Rare Tumors and Lesions of the Pancreas

John A. Stauffer, MD, Horacio J. Asbun, MD*

KEYWORDS

• Pancreatectomy • Pancreatic neoplasm • Anaplastic carcinoma
• Adenosquamous carcinoma • Solid pseudopapillary tumor • Acinar cell carcinoma
• Primary pancreatic lymphoma • Unusual pancreas tumors

KEY POINTS

- Rare pancreatic tumors of the pancreas include adenocarcinoma variants, such as anaplastic carcinoma, adenosquamous carcinoma, colloid, hepatoid, and medullary carcinoma.
- Other neoplasms include acinar cell carcinoma, solid pseudopapillary tumor, sarcomas, or lymphomas.
- Benign solid or cystic masses, such as hamartoma, hemangioma, lymphangioma, or others also may mimic neoplastic disease.
- The pancreas may be the site of isolated metastatic disease, such as renal cell cancer, colorectal cancer, melanoma, and other carcinomas.
- Pancreatic inflammatory diseases may mimic solid neoplasms of the pancreas.

Primary pancreatic ductal adenocarcinoma (PDAC) is the most common neoplasm of the pancreas. Pancreatic neuroendocrine tumors (PNETs) are much less common but their incidence has increased over the past decade due to the increased use of cross-sectional imaging.[1] Cystic lesions, such as intraductal papillary mucinous neoplasm (IPMN), mucinous cystic neoplasms (MCN), and serous cystic neoplasms (SCN) are also relatively common. The pancreas is a complex organ that harbors a wide array of diseases. There are a variety of non-neoplastic conditions that mimic PDAC, such as groove pancreatitis (GP) and autoimmune pancreatitis (AIP).[2,3] Additionally, there are a handful of other rare neoplastic lesions infrequently found in patients with pancreatic masses that range from well known (eg, solid pseudopapillary neoplasm and acinar cell carcinoma) to less well known (eg, leiomyosarcoma and hepatoid carcinoma). Rare cystic lesions can be misdiagnosed for the more common

Disclosures: The authors have nothing to disclose.
Department of Surgery, Mayo Clinic, 4500 San Pablo Road South, Jacksonville, FL 32224, USA
* Corresponding author. Division of General Surgery, Mayo Clinic, 4500 San Pablo Road South, Jacksonville, FL 32224.
E-mail address: asbun.horacio@mayo.edu

Surg Clin N Am 98 (2018) 169–188
https://doi.org/10.1016/j.suc.2017.09.013 **surgical.theclinics.com**

mucinous, serous, or inflammatory pancreatic lesions. Peripancreatic solid lesions or duodenal pathology occasionally can be mistaken for pancreatic pathology as well. Finally, the pancreas is a potential site for metastatic disease, such as renal cell carcinoma (RCC), or can be involved with other diseases, such as primary pancreatic lymphoma. Any of these lesions can be mistaken for PDAC.

Contrast-enhanced computerized tomography (CT) is the most common modality to detect and diagnose pancreatic pathology. Endoscopic ultrasound (EUS) and MRI with cholangiopancreatography (MRCP) have distinct advantages in hepatopancreatobiliary imaging that may clarify the diagnosis of an unknown pancreatic mass. EUS allows gastroduodenal mucosal evaluation, and has perhaps the highest sensitivity for small lesions of the pancreas (eg, subcentimeter PNET and mural nodules within IPMN), as well as enabling direct tissue sampling with fine-needle aspiration. High-quality MRI with MRCP provides detailed anatomic information of the pancreas and ductal structures that cannot be obtained with any other modality. Additionally, with an appropriate protocol, the MRI can provide conspicuity of any liver lesions associated with pancreatic disease surpass the images of the highest-quality triple-phase CT.[4,5] Complete evaluation by an experienced team is warranted for all with pancreatic neoplasms. A multidisciplinary approach with knowledgeable surgeons, gastroenterologists, radiologists, oncologists, pathologists, and others limit misdiagnosis and/or mismanagement of the following rare pancreatic findings.

ADENOCARCINOMA VARIANTS

Ductal adenocarcinoma of the pancreas with tubular morphology accounts for more than 90% of pancreatic carcinoma. There are variants of adenocarcinoma with a different prognosis that should be distinguished from PDAC.

Anaplastic (Undifferentiated) Adenocarcinoma (Also with Osteoclastlike Giant Cells)

Anaplastic pancreatic carcinomas (APCs) are rare neoplasms that represent 2% to 7% of all exocrine pancreatic tumors. First described by Sommer and Meissner in 1954[6] they are referred to as undifferentiated carcinoma with or without osteoclastlike giant cells, carcinosarcoma, sarcomatoid carcinoma, pleomorphic carcinoma, pleomorphic giant-cell carcinoma, and pleomorphic large-cell carcinoma of the pancreas. This undifferentiated carcinoma is an aggressive epithelial neoplasm that does not display significant components of differentiated lesions. Anaplastic foci can be seen within PDAC but as a minor component. The male-to-female ratio is 3 to 1 and generally affects older men (**Fig. 1**). The lesions are distributed throughout the pancreas and are often quite large when diagnosed (average of up to 9–10 cm).[7,8] The literature focuses on histology, immunohistochemistry, electron microscopy, and gene expression of APCs. Many studies note a poor outcome after resection due to its systemic nature, but other larger studies have shown benefit to resection.[7,9] Hoshimoto and colleagues[10] reported 60 cases of APC resected in Japan with a mean age at diagnosis of 61.5 years, 63% male, and a median size of 6 cm. Nearly one-fourth required resection of adjacent organs and vascular involvement was present in (12%). Although half died within 1 year of surgery, the 5-year survival rate was 12%.[10] Strobel and colleagues[11] reported a single institutional experience of 18 patients with APC who underwent attempted resection and compared them to a similar group with PDAC. They noted a median survival of only 5.7 months, but a margin-negative resection extended survival and 17% were long-term survivors.[11] Paniccia and colleagues[12] matched 192 patients with APC from the National Cancer Data Base with 960 PDAC patients. They too noted a 1-year survival that was lower than PDAC with a similar overall long-term survival.

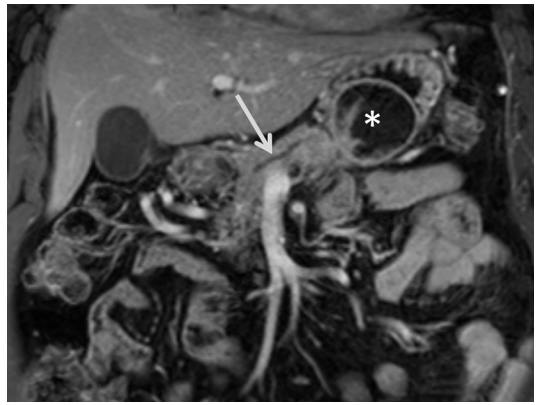

Fig. 1. Coronal MRI showing 6-cm mass in the tail of the pancreas in a 69-year-old man. Distal pancreatectomy with en bloc partial gastrectomy, splenectomy, and adrenalectomy was performed with pathology revealing anaplastic (undifferentiated) carcinoma with extensive necrosis. The tumor had focal areas (<10%) of conventional adenocarcinoma and 0/40 lymph nodes involved. The patient was alive without disease 2 years later. Asterisk indicates tumor with invasion into the posterior wall of the stomach, arrow indicates main pancreatic duct.

The presence of osteoclastlike giant cells implied a significantly better prognosis.[12] Clark and colleagues[13] evaluated the Surveillance, Epidemiology, and End Results (SEER) database over 20 years and found that the median survival of 353 APC patients was only 3 months, significantly worse than 5859 patients with PDAC (11 months). However, for those who underwent surgical resection, the overall survival was not significantly different (12% vs 24%).[13] Multiple single-center and population-based studies have confirmed the aggressive nature of APCs but operative intervention is advised when technically feasible and patient comorbidities are acceptable.

Adenosquamous Carcinoma

Adenosquamous carcinoma (ASC) is a rare and aggressive subtype of pancreatic carcinoma with glandular and squamous differentiation, the latter of which accounts for at least 30% of the neoplasm (Fig. 2).[8] First reported by G. Herxheimer in 1907,[14] the

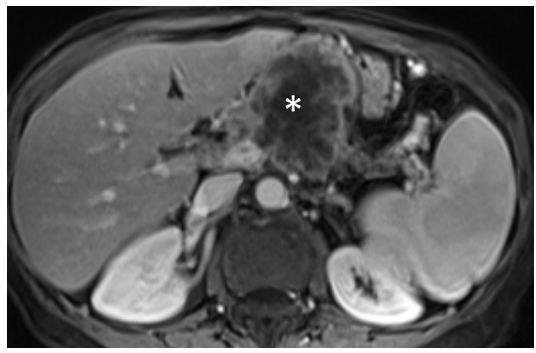

Fig. 2. Axial MRI showing 5-cm locally advanced mass in the head and body of the pancreas in an 83-year-old woman. EUS with fine needle aspiration confirmed adenosquamous carcinoma. Asterisk indicates tumor with obliteration of the superior mesenteric vein.

lesion has acquired several names, including adenoacanthoma, adenocarcinoma with squamous metaplasia, and mucoepidermoid carcinoma. This tumor is differentiated from metastatic squamous cell carcinoma to the pancreas by its glandular elements.[8] ASC has a poor prognosis and a short survival. Katz and colleagues[15] matched 95 California Cancer Registry patients over 8 years and with a similar group with PDAC. Despite a larger tumor (4.6 cm vs 3.4 cm), ASC patients were more likely to undergo surgery (33% vs 17%) Involved lymph nodes and adjuvant therapy were similar in both groups. Overall survival was equally poor with unresectable disease, but better after resection.[15] The SEER database from 1998 to 2007 was used to compare 415 ASC patients to 45,693 with PDAC. ASC was more likely to occur in the tail of the pancreas, be poorly differentiated, larger, and have more positive nodes than PDAC. Katz and colleagues[15] found that disease-specific one and 2 year survival was only 30.5% and 19.7% (median survival of 7 months) which was significantly worse than PDAC.[16] Similarly, a single-center study of 28 ASC cases by Imaoka and colleagues[17] reported that ASC had a worse survival than PDAC compared 56 matched with PDAC. Resection may improve the chance for long-term survival and is recommended when feasible.

Hepatoid Carcinoma

Hepatoid carcinomas (HCs) are malignant extrahepatic epithelial neoplasms with morphologic and immunohistologic features of hepatocellular carcinoma (HCC). Like HCC, they have elevated serum alpha-fetoprotein (AFP) and an older age at diagnosis. The main differential lesion is metastases from a liver primary.[18] Because both acinar cell and pancreatoblastoma have acinar cell differentiation that may secrete lipase, trypsin, chymotrypsin, or serum alpha-fetoprotein, lesions that must be differentiated from HC. Immunohistochemical labeling for HC is positive for hepatocyst paraffin-1, polyclonal carcinoembryonic antigen, and CD10.[8] HC lesions are often large and late stage at presentation. Marchegiani and colleagues[18] reported 22 HCs in the world literature. Only 15 patients underwent surgical resection but resected patients had a better long-term survival.[18] Systemic therapies are neither standardized nor very effective, but some report limited success with the tyrosine kinase inhibitor sorafenib.[19] Kuo and colleagues[20] reported that 40% of these tumors had other tumor components, such as PNET, PDAC, or acinar cell carcinoma (ACC) and that radical surgery was the only chance for long-term survival.

Colloid Carcinoma (Mucinous Noncystic Carcinoma)

Colloid carcinoma of the pancreas is a mucin-producing epithelial cell adenocarcinoma "floating" within large pools of extracellular mucin. The colloid generally comprises at least 80% of the neoplasm plus a tubular component, and the lesion is also known as mucinous noncystic carcinoma.[8] This is a subtype of IPMN with more indolent behavior which is attributed to 2 morphologic features of mucin overproduction. First, the mucin is secreted toward the cell-stroma interface and detaches the epithelial cells from the stroma. Second, the mucin acts as a barrier limiting the spread of neoplastic cells.[21] The differential diagnosis includes MCN and IPMN. Overall survival is as high as 70% and 57% at 2 and 5 years.[22]

Medullary Carcinoma

Medullary carcinoma of the pancreas is a rare variant of a malignant epithelial neoplasm that is characterized by poor differentiation, syncytial growth pattern, well-defined borders, and areas of focal necrosis.[8] It was first described in 1998 and often has DNA replication errors associated with wild-type K-RAS or microsatellite

instability.[23] Because of this, medullary carcinoma may be a focal point for clinicians who study inherited pancreatic cancer syndromes.[24] Because of limited data, survival of medullary carcinoma compared with PDAC is unknown.

MISCELLANEOUS NEOPLASMS

Neoplastic Potential

Acinar cell carcinoma

ACC was first described in 1908 by Berner[25] as a syndrome of fever, polyarthritis, subcutaneous fat nodular necrosis, and eosinophilia. This syndrome is initiated by tumor hypersecretion of lipase. ACC tumors are very large, exophytic, well-circumscribed, and hypovascular with minimal stroma throughout the pancreas.[26] These tumors occur in older patients and are quite rare, accounting for fewer than 1% of all pancreatic tumors despite that the pancreas has more than 80% volume of acinar cells. ACC may be found in the pediatric population, where it accounts for 15% of all pediatric pancreatic neoplasms.[8] Although most acinar cell neoplasms are solid malignant tumor, rare subtypes, such as acinar cell cystadenoma, acinar cell cystadenocarcinoma, or a mixed tumor are found. A characteristic paraneoplastic process, lipase hypersecretion syndrome is found in 10% to 15% of patients, and is identified by a serum lipase >10,000 U/dL. It is characterized by multiple nodular foci of subcutaneous fat necrosis and polyarthralgia due to sclerotic bone lesions from fat necrosis. The syndrome usually resolves after tumor resection (**Fig. 3**).[27] Alternatively, in diffuse metastatic or unresectable disease, combined chemotherapy with oxaliplatin, irinotecan, and fluorouracil (FOLFIRINOX) may alleviate symptoms from lipase hypersecretion.[28]

The overall prognosis of ACC is unclear. In a recent report from China, Wang and colleagues[26] described 19 patients treated over 20 years. The predominate symptoms were abdominal pain and weight loss, and the ACC tumors were equally distributed in the head and tail. Interestingly, no patient developed jaundice despite large tumors in the head, and only 2 had elevated serum lipase. CA 19-9 was normal in all. Only 14 patients underwent an R0 resection with a median tumor size of 5.4 cm with 1 postoperative mortality. Surgical resection was associated with a longer median survival (19 vs 9 months), as was adjuvant chemotherapy. When matched to a similar group with PDAC, ACC patients were younger (54 vs 65 years), more often (84 vs 53%), with larger tumors (5.3 vs 3.1 cm), earlier stage, and a longer median survival (18 vs 4 months).[26] Matos and colleagues[29] reported a multi-institutional review of 17 ACC patients over 20 years. Four had elevated serum lipase, but none had lipase hypersecretion syndrome. Most (15) underwent resection, with a 1-year and 5-year survival rates of 88% and 50%.[29]

ACC is a rare pancreatic tumor that may be difficult to differentiate from PDAC, but is best treated by surgical resection when feasible. Long-term outcomes and prognosis are similar if not slightly better than that of PDAC.

Solid pseudopapillary neoplasm

Solid pseudopapillary neoplasms (SPNs) are a distinct, low-grade, malignant epithelial tumor first described by Frantz in 1959.[30] The lesions are distinct, a solid mass with cystic degeneration often with intracystic hemorrhage. They are also classified as papillary epithelial neoplasm, papillary cystic neoplasm, solid and papillary neoplasm, low-grade papillary neoplasm, and Hamoudi or Frantz tumor.[8] The female-to-male ratio is 10:1 and it usually presents in the second or third decade with a large mass causing abdominal symptoms, but rarely jaundice or pancreatitis despite its large size. SPNs are located throughout the pancreas, but are more frequent in the body and tail. The differential diagnosis includes PDAC, cystadenoma, cystadenocarcinoma, neuroendocrine

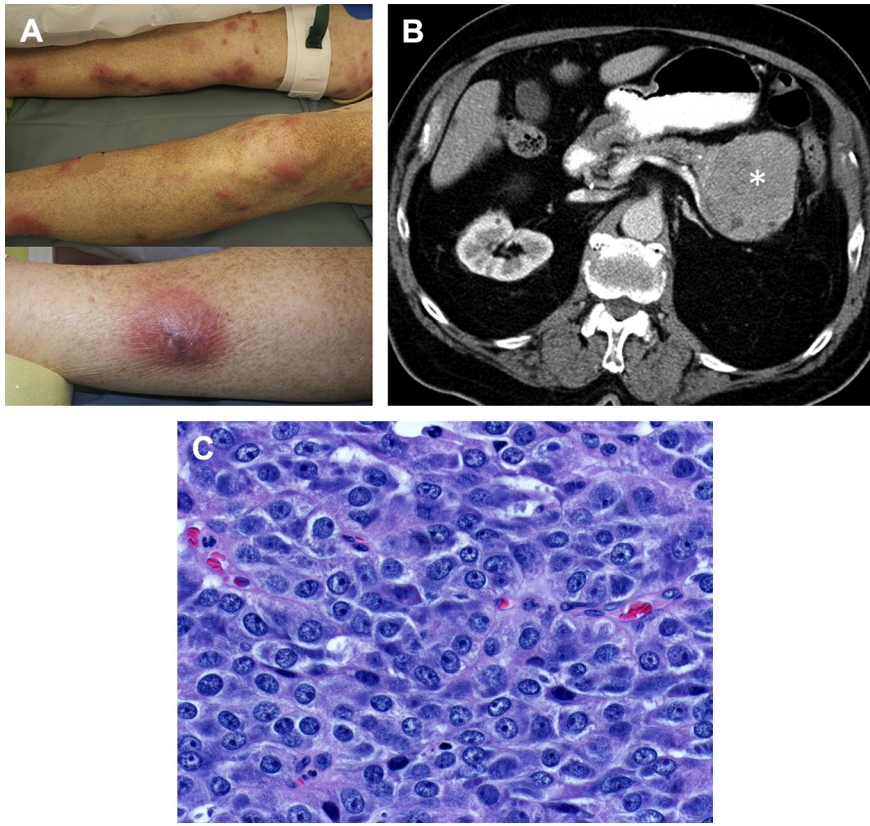

Fig. 3. (*A*) Photographs of diffuse subcutaneous nodules found on a 79-year-old man. The nodules were erythematous, firm, and cystic, with overlying epithelial exfoliation. They started on the lower extremities but spread to the whole body. Serum lipase was noted to be >13,000 U/L. (*B*) Axial CT showing 9-cm mass in the tail of the pancreas in this same patient. Asterisk indicates tumor (*C*) The serum lipase returned to normal after distal pancreatectomy. High-powered magnification of the pancreas mass showed poorly differentiated ACC. The tumor predominantly had a solid growth with a trabecular pattern. The cells had abundant basophilic cytoplasm with large nuclei and prominent nucleoli (hematoxylin-eosin, original magnification × 20).

tumor, or pancreatic cyst.[31] Usually serum tumor markers are normal and cross-sectional imaging shows a well-encapsulated complex mass containing solid and cystic components. SPNs should be suspected when hemorrhage into a nonseptated cystic mass is seen in the distal part of the pancreas in a young woman. For female patients below 40, this tumor accounts for more than 70% of pancreatic resections.

Although SPN is generally indolent, malignancy develops in up to 15% of patients. Nodal disease is rare and metastases are by local or hematogenous invasion, which most frequently involves the liver, regional lymph nodes, mesentery, omentum, and peritoneum. Vascular and/or visceral invasion is not uncommon due to their large size (**Figs. 4** and **5**).

Margin-negative surgical resection is the curative goal. Despite locally advanced or metastatic disease, the prognosis is generally quite good. Lubezky and colleagues[32] recently published their experience with 32 margin-negative SPN's. The mean tumor

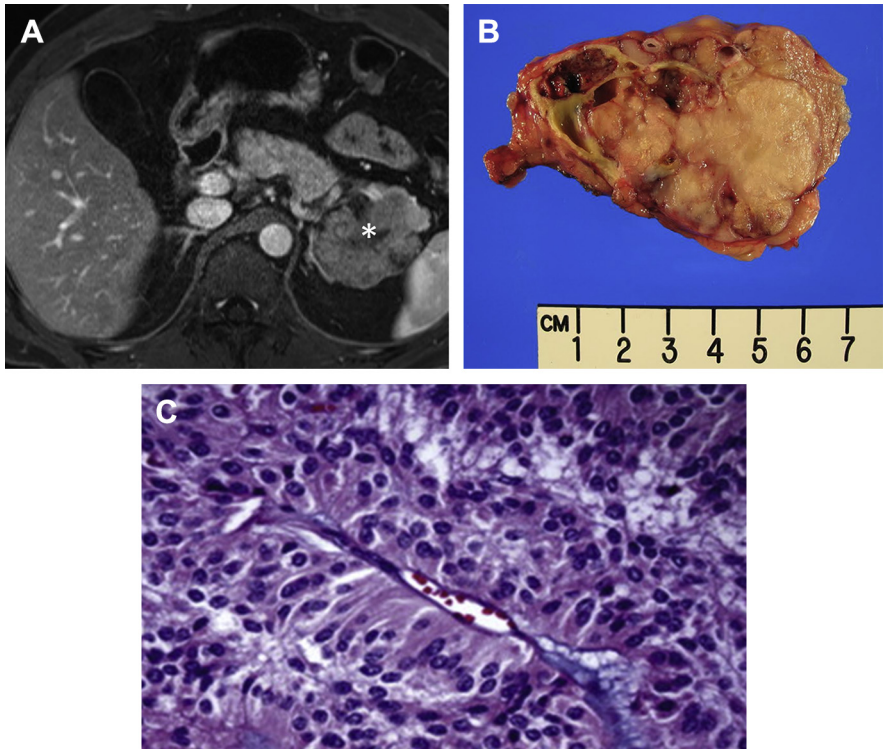

Fig. 4. (*A*) Axial MRI showing a 5.6-cm lobulated solid mass with areas of cystic changes and necrosis in the tail of the pancreas in a 39-year-old man. The splenic vessels were draped over the lesion and patent. Asterisk indicates tumor. (*B*) Distal pancreatectomy was performed and gross pathology pictures show an encapsulated, heterogeneous solid and cystic mass in the tail of the pancreas; 0/10 lymph nodes were involved. (*C*) Microscopic pictures of pseudopapillae arranged around vascular stalks indicated SPN. The tumor stained positive for synaptophysin, CD 10, and beta-catenin and negative for chromogranin and pancytokeratin (hematoxylin-eosin, original magnification × 20).

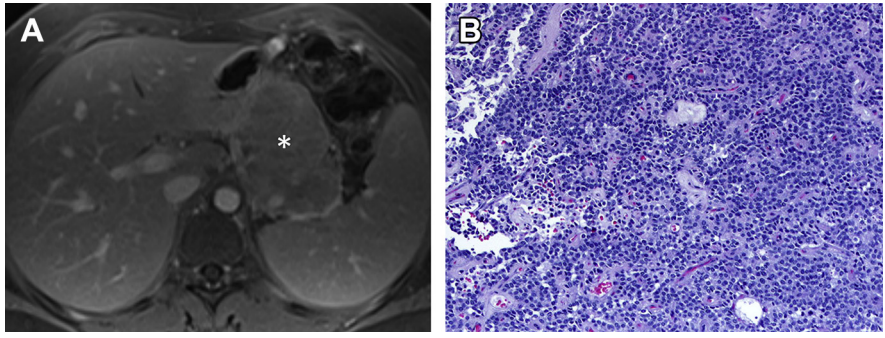

Fig. 5. (*A*) Axial MRI of a 17-year-old female patient with an 8.8-cm solid cystic mass of the tail of the pancreas. Asterisk indicates tumor. (*B*) Microscopic picture of SPN. Immunohistochemistry stains were positive for vimentin, CD 10, progesterone, beta-catenin, cytokeratin, and synaptophysin, and negative for chromogranin, E-cadherin, and trypsin (hematoxylin-eosin, original magnification × 10).

size was 5.9 cm, and 91% of the patients were women with a mean age of 28 years. The 5-year and 10-year disease-free survival was 97% and 90%. Four patients had metastatic disease, including 1 with multiple bilobar liver metastases which was stable at 37 months post resection. Three others underwent hepatectomy or observation and remained disease-free or stable in a lengthy follow-up.[32] In a recent multi-institutional report of 131 SPN patients, two with metastases underwent synchronous hepatopancreatectomy with good outcomes. Only two had recurrence 5 and 6 years after partial pancreatectomy. Disease-specific survival and disease-free survival were 98% at 5 years.[33]

Overall, SPN is a rare, indolent tumor that should be classified "malignant" only when metastatic or recurrent is evident. When indicated surgical resection is the treatment of choice for localized, metastatic, or recurrent SPN.

Pancreatoblastoma

Pancreatoblastoma is a malignant epithelial tumor that includes acinar, squamoid nests, endocrine, and ductal differentiation. They may be large at presentation and have elevated AFP levels.[8] This is the most common pancreatic neoplasm of childhood and young adults, in whom the prognosis is worse.[34] Surgical resection is indicated, although the disease often is advanced at presentation with an aggressive course and poor outcome, similar to ACC.

Schwannoma

Schwann cell tumors (Schwannoma) are mesenchymal tumors of peripheral nerve sheaths that are located throughout the body, including the pancreas. Pancreatic schwannoma are rare with fewer than 70 reported cases in the past 4 decades. Pathology shows a well-encapsulated lesion of spindle-shaped cells without atypia. Immunohistochemical staining is positive for protein S-100. The age at diagnosis is relatively young, and surgical resection is preferred.[35] These tumors are often incidental findings with an excellent overall prognosis. There are 5 reported malignant pancreatic schwannomas.[36] Degenerative changes, such as cystic formation, calcification, hemorrhage, hyalinization, or xanthomatous infiltration, are present in two-thirds of patients. Preoperative diagnosis by EUS with fine-needle aspiration will differentiate this tumor from cystic PNET, SPN, MCN, or pseudocysts.[37]

Angiosarcoma

Primary angiosarcoma of the pancreas are aggressive and extremely rare lesions, with only 5 reported cases. They present with gastrointestinal bleeding, weight loss, and abdominal pain. Surgical resection for localized disease may be curative. Risk factors for angiosarcoma include radiation, chronic lymphedema, certain familial syndromes and chemical carcinogens, but specific risk factors are not known.[38,39]

Perivascular epithelioid cell neoplasms

Perivascular epithelioid cell neoplasm (PEComa) are another mesenchymal neoplasm that arise from perivascular epithelioid cells and may occur in the pancreas. Composed of large epithelioid and spindle cells with a characteristic nuclei pattern, HMB45 immunostaining will be strongly positive. These tumors are also known as clear-cell "sugar" tumors, and angiomyolipoma (AML). AML typically occurs in the kidney.[40] Fewer than 10 cases of PEComa have been reported, including patients with local recurrence and metastatic disease after primary tumor resection. Metastatic melanoma, gastrointestinal stromal tumor (GIST), and clear-cell carcinoma are diagnostic considerations. Resection and frequent follow-up are warranted, as the prognosis is generally very good.[41–43]

Primary leiomyosarcoma

Primary pancreatic leiomyosarcoma is rare and accounts for most pancreatic sarcomas. It may mimic other rare neoplasms, such as GIST, solitary fibrous tumor, inflammatory myofibroblastic tumor, malignant schwannoma, liposarcoma, rhabdomyosarcoma, and anaplastic carcinoma. They are highly aggressive neoplasms with fewer than 40 cases in the English literature,[44,45] including 9 patients by Zhang and colleagues[46] who noted an equal male:female distribution, and a mean age and tumor size of 63 years and 1. Resection was possible in 4 (no lymph nodes were involved), but liver metastases were evident in 5 and overall mean survival was only 31 months with 5 having disease-related deaths.[46] This tumor presents late and is treated with doxorubicin-based chemotherapy with a poor response rate.[47] Surgical resection may benefit localized disease.[48]

Solitary fibrous tumor

Solitary fibrous tumor of the pancreas is a rare benign entity with fewer than 20 reported cases.[44,49,50] Most (81%) were women with a median age of 54 years, and a mean tumor size of 5.8 cm, with lesions distributed throughout the pancreas. Excision reveals a well-circumscribed encapsulated mass that is positive on immunohistochemical staining for CD34, vimentin, CD 99, and/or Bcl-2 but not CD117.

Primary pancreatic lymphoma

Primary pancreatic lymphoma (PPL) is another rare entity that can be very difficult to diagnose and is the "mimicker" of the more common PDAC. An accurate diagnosis is important because the treatment is chemotherapy and radiotherapy. Diagnostic criteria for PPL include (1) no superficial or mediastinal lymphadenopathy, (2) a normal leukocyte count, (3) a pancreatic or lymph-node mass in the peripancreatic region, and (4) absent hepatic and splenic involvement.[51] The most common pancreatic variant is diffuse large B-cell lymphoma, accounting for 80% of PPL. Common presenting symptoms are abdominal pain, jaundice, pancreatitis, small bowel obstruction, and diarrhea. Classic symptoms of fever, chills, and night sweats are uncommon.[52] Imaging characteristics include a large infiltrative mass with peripancreatic stranding and infrequent biliary, pancreatic duct, or venous obstruction. Some PPLs present as well-circumscribed tumors with infrarenal lymphadenopathy (**Fig. 6**).[53] The differential

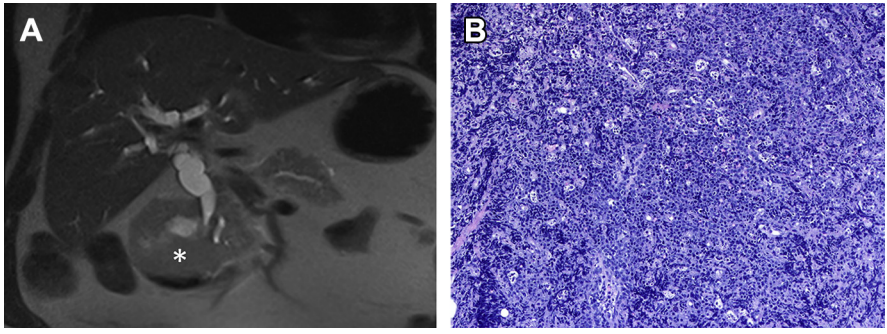

Fig. 6. (*A*) Coronal MRCP with a 7-cm mass of the head of the pancreas causing biliary and duodenal obstruction in a 64-year-old man. Asterisk indicates mass. (*B*) EUS and fine-needle aspiration showed PPL. Staining was positive for CD20, PAX-5, Bcl-6, and CD10 and negative for CD3. There was c-Myc/immunoglobulin H translocation consistent with B-cell lymphoma (hematoxylin-eosin, original magnification × 4). The patient was successfully treated with biliary stenting followed by rituximab, cyclophosphamide, vincristine, Adriamycin, and prednisone (R-CHOP).

diagnosis beside PDAC includes secondary lymphoma, pancreatitis, AIP, PNET, or ACC. Biopsy is indicated for a large bulky pancreatic mass that infiltrates beyond normal anatomic barriers, stretches local vasculature without infiltration, normal PDAC tumor markers, and elevated serum lactate dehydrogenase. This disease is treatable in all stages and endoscopic or percutaneous diagnosis is preferred.[51] Sadot and colleagues[54] reported 44 patients with PPL. Three-fourths of patients achieved complete remission, with a median overall survival of 6.1 years and a 10-year disease-specific survival of 69%. The follicular lymphoma subtype has the best prognosis, with a 100% 5-year survival. Long-term surveillance is indicated to exclude relapse.[54]

Collision/mixed tumors

Collision tumors are defined and classified by the World Health Organization as at least 2 different malignant components occurring within a tumor in the same organ or anatomic site.[55] Various combinations have been noted, including combinations of PDAC and PNET,[56] IPMN and PNET,[57,58] SPN and PNET,[59] hepatoid carcinoma and PNET,[20] mixed ACC with either PNET or PDAC,[27,60] or PDAC and biliary carcinoma.[61] For collision tumors, the possibility of metastatic disease must be ruled out, but the incidence of diagnosed dual cancers is increasing and more frequently recognized.[61]

BENIGN SOLID/CYSTIC

Hamartomas

Pancreatic hamartomas are rare with fewer than 31 reported cases. They are a malformation rather than a neoplasm and are quite benign. The median age at presentation is 50.4 years with equal sex predilection. They present as solid or solid/cystic patterns and are isolated or multiple. The average size is <5 cm and they occur anywhere within the pancreas. Most have been resected due to the uncertain nature of a pancreatic mass, but if the diagnosis is known they can and should be observed.[62–64]

Hemangioma

Pancreatic cavernous hemangioma is rare in adults. They are benign variants of vascular tumors that include lymphangioma, hemolymphangioma, hemangioendothelioma, hemangiopericytoma, hemangioblastoma, and angiosarcoma. Visceral hemangiomas are most common in the liver, but are found anywhere in the gastrointestinal tract. In a review of pancreatic hemangiomas, Mondal and colleagues[65] identified 21 cases with an average age of 48 years and male-to-female ratio of 1:3. Symptoms included abdominal pain in half. Hemangiomas occur with von Hippel-Lindau disease. They are quite benign and surgical resection should be avoided.[65] Pediatric hemangiomas may involute but adult pancreatic hemangiomas do not. They rarely obstruct or infiltrate despite large size or continued slow growth. They may be difficult to distinguish from other highly vascular tumors, especially metastatic RCC.[66] Some advise surgical resection in a pregnant patient to avoid rupture, but this is controversial and should be performed selectively.[67]

Lymphangioma

Pancreatic lymphangioma is an uncommon benign cystic tumor of the pancreas. There are 4 subtypes, dependent on the depth and size of abnormal lymph vessels: capillary lymphangioma, cavernous lymphangioma, cystic hygroma, or hemolymphangioma. They are congenital and originate from mesenchymal tissue. Less often they develop from poor lymph drainage or lymphatic injury. They are identified

macroscopically as thin-walled cysts with multiple septa and variable-sized cystic cavities containing clear or hemorrhage lymph fluid. They are generally asymptomatic and are diagnosed incidentally. Surgical removal is indicated for symptomatic disease or to exclude other disease when the diagnosis is uncertain (**Fig. 7**). Incomplete resection can lead to recurrence.[68,69]

Pancreatic Lymphoepithelial Cyst

Lymphoepithelial cysts (LECs) consist of keratinized material lined by mature squamous epithelium surrounded by lymphatic tissue. Pancreatic LECs are true cystic lesions with no malignant potential and are very similar to squamoid cysts, mucinous non-neoplastic cysts, enterogenous cysts, endometrial cysts, and retention cysts or simple cysts. They account for less than 2% of pancreatectomy.[70] These cysts do not have any solid components but may occasionally have septations. The differential diagnoses of LECs includes MCN, SCN, and IPMN. EUS-guided biopsy with aspiration can be diagnostic and is recommended for all unknown cystic lesions of the pancreas. However, the clinician should be aware that a simple cyst may become complex on imaging after fine-needle aspiration with intracystic hemorrhage.[71,72]

Intrapancreatic Accessory Spleen

Intrapancreatic accessory spleen (IPAS) is a congenital anomaly caused by failure of fusion during embryology. The incidence is 10% to 15% in the general population and the tail of the pancreas is the second most common site after the hilum of the spleen.[73] They are commonly detected because of the increased frequency and sensitivity of abdominal imaging. IPASs are generally small and match the density of the spleen on all contrast phases. They can, however, be mistaken for other enhancing pancreatic lesions of the tail, including PNET, SPN, and metastatic disease. Nuclear medicine imaging can be used to confirm this diagnosis, and biopsy is rarely required.[74,75]

Plasmacytoma

Pancreatic plasmacytoma is most commonly associated with multiple myeloma and results from extramedullary plasmacytoma, which is a discrete collection of monoclonal plasmocytes arising in tissues other than bone. In the gastrointestinal tract, the liver and spleen are more commonly involved and pancreatic involvement is

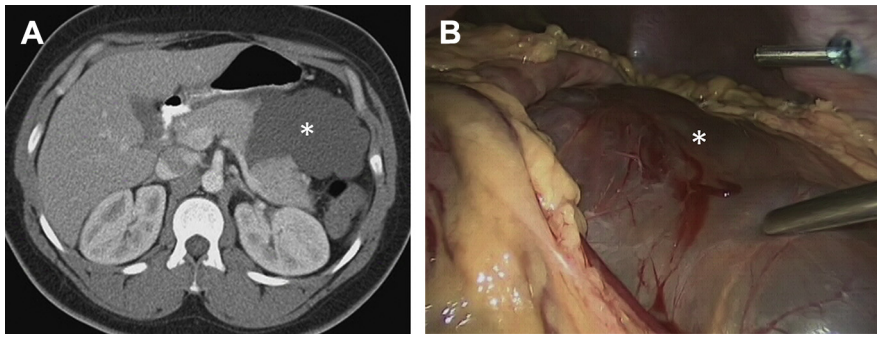

Fig. 7. (*A*) Axial CT showing a large multilobulated cystic mass in the lesser sac arising from the body of the pancreas causing abdominal pain in a 22-year-old woman. Asterisk indicates cyst. (*B*) Intraoperative picture of a cystic lesion of the tail of the pancreas. Limited pancreatic resection and excision of the mass confirmed complete resection of a 15-cm lymphangioma with resolution of the patient's symptoms. Asterisk indicates cyst.

rare.[76] Williet and colleagues[77] identified 63 reported cases of pancreatic plasmacytoma with a mean age of 58.5 years. Seventy percent presented with jaundice and only 2 cases were in the body or tail of the pancreas. Biopsy, whether percutaneous, endoscopic, or surgical, is indicated, and treatment with chemotherapy or radiotherapy resulted in 100% response rates.[77]

Pancreatic Sarcoidosis

Sarcoidosis is a granulomatous syndrome of unknown etiology that can involve all organ systems in the body, most commonly lung and lymph. Gastrointestinal involvement occurs in fewer than 1% and pancreatic sarcoidosis is rare; however, it can present with pancreatic involvement and be mistaken for pancreatitis or PDAC. Abdominal symptoms and lymphadenopathy can be seen, but high-quality imaging and tissue diagnosis will differentiate this from similar entities, and surgical intervention can be avoided.[78,79]

Pancreatic Tuberculosis

Pancreatic tuberculosis (TB) is an extremely rare presentation of abdominal TB. The retroperitoneal location and enzymatic environment of the pancreas is thought to protect it from exposure and mycobacterium invasion. However, there are reports of isolated pancreatic TB causing symptoms that mimic pancreatic malignancy. EUS with biopsy and findings of caseating necrosis, granuloma, and acid-fast bacteria have become the method of choice for the diagnosis of pancreatic TB.[80–82]

METASTATIC TUMORS

Renal Cell Carcinoma

RCC has a propensity to metastasize to the pancreas and can present as a solitary mass or multiple masses within the pancreas. It can present many years after the initial diagnosis of RCC and it should be considered in all patients with a history of RCC who present with a pancreatic mass (**Fig. 8**). Adler and colleagues[83] reported in a literature review of 399 patients who underwent pancreatectomy for metastases, that RCC was responsible for 62.6% of all operations. The prognosis is quite good for isolated RCC involvement of the pancreas after surgical resection with a 5-year survival of 70.4%. This was significantly better than for non-RCC pancreatic metastasectomies.[83]

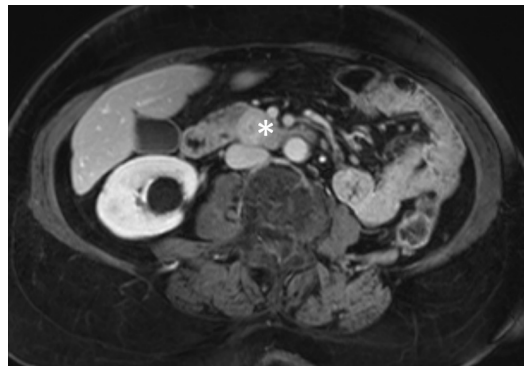

Fig. 8. Axial MRI showing a 2.3-cm mass in the head of the pancreas in a 70-year-old woman with a history of left-sided renal cell cancer 4 years prior. Pancreatic resection revealed isolated metastatic RCC. Asterisk indicates mass.

Konstantinidis and colleagues[84] reported 20 patients who underwent pancreatic resection for RCC, with most being male (65%) and a median age of 68.5 years. The right and left kidneys were the equally involved and 25% had multiple metastases in the pancreas. These lesions were equally distributed throughout the pancreas and 19 of 20 presented with metachronous disease at a median of 8.7 years after nephrectomy. Total pancreatectomy, central pancreatectomy, and enucleation were used as indicated, as well as Whipple and distal pancreatectomy. Actual 5-year survival was 61%.[84] RCC is the most common metastatic lesion to the pancreas requiring surgical resection. These tumors may mimic PNET and are generally very well circumscribed and may have cystic degeneration. For isolated RCC in the pancreas, surgical intervention is clearly indicated.[85]

Melanoma

Malignant melanoma can develop multiple distant metastases in the gastrointestinal tract; however, pancreatic involvement is rare.[86] The literature is limited regarding metastatic pancreatic melanoma and its surgical treatment. Most patients present with a symptomatic mass with or without a known previous melanoma.[86,87] The tumor is commonly discovered after cross-imaging techniques, and the diagnosis of metastatic melanoma is established by fine-needle biopsy. Goyal and colleagues[87] reported 5 patients treated with pancreatoduodenectomy and distal pancreatectomy and the median survival was only 11.4 months.

Lung Carcinoma

Common sites of lung cancer metastasis are brain, bones, liver, and adrenal with the pancreas rarely involved.[88,89] A retrospective study of 2872 patients with non–small-cell lung carcinoma revealed pancreatic disease in just 17 patients (0.59%).[90] Small-cell lung cancer is the most common histologic subtype that metastasizes to the pancreas from the lung.[88] In most cases, metachronous pancreatic metastases are found incidentally during the evaluation of patients with lung cancer, indicating stage IV disease. Lung metastases to the pancreas have poor outcomes.[88,90] There is controversy regarding attempted curative pancreatectomy for metachronous pancreatic metastasis from lung carcinoma (Fig. 9). A single study reported 3 resections with

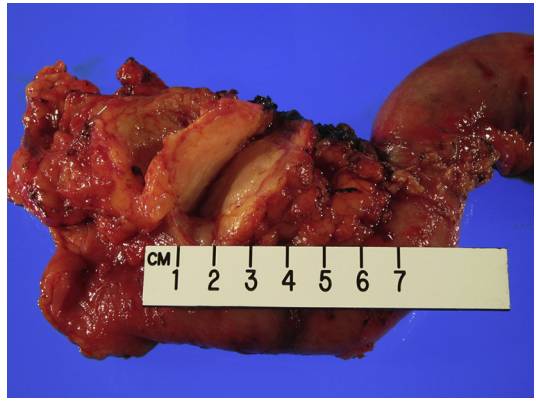

Fig. 9. Gross photograph of an isolated metastatic lung adenocarcinoma lesion within the head of the pancreas in an 84-year-old man. He remained disease-free 5 years after undergoing pancreaticoduodenectomy.

recurrence in all.[91] Others report better results and recommend resection and systemic therapy in select patients.[90,92]

Breast Carcinoma

Breast adenocarcinoma metastasis to the pancreas is extremely rare compared with other distant sites, such as kidney, lung, and colon.[93] The literature is limited to a few case reports. According to Bednar and colleagues,[94] approximately 5% of patients operated for pancreatic metastasis were found to have breast adenocarcinoma, and an autopsy series reported pancreatic involvement in 13%.[95] They present as mass lesions in the pancreas on follow-up imaging studies, and patients may have jaundice, abdominal pain, or disseminated disease.[93] Surgery relieves symptoms in select patients. In combination with chemoradiation and hormonal therapy, surgery may have a palliative role with a low perioperative mortality[95] and a 25% 5-year survival.[96]

Colorectal Cancer

Studies reporting patients with colorectal metastasis to the pancreas are also limited to single case reports or small series. Sperti and colleagues[95] reported 18 resections for metastatic disease with 9 from colorectal adenocarcinoma. Most presented with abdominal pain and jaundice, and imaging studies revealed a mass in the pancreas and a history of colorectal cancer.[93,95,97] Surgical resection or metastasectomy without other organ involvement may relieve symptoms and be adequate treatment, usually combined with other modalities.[95,96]

Other Rare Metastases from Different Sites

Three percent to 15% of resected pancreatic metastases are from the urinary bladder, ovary, and prostate.[83,93,96] Limited conclusions can be drawn due to rarity of the disease, but surgeons can apply similar reasoning to determine treatment for these lesions, Parenchyma-sparing operations, such as central pancreatectomy and enucleation can be considered when feasible.

PANCREATIC INFLAMMATORY LESIONS

Fewer than 5% of all pancreatectomies done for suspected carcinoma are benign. There are a few pancreatic inflammatory conditions, such as chronic pancreatitis, AIP, GP (**Fig. 10**), eosinophilic pancreatitis, and pyogenic abscess that mirror

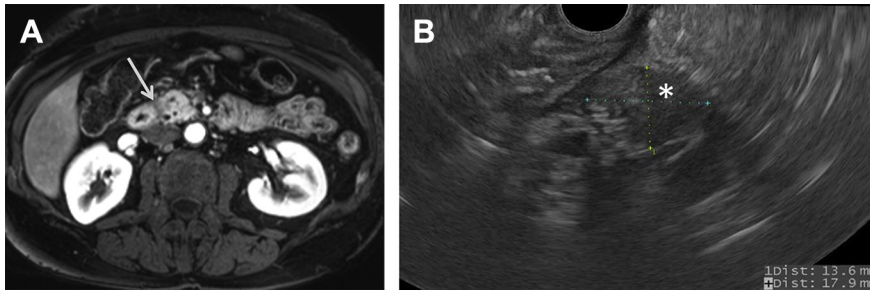

Fig. 10. (*A*) Axial MRI showing a 1-cm heterogeneous mass in a 57-year-old woman with recurrent pancreatitis (*arrow indicates mass*). (*B*) EUS of this patient confirming a 13.6 × 17.9-mm mass in the head of the pancreas. Surgical resection was performed and pathologic findings confirmed GP. The patient's recurrent pancreatitis symptoms resolved. Asterisk indicates mass.

PDAC. Clinical, biochemical, and radiographic findings may overlap, and uncertainty may infrequently require pancreatectomy for definitive diagnosis.[2,3] AIP, in particular (also known as lymphoplasmacytic sclerosing pancreatitis), now accounts for most "pseudotumors" and should be suspected if serum immunoglobulin G4 is elevated (Type I only) in younger patients with or without other autoimmune diseases. Surgical resection is not the primary treatment, and response to a short course of steroids is diagnostic.[98,99]

SUMMARY

PDAC, PNET, IPMN, mucinous cystic neoplasm, and serous cystic neoplasm account for the vast majority of solid and cystic lesions of the pancreas. However, other neoplasms may rarely involve the pancreas and require different treatment with varying prognosis. Additionally, the pancreas may be involved with other solid or cystic lesions that require pancreatectomy for diagnosis or therapy. Therefore, the clinician needs to be aware of these infrequent and rare lesions and evaluate, treat, or refer as needed.

REFERENCES

1. Liu JB, Baker MS. Surgical management of pancreatic neuroendocrine tumors. Surg Clin North Am 2016;96:1447–68.
2. Adsay NV, Basturk O, Klimstra DS, et al. Pancreatic pseudotumors: non-neoplastic solid lesions of the pancreas that clinically mimic pancreas cancer. Semin Diagn Pathol 2004;21:260–7.
3. Al-Hawary MM, Kaza RK, Azar SF, et al. Mimics of pancreatic ductal adenocarcinoma. Cancer Imaging 2013;13:342–9.
4. Feldman MK, Gandhi NS. Imaging evaluation of pancreatic cancer. Surg Clin North Am 2016;96:1235–56.
5. Singh A, Faulx AL. Endoscopic evaluation in the workup of pancreatic cancer. Surg Clin North Am 2016;96:1257–70.
6. Sommers SC, Meissner WA. Unusual carcinomas of the pancreas. AMA Arch Pathol 1954;58:101–11.
7. Paal E, Thompson LD, Frommelt RA, et al. A clinicopathologic and immunohistochemical study of 35 anaplastic carcinomas of the pancreas with a review of the literature. Ann Diagn Pathol 2001;5:129–40.
8. Hruban RH, Pitman MB, Klimstra DS. Tumors of the pancreas. Washington, DC: American Registry of Pathology in collaboration with Armed Forces Institute of Pathology; 2007.
9. Yamaguchi K, Nakamura K, Shimizu S, et al. Pleomorphic carcinoma of the pancreas: reappraisal of surgical resection. Am J Gastroenterol 1998;93:1151–5.
10. Hoshimoto S, Matsui J, Miyata R, et al. Anaplastic carcinoma of the pancreas: case report and literature review of reported cases in Japan. World J Gastroenterol 2016;22:8631–7.
11. Strobel O, Hartwig W, Bergmann F, et al. Anaplastic pancreatic cancer: presentation, surgical management, and outcome. Surgery 2011;149:200–8.
12. Paniccia A, Hosokawa PW, Schulick RD, et al. A matched-cohort analysis of 192 pancreatic anaplastic carcinomas and 960 pancreatic adenocarcinomas: a 13-year North American experience using the National Cancer Data Base (NCDB). Surgery 2016;160:281–92.
13. Clark CJ, Graham RP, Arun JS, et al. Clinical outcomes for anaplastic pancreatic cancer: a population-based study. J Am Coll Surg 2012;215:627–34.
14. Herxheimer G. Uber heterologe cancroide. Beitr Pathol Anat 1907;41:348–412.

15. Katz MH, Taylor TH, Al-Refaie WB, et al. Adenosquamous versus adenocarcinoma of the pancreas: a population-based outcomes analysis. J Gastrointest Surg 2011;15:165–74.
16. Boyd CA, Benarroch-Gampel J, Sheffield KM, et al. 415 patients with adenosquamous carcinoma of the pancreas: a population-based analysis of prognosis and survival. J Surg Res 2012;174:12–9.
17. Imaoka H, Shimizu Y, Mizuno N, et al. Clinical characteristics of adenosquamous carcinoma of the pancreas: a matched case-control study. Pancreas 2014;43:287–90.
18. Marchegiani G, Gareer H, Parisi A, et al. Pancreatic hepatoid carcinoma: a review of the literature. Dig Surg 2013;30:425–33.
19. Petrelli F, Ghilardi M, Colombo S, et al. A rare case of metastatic pancreatic hepatoid carcinoma treated with sorafenib. J Gastrointest Cancer 2012;43:97–102.
20. Kuo PC, Chen SC, Shyr YM, et al. Hepatoid carcinoma of the pancreas. World J Surg Oncol 2015;13:185.
21. Adsay NV, Merati K, Nassar H, et al. Pathogenesis of colloid (pure mucinous) carcinoma of exocrine organs: coupling of gel-forming mucin (MUC2) production with altered cell polarity and abnormal cell-stroma interaction may be the key factor in the morphogenesis and indolent behavior of colloid carcinoma in the breast and pancreas. Am J Surg Pathol 2003;27:571–8.
22. Adsay NV, Pierson C, Sarkar F, et al. Colloid (mucinous noncystic) carcinoma of the pancreas. Am J Surg Pathol 2001;25:26–42.
23. Goggins M, Offerhaus GJ, Hilgers W, et al. Pancreatic adenocarcinomas with DNA replication errors (RER+) are associated with wild-type K-ras and characteristic histopathology. Poor differentiation, a syncytial growth pattern, and pushing borders suggest RER+. Am J Pathol 1998;152:1501–7.
24. Wilentz RE, Goggins M, Redston M, et al. Genetic, immunohistochemical, and clinical features of medullary carcinoma of the pancreas: a newly described and characterized entity. Am J Pathol 2000;156:1641–51.
25. Berner O. Subkutane fettgewebsnekose. Virchow Arch Path Anat 1908;193:510–8.
26. Wang Y, Wang S, Zhou X, et al. Acinar cell carcinoma: a report of 19 cases with a brief review of the literature. World J Surg Oncol 2016;14:172.
27. Chaudhary P. Acinar cell carcinoma of the pancreas: a literature review and update. Indian J Surg 2015;77:226–31.
28. Yoshihiro T, Nio K, Tsuchihashi K, et al. Pancreatic acinar cell carcinoma presenting with panniculitis, successfully treated with FOLFIRINOX: a case report. Mol Clin Oncol 2017;6:866–70.
29. Matos JM, Schmidt CM, Turrini O, et al. Pancreatic acinar cell carcinoma: a multiinstitutional study. J Gastrointest Surg 2009;13:1495–502.
30. Frantz VK. Tumors of the pancreas. Atlas of tumor pathology. Washington, DC: Armed Forces Institute of Pathology; 1959. p. 32–3.
31. Yu PF, Hu ZH, Wang XB, et al. Solid pseudopapillary tumor of the pancreas: a review of 553 cases in Chinese literature. World J Gastroenterol 2010;16:1209–14.
32. Lubezky N, Papoulas M, Lessing Y, et al. Solid pseudopapillary neoplasm of the pancreas: management and long-term outcome. Eur J Surg Oncol 2017;43:1056–60.
33. Marchegiani G, Andrianello S, Massignani M, et al. Solid pseudopapillary tumors of the pancreas: specific pathological features predict the likelihood of postoperative recurrence. J Surg Oncol 2016;114:597–601.

34. Dhebri AR, Connor S, Campbell F, et al. Diagnosis, treatment and outcome of pancreatoblastoma. Pancreatology 2004;4:441–51 [discussion: 452–3].
35. Xu SY, Sun K, Owusu-Ansah KG, et al. Central pancreatectomy for pancreatic schwannoma: a case report and literature review. World J Gastroenterol 2016; 22:8439–46.
36. Moriya T, Kimura W, Hirai I, et al. Pancreatic schwannoma: case report and an updated 30-year review of the literature yielding 47 cases. World J Gastroenterol 2012;18:1538–44.
37. Nishikawa T, Shimura K, Tsuyuguchi T, et al. Contrast-enhanced harmonic EUS of pancreatic schwannoma. Gastrointest Endosc 2016;83:463–4.
38. Meeks M, Grace S, Veerapong J, et al. Primary angiosarcoma of the pancreas. J Gastrointest Cancer 2016. [Epub ahead of print].
39. Worth PJ, Turner M, Hammill CW. Incidental angiosarcoma of the pancreas: a case report of a rare, asymptomatic tumor. J Pancreat Cancer 2017;3:24–7.
40. Heywood G, Smyrk TC, Donohue JH. Primary angiomyolipoma of the pancreas. Pancreas 2004;28:443–5.
41. Nagata S, Yuki M, Tomoeda M, et al. Perivascular epithelioid cell neoplasm (PEComa) originating from the pancreas and metastasizing to the liver. Pancreas 2011;40:1155–7.
42. Mourra N, Lazure T, Colas C, et al. Perivascular epithelioid cell tumor: the first malignant case report in the pancreas. Appl Immunohistochem Mol Morphol 2013; 21:e1–4.
43. Mizuuchi Y, Nishihara K, Hayashi A, et al. Perivascular epithelial cell tumor (PEComa) of the pancreas: a case report and review of previous literature. Surg Case Rep 2016;2:59.
44. Kim JY, Song JS, Park H, et al. Primary mesenchymal tumors of the pancreas: single-center experience over 16 years. Pancreas 2014;43:959–68.
45. Soreide JA, Undersrud ES, Al-Saiddi MS, et al. Primary leiomyosarcoma of the pancreas—a case report and a comprehensive review. J Gastrointest Cancer 2016;47:358–65.
46. Zhang H, Jensen MH, Farnell MB, et al. Primary leiomyosarcoma of the pancreas: study of 9 cases and review of literature. Am J Surg Pathol 2010;34:1849–56.
47. ESMO/European Sarcoma Network Working Group. Soft tissue and visceral sarcomas: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 2012;23(Suppl 7):vii92–9.
48. Aihara H, Kawamura YJ, Toyama N, et al. A small leiomyosarcoma of the pancreas treated by local excision. HPB (Oxford) 2002;4:145–8.
49. Paramythiotis D, Kofina K, Bangeas P, et al. Solitary fibrous tumor of the pancreas: case report and review of the literature. World J Gastrointest Surg 2016;8:461–6.
50. D'Amico FE, Ruffolo C, Romano M, et al. Rare neoplasm mimicking neuoroendocrine pancreatic tumor: a case report of solitary fibrous tumor with review of the literature. Anticancer Res 2017;37:3093–7.
51. Saif MW. Primary pancreatic lymphomas. JOP 2006;7:262–73.
52. Anand D, Lall C, Bhosale P, et al. Current update on primary pancreatic lymphoma. Abdom Radiol (NY) 2016;41:347–55.
53. Yu L, Chen Y, Xing L. Primary pancreatic lymphoma: two case reports and a literature review. Onco Targets Ther 2017;10:1687–94.
54. Sadot E, Yahalom J, Do RK, et al. Clinical features and outcome of primary pancreatic lymphoma. Ann Surg Oncol 2015;22:1176–84.

55. Kloppel G, Hruban RH, Longnecker DS, et al. Ductal adenocarcinoma of the pancreas. In: Hamilton SR, Aaltonen LA, editors. World Health Organization classification of tumours. Pathology and genetics of tumours of the digestive system. Lyon (France): International Agency for Research on Cancer; 2000. p. 221–30.
56. Serafini S, Da Dalt G, Pozza G, et al. Collision of ductal adenocarcinoma and neuroendocrine tumor of the pancreas: a case report and review of the literature. World J Surg Oncol 2017;15:93.
57. Tewari N, Zaitoun AM, Lindsay D, et al. Three cases of concomitant intraductal papillary mucinous neoplasm and pancreatic neuroendocrine tumour. JOP 2013;14:423–7.
58. Ishida M, Shiomi H, Naka S, et al. Concomitant intraductal papillary mucinous neoplasm and neuroendocrine tumor of the pancreas. Oncol Lett 2013;5:63–7.
59. Yan SX, Adair CF, Balani J, et al. Solid pseudopapillary neoplasm collides with a well-differentiated pancreatic endocrine neoplasm in an adult man: case report and review of histogenesis. Am J Clin Pathol 2015;143:283–7.
60. Jakobsen M, Kloppel G, Detlefsen S. Mixed acinar-neuroendocrine carcinoma of the pancreas: a case report and a review. Histol Histopathol 2016;31:1381–8.
61. Izumi H, Furukawa D, Yazawa N, et al. A case study of a collision tumor composed of cancers of the bile duct and pancreas. Surg Case Reps 2015;1:40.
62. Matsushita D, Kurahara H, Mataki Y, et al. Pancreatic hamartoma: a case report and literature review. BMC Gastroenterol 2016;16:3.
63. Zhang J, Wang H, Tang X, et al. Pancreatic hamartoma, a rare benign disease of the pancreas: a case report. Oncol Lett 2016;11:3925–8.
64. Kawakami F, Shimizu M, Yamaguchi H, et al. Multiple solid pancreatic hamartomas: a case report and review of the literature. World J Gastrointest Oncol 2012;4:202–6.
65. Mondal U, Henkes N, Henkes D, et al. Cavernous hemangioma of adult pancreas: a case report and literature review. World J Gastroenterol 2015;21:9793–802.
66. Kim SH, Kim JY, Choi JY, et al. Incidental detection of pancreatic hemangioma mimicking a metastatic tumor of renal cell carcinoma. Korean J Hepatobiliary Pancreat Surg 2016;20:93–6.
67. Soreide JA, Greve OJ, Gudlaugsson E. Adult pancreatic hemangioma in pregnancy–concerns and considerations of a rare case. BMC Surg 2015;15:119.
68. Figueroa RM, Lopez GJ, Servin TE, et al. Pancreatic hemolymphangioma. JOP 2014;15:399–402.
69. Chung JC, Kim HC, Chu CW, et al. Huge cystic lymphangioma of the pancreas. Can J Surg 2009;52:E303–5.
70. Assifi MM, Nguyen PD, Agrawal N, et al. Non-neoplastic epithelial cysts of the pancreas: a rare, benign entity. J Gastrointest Surg 2014;18:523–31.
71. Oh Y, Choi Y, Son SM, et al. Pancreatic lymphoepithelial cysts diagnosed with endosonography-guided fine needle aspiration. Korean J Gastroenterol 2017;69:253–8.
72. Terakawa H, Makino I, Nakagawara H, et al. Clinical and radiological feature of lymphoepithelial cyst of the pancreas. World J Gastroenterol 2014;20:17247–53.
73. Rodriguez E, Netto G, Li QK. Intrapancreatic accessory spleen: a case report and review of literature. Diagn Cytopathol 2013;41:466–9.
74. Spencer LA, Spizarny DL, Williams TR. Imaging features of intrapancreatic accessory spleen. Br J Radiol 2010;83:668–73.
75. Guo W, Han W, Liu J, et al. Intrapancreatic accessory spleen: a case report and review of the literature. World J Gastroenterol 2009;15:1141–3.

76. Miljkovic M, Senadhi V. Use of endoscopic ultrasound in diagnosing plasmacytoma of the pancreas. JOP 2012;13:26–9.
77. Williet N, Kassir R, Cuilleron M, et al. Difficult endoscopic diagnosis of a pancreatic plasmacytoma: case report and review of literature. World J Clin Oncol 2017; 8:91–5.
78. Mony S, Patil PD, English R, et al. A rare presentation of sarcoidosis as a pancreatic head mass. Case Rep Pulmonol 2017;2017:7037162.
79. Kersting S, Janot MS, Munding J, et al. Rare solid tumors of the pancreas as differential diagnosis of pancreatic adenocarcinoma. JOP 2012;13:268–77.
80. Gupta D, Patel J, Rathi C, et al. Primary pancreatic head tuberculosis: great masquerader of pancreatic adenocarcinoma. Gastroenterol Res 2015;8:193–6.
81. Kaur M, Dalal V, Bhatnagar A, et al. Pancreatic tuberculosis with markedly elevated CA 19-9 levels: a diagnostic pitfall. Oman Med J 2016;31:446–9.
82. Waintraub DJ, D'Souza LS, Madrigal E, et al. A rare case of isolated pancreatic tuberculosis. ACG Case Rep J 2016;3:e91.
83. Adler H, Redmond CE, Heneghan HM, et al. Pancreatectomy for metastatic disease: a systematic review. Eur J Surg Oncol 2014;40:379–86.
84. Konstantinidis IT, Dursun A, Zheng H, et al. Metastatic tumors in the pancreas in the modern era. J Am Coll Surg 2010;211:749–53.
85. Hung JH, Wang SE, Shyr YM, et al. Resection for secondary malignancy of the pancreas. Pancreas 2012;41:121–9.
86. De Moura DT, Chacon DA, Tanigawa R, et al. Pancreatic metastases from ocular malignant melanoma: the use of endoscopic ultrasound-guided fine-needle aspiration to establish a definitive cytologic diagnosis: a case report. J Med Case Rep 2016;10:332.
87. Goyal J, Lipson EJ, Rezaee N, et al. Surgical resection of malignant melanoma metastatic to the pancreas: case series and review of literature. J Gastrointest Cancer 2012;43:431–6.
88. Sperti C, Moletta L, Patane G. Metastatic tumors to the pancreas: the role of surgery. World J Gastrointest Oncol 2014;6:381–92.
89. Mokhtar Pour A, Masir N, Isa MR. Obstructive jaundice in small cell lung carcinoma. Malays J Pathol 2015;37:149–52.
90. Niu FY, Zhou Q, Yang JJ, et al. Distribution and prognosis of uncommon metastases from non-small cell lung cancer. BMC Cancer 2016;16:149.
91. Hiotis SP, Klimstra DS, Conlon KC, et al. Results after pancreatic resection for metastatic lesions. Ann Surg Oncol 2002;9:675–9.
92. Mourra N, Arrive L, Balladur P, et al. Isolated metastatic tumors to the pancreas: Hopital St-Antoine experience. Pancreas 2010;39:577–80.
93. Pan B, Lee Y, Rodriguez T, et al. Secondary tumors of the pancreas: a case series. Anticancer Res 2012;32:1449–52.
94. Bednar F, Scheiman JM, McKenna BJ, et al. Breast cancer metastases to the pancreas. J Gastrointest Surg 2013;17:1826–31.
95. Sperti C, Pasquali C, Berselli M, et al. Metastasis to the pancreas from colorectal cancer: is there a place for pancreatic resection? Dis Colon Rectum 2009;52: 1154–9.
96. Reddy S, Wolfgang CL. The role of surgery in the management of isolated metastases to the pancreas. Lancet Oncol 2009;10:287–93.
97. Matsubara N, Baba H, Okamoto A, et al. Rectal cancer metastasis to the head of the pancreas treated with pancreaticoduodenectomy. J Hepatobiliary Pancreat Surg 2007;14:590–4.

98. Farris AB 3rd, Basturk O, Adsay NV. Pancreatitis, other inflammatory lesions, and pancreatic pseudotumors. Surg Pathol Clin 2011;4:625–50.
99. Asbun H, Conlon K, Fernandez-Cruz L, et al, International Study Group of Pancreatic Surgery. When to perform a pancreatoduodenectomy in the absence of positive histology? A consensus statement by the International Study Group of Pancreatic Surgery. Surgery 2014;155(5):887–92.