Squamoid cystosis of pancreatic ducts: a variant of a newly-described cystic lesion, with evidence for an obstructive etiology

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Abstract

We describe a 40-year-old man who was found to have a cystic mass in the pancreatic tail during workup for weight loss and abdominal discomfort. Although computed tomography scan showed a single cyst associated with dilatation of the main pancreatic duct, gross and histologic examination of the distal pancreatectomy specimen actually revealed a central cyst that was surrounded by multiple smaller cystic spaces. This distinctive appearance was formed from extensive cystic dilatation and squamous metaplasia of the native pancreatic duct system. Further, a traumatic neuroma was discovered near the junction between normal and abnormal parenchyma. We believe that this case represents a variant of the newly-described squamoid cyst of pancreatic ducts which we term *squamoid cystosis* of pancreatic ducts. The presence of chronic pancreatitis and a traumatic neuroma supports the hypothesis that squamoid cysts are non-neoplastic lesions arising from prior duct obstruction.

Introduction

Until quite recently only three major types of squamous-lined pancreatic cysts were recognized: dermoid cysts (teratomatous neoplasms containing squamous, sebaceous, and/or respiratory epithelium and hair follicles), lymphoepithelial cysts (non-neoplastic, intra- or peripancreatic keratinizing cysts with surrounding stroma that resembles lymph node), and epidermoid cysts of intrapancreatic accessory spleen (non-neoplastic keratinizing cysts surrounded by splenic parenchyma, including red pulp). Although recognition of pancreatic dermoid cyst dates back to at least 1918,[1] squamous cyst of intrapancreatic accessory spleen was not described until 1980,[2] and lymphoepithelial cyst until 1985.[3] Recently, detailed characterization of these and other uncommon pancreatic cysts has been aided by the increasing use of radiologic examinations – which promote detection of small or otherwise clinically indolent lesions – as well as the increasing safety of pancreatic surgery relative to prior decades.

In 2007, Othman and colleagues reported a new type of squamous-lined pancreatic cyst termed *squamoid cyst of pancreatic ducts* (SCOP).[4] The six clinically-manifest cases of SCOP comprised cysts of 0.8-9 cm which were variably lined by flat, transitional, and stratified squamous epithelial cells that lacked a granular cell layer and lacked ortho- or parakeratosis. These cysts appeared to arise from non-neoplastic, unilocular dilatation and metaplasia of pancreatic ducts in a manner that suggested localized duct obstruction as the most likely etiology. However, neither direct nor surrogate evidence for duct obstruction could be demonstrated in any of the six patients to support the authors' hypothesis.

In this report we describe a case of multifocal cystic dilatation and squamoid metaplasia of the distal pancreatic duct system, a process that we believe represents an extreme variant of SCOP which we have termed *squamoid cystosis* of pancreatic ducts. The patient, who had a clinical history of heavy alcohol use and marked chronic pancreatitis around the involved ducts, also harbored a small traumatic neuroma near the junction between affected and unaffected pancreatic parenchyma. Together, these unusual features support the idea that SCOP results from prior duct obstruction.

Case Report

This 40-year-old African American man presented for evaluation of microhematuria, weight loss, and abdominal discomfort. His past medical history included type 2 diabetes mellitus, a long history of tobacco use, and heavy alcohol consumption in the past. Current alcohol use was 4 or fewer beverages/day. Although his body mass index was elevated at 29, he had unintentionally lost 50 lbs due to lack of appetite and periumbilical discomfort. He denied any radiation of pain to his back. On physical examination there was no abdominal tenderness, nor was there hepatosplenomegaly, palpable mass, or ascites. Laboratory testing was significant only for elevated levels of fasting blood glucose (385 mg/dL, normal 70-110 mg/dL) and glycohemoglobin A1C (10.8%, normal ≤6.0%). Tumor markers such as CEA and CA 19.9 were not measured.

Computed tomography (CT) scans of the abdomen and pelvis revealed a 2-3 cm cystic mass in the tail of the pancreas along with dilatation of the main pancreatic duct (Figure 1A). The radiologic appearance was nonspecific, with the differential diagnosis including both neoplastic and non-neoplastic cysts. The lesion had also been present on outside abdominal CT scan from the prior year; on questioning, the patient disclosed that he had been made aware of the cyst, which was apparently ascribed to *chronic pancreatitis*, although there was no history of acute pancreatitis in the past.

The patient elected to undergo laparoscopic-assisted distal pancreatectomy because of clinical concern for intraductal papillary mucinous neoplasm, especially given the presence of a dilated main pancreatic duct. Recovery was uneventful.

Gross pathological findings

We removed 8.7 cm of the distal pancreas, along with a separately submitted section of the proximal parenchymal margin. The largest cyst – and the one that was evident radiologically – was unilocular, 2.5 cm in diameter, smooth-lined, and filled with clear fluid (Figure 1B). This cyst was connected to a dilated (0.5 cm luminal diameter) main pancreatic duct. The parenchyma throughout most of the specimen was grossly fibrotic and contained multiple tiny cystic spaces. Near the proximal margin, the pancreas became more normal in its appearance, with areas of tan, lobulated parenchyma intermixed with fibrosis. Diameter of the pancreatic duct in the separately submitted section of proximal margin was only 0.1 cm.

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Key words: pancreas, tumors, benign.

Contributions: the authors contributed equally.

Conflict of interests: the authors declare no potential conflict of interests.

Received for publication: 6 January 2014.
Accepted for publication: 7 March 2014.

Rare Tumors 2014; 6:5286
doi:10.4081/rt.2014.5286

Microscopic pathological findings

All of the cysts were formed from dilatation of the native pancreatic duct system. In general, the cyst lumens appeared empty following processing, but very focally there were dense eosinophilic secretions and a few foamy histiocytes. Thin bands of fibrous tissue surrounded most of the cysts. The intervening parenchyma was markedly atrophic – with preservation of islets but only scant acini – and contained slight to mild lymphocytic infiltrates (Figure 2A). The cysts were variably lined by flattened/attenuated squamoid cells, squamous cells of several layers' thickness, to stratified squamous epithelium that lacked a granular cell layer and lacked keratinization. In the largest cyst, much of the epithelium was attenuated and there were areas of denudation. Stratified squamous epithelium was easiest to appreciate in the smaller ducts, which ranged from minimally ectatic to ~1 cm. Only a few of the smallest ducts contained a normal, cuboidal epithelial lining and in some a process of *immature* squamous metaplasia could be seen, with stratified squamous epithelium undermining the cuboidal lining (Figure 2B). Rare foci of pancreatic intraepithelial neoplasia (PanIN)-1A and -1B were also present, with a single small focus of PanIN-2.[5] Immunohistochemical stains for p63 and CK 5/6 strongly labeled the squamoid/transitional cells, but frequently spared the most superficial layer of cuboidal, ductal-type cells and spared the foci of PanIN (Figure 2B). At the proximal resection margin the parenchyma was nearly normal, with only patchy areas of mild fibrosis. The main pancreatic duct at that level was of normal caliber and predominantly lined by cuboidal epithelium. A few areas of squamous metaplasia persisted in the main duct and in some smaller ducts.

Near the junction between affected and nonaffected parenchyma, we noted a proliferation of spindled and plump epithelioid cells that had granular eosinophilic cytoplasm, intermixed nerve twigs, and a somewhat *infiltrative* appearance around ducts and residual pancreatic islets (Figure 3). This lesion was not grossly evident – being set in a background of fibrotic parenchyma – but measured ~0.8 cm from the glass slides.

Nuclei of the granular cells were small, centrally placed, and lacked discernable mitotic activity. Their cytoplasmic granularity was highlighted by diastase-treated periodic acid-Schiff (PAS-D) stain. By immunohistochemistry, the granular cells were intensely S100 positive (Figure 3) but lacked labeling for CD68 and smooth muscle actin; they were intimately associated with numerous NF+ cytoplasmic strands. EMA highlighted perineural cells around hyperplastic nerves.

Discussion and Conclusions

The cytologic findings and intraductal nature of the squamoid proliferation in our case are identical to those described recently by Othman *et al.* as SCOPs.[4] The present case differs mainly in its wide extent – a process more akin to *squamoid cystosis* than solitary cyst – and in its background of marked chronic pancreatitis. Importantly, we believe that the presence of chronic pancreatitis and history of heavy alcohol use in this patient lend support to Othman's hypothesis that SCOP is a type of nonneoplastic *retention cyst* caused by prior duct obstruction.[4] The finding of a traumatic neuroma within the pancreatic parenchyma near the junction between normal and abnormal ducts further supports this concept.

A single case of traumatic neuroma in the pancreas has been previously reported, involving a 50-year-old man who developed the lesion after splenectomy for abdominal trauma that had occurred 26 years before his presentation.[6] As in our case, the traumatic neuroma in that patient was also associated with morphologic features of chronic pancreatitis in the adjacent parenchyma of the surgical specimen. Although many cases of traumatic neuroma develop after surgical severance of a nerve, they have also been reported in association with nonsurgical and clinically inapparent forms of trauma such as chronic duct obstruction. For example, Giménez-Bascuñana and Piqueras-Pérez described a traumatic neuroma found in the salivary gland of a 74-year-old man who had a 2 cm calcified sialolith, ductal dilatation, and chronic sialadenitis of the submaxillary gland (including squamous metaplasia of the submaxillary ducts).[7]

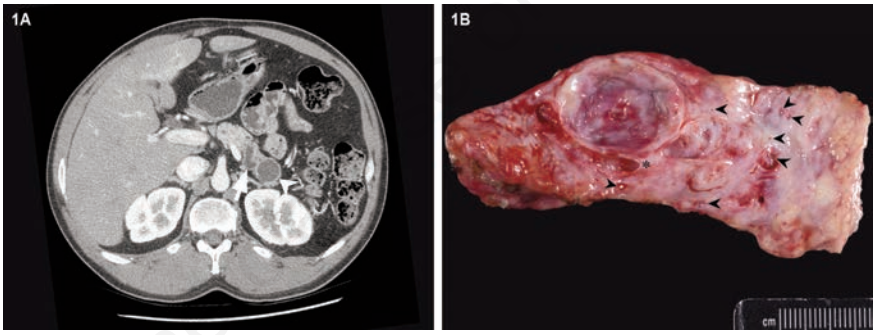

Figure 1. A) Computed tomography scan of the abdomen shows a cyst in the tail of the pancreas (arrowhead), which appears connected to the dilated main pancreatic duct (arrow). B) Gross photograph of the pancreatic tail reveals a 2.5 cm unilocular cyst adjacent to the dialted main pancreatic duct (asterisk). The surrounding parenchyma is fibrotic and contains multiple smaller cystic spaces (arrowheads); near the resection margin at right, the pancreatic parenchyma assumes a more normal gross appearance.

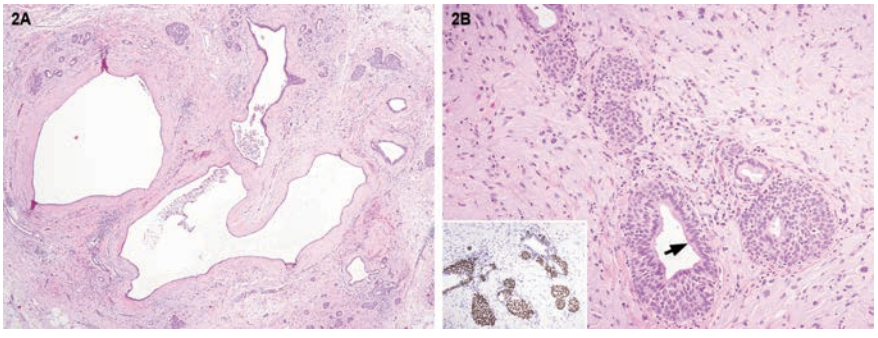

Figure 2. A) Cluster of cystically-dilated pancreatic ducts. The intervening parenchyma shows chronic pancreatitis with mild lymphocytic inflammation, scattered islets, and near-total loss of acini (Hematoxylin and Eosin, ×20). B) Nodules of squamous metaplasia surrounding the smallest pancreatic ducts; focally the luminal epithelium is cuboidal (arrow) (Hematoxylin and Eosin, ×100). Immunostaining for p63 (inset, ×100) highlights the squamoid epithelium but spares the overlying ductal epithelial cells in these small ducts.

The traumatic neuroma in our patient represents an unusual morphologic variant, termed *granular cell traumatic neuromas* by Rosso *et al.* because their histologic features overlap both granular cell tumors and traumatic neuromas.[8] The lesions reported by Rosso occurred in mastectomy scars following surgeries for ductal carcinoma of the breast, and similar to our patient they were small (0.4 cm and 0.6 cm) nodules composed of cytologically bland but locally infiltrative proliferations of S100+, PAS-D+, SMA- granular cells set haphazardly in a collagenous matrix that also contained several hypertrophic nerve bundles.[8] Granular cell change, of course, is not restricted to traumatic neuromas but can be seen as a degenerative phenomenon due to accumulation of lysosomal structures in various cell types including smooth muscle.[9,10]

All of the abnormalities in our case – pancreatic duct dilatation, squamoid cysts, and granular cell traumatic neuroma – are benign processes related to chronic pancreatitis. None would warrant surgical resection except for their mimicry of potentially neoplastic lesions. The granular cell traumatic neuromas reported by Rosso *et al.* clinically mimicked recurrent breast carcinoma and were excised for that reason.[8] The SCOPs reported by Othman *et al.* were generally excised because of a clinical suspicion for mucinous neoplasms such as mucinous cystic neoplasm.[4] In our patient, the granular cell traumatic neuroma was an incidental finding only, and the clinical concern was exclusion of intraductal papillary mucinous neoplasm based on the radiologic appearance of a cystic lesion in a male patient who also had dilatation of the main pancreatic duct.

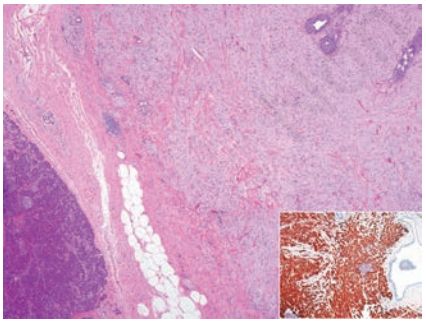

Figure 3. Granular cell traumatic neuroma, which shows infiltration around small pancreatic ducts with squamous metaplasia (upper right); normal acinar parenchyma can be seen in the lower left corner (Hematoxylin and Eosin, ×20). Lesional cells are intensely S100+ (inset, ×100).

Despite their radiologic similarity to neoplastic lesions, resected SCOPs should be easily distinguishable by their distinctive histologic features, provided that pathologists are aware of this entity. They are clearly not mucinous lesions, even if – as in our case – focal PanIN is encountered. They lack the features of other squamous-lined pancreatic lesions including the lymphoid stroma of lymphoepithelial cysts, the splenic parenchyma of epidermoid cysts of intrapancreatic spleen, and the hair follicles or other adnexal elements of dermoid cysts. Finally, there is no cytologic atypia or stromal extension that could cause confusion with the rare squamous or adenosquamous carcinomas of the pancreas that show cystic degeneration.[11]

Several recent publications have emphasized the increasing frequency of diagnosis of small, benign pancreatic cysts, because of increased detection of previously silent tumors by abdominal imaging studies and because of their relative safety of surgical excision, given the (now) low mortality of pancreatic surgery in high-volume centers.[12,13] For example, most of the SCOPs described by Othman *et al.* were incidental findings on CT scans performed for other reasons.[4] Although focal squamous metaplasia of pancreatic ducts has been a long-recognized phenomenon in pancreata removed for carcinoma or for severe chronic pancreatitis,[14,15] the formation of a distinct cystic lesion comprised solely of squamous or squamoid epithelium in a dilated pancreatic duct was not described until Othman's publication in 2007. Our patient, like those reported by Othman *et al.*, was thought to have a single cyst by CT scan. Gross and microscopic evaluation of the resected pancreatic tail, however, revealed a dominant 2.5 cm cyst surrounded by innumerable smaller cysts, all of which represented squamous- or squamoid-lined dilated pancreatic ducts.

In summary, the *squamoid cystosis* in this patient appears to represent a variant of the solitary squamoid cysts of pancreatic ducts reported by Othman *et al.*; and the co-existence of chronic pancreatitis, history of heavy alcohol use, and traumatic neuroma near the junction between affected and unaffected pancreatic parenchyma supports the contention that SCOPs are non-neoplastic and result from prior duct obstruction. Although rare, these distinctive lesions may be encountered more frequently in the future, as the use of abdominal imaging expands and imaging resolution increases.

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