not related to the IPMN *per se* and is related to chronic pancreatitis resulting from obstruction within the pancreatic duct system. The most frequent location for calcification in IPMN is within the lumen and related to the mucus [1, 2, 3, 4].

In a detailed study looking specifically at calcification in IPMN, Perez-Johnston and colleagues examined 164 IPMN and found calcification in 33 cases (20%) [5]. They classified the calcification as punctate, coarse and eggshell that were distributed in the wall most frequently (mural), septum, ducts, solid component and combinations of the aforementioned sites [5]. The cyst wall either alone or in combination with other sites was seen in 84% of the 33 cases with calcification [5]. Interestingly, there is no mention of any cases containing any osseous metaplastic foci, attesting to the rarity of its occurrence and as a dominant histologic feature. Calcification tends to occur more frequently in larger cysts especially with accompanying dilatation of the main pancreatic duct [5]. Of itself, the presence of calcification did not portend the presence of invasive carcinoma.

Intraductal tubular or tubulo-papillary adenomas are a frequent feature of gastric-type IPMN and occur in approximately 50% of these IPMN [7, 8]. Its occurrence in IPMN is thought to be a localized proliferation of the neoplastic epithelium lining the cyst resulting in an intraluminal polypoid lesion. The lining epithelium of intraductal tubulo-papillary adenomas is morphologically and molecularly identical to that of gastric-type IPMN, and these tubulo-papillary lesions should not be regarded as separate or distinct from IPMN-gastric (pyloric gland) type [9]. From a clinical point of view, extensive radiological opacification in an IPMN should not automatically invoke the possibility of invasive malignancy.

CONCLUSION

This case thus highlights three distinct features that can accompany IPMN. The radiological appearance of eggshell calcification is an uncommon but recognized feature of IPMN, histologically this was due mainly to complete osseous metaplasia (bone and marrow elements), and finally that intraductal tubular/tubulo-papillary adenomas lined by identical epithelium as the gastric-type IPMN, is a cause of an intraluminal mass and a frequent accompaniment of IPMN-gastric type.

Conflict of Interest

Authors are declared that there is no conflict of interest.

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