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Rare tumors in the pancreatic region

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Abstract
Pancreatic cancer is still considered to be one of the leading causes of cancer deaths. The most common of all the different types of pancreatic cancer is ductal original malignant tumors, and their clinical features are commonly characterized. However, for the rare tumors in the pancreatic region, the clinical features often vary, and detection of the cancers are detected late. Limited data are available to guide the management of very rare neoplasms of the pancreas. Therefore, to recognize or detect the rare tumors in the pancreatic region are of importance for the clinical practice.

Keywords: Pancreatic cancer, region, rare tumors, clinical practice,

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Introduction
Limited data are available to guide the management of very rare exocrine neoplasms of the pancreas (VREP). Available evidence suggests that VREP have different risk factors and prognoses from those of adenocarcinoma of the pancreas. The primary objectives for one study were to determine the survival, comorbidities, and response to treatment of patients seen at Mayo Clinic with VREP. It was reviewed patients from 1975 to 2005 who had VREP and compared them to patients with adenocarcinomas that were matched for TNM, grade, and decade of treatment. Sixty-six patients with VREP were identified. The most commonly identified neoplasms were acinar cell carcinoma (n=15), small cell carcinoma (n=12), and squamous cell carcinoma (n=8). Abdominal discomfort and jaundice were the most common presenting symptoms. The median overall survival for patients with VREP, 10 months (range 4-23 months), was significantly better than that for matched controls, 8 months (range, 4-15 months). There was no difference in the survival of patients with stage 4 disease between cases, 8 months (range 2-22 months), and controls, 7 months (range 2-11 months) (P = 0.17). It was concluded that the overall survival of all patients with VREP was better than matched controls, but no statistical difference was seen between the groups with stage 4 disease [1].

Solid Pseudopapillary Tumors
Solid pseudopapillary tumors of the pancreas (SPT) are rare neoplasms, and the natural history is poorly defined. The aim of one study was to define the natural history and compare patient and tumor factors between patients with malignant and non-malignant disease. Data for all patients with SPT who underwent surgical exploration between 1987 and 2009 were collected and analyzed. Patient, tumor, treatment, and survival variables were examined. Malignant tumors were defined as any tumor that was locally unresectable, metastatic, or recurrent. Forty-five patients had an SPT during the study period. Median age was 38 years (10-63) and 38 (84 %) were women. At the time of diagnosis, 38 were symptomatic, with the most common symptom being abdominal pain (n=35). The most frequent imaging characteristic was a solid and cystic tumor (n=29), most commonly located in the tail of the pancreas (n=23). Resection of the primary tumor (n=41) (41/2,919 = 1.4 % of all resections) included distal pancreatectomy in 26, pancreatoduodenectomy in 11, central pancreatectomy in two, and enucleation in two. Nine patients had malignant disease defined by a locally unresectable tumor in three, liver metastases in three, locally unresectable tumor and liver metastases in one, local recurrence and liver metastases in one, and local recurrence in another. Patients with malignant disease presented with significantly larger tumors (7.8 vs. 4.2 cm). After median follow-up of 44 months, 34 patients were without evidence of disease, four

patients were alive with disease, three patients died of disease, and four patients died of other causes. These results demonstrate that SPT occurs in young women, and the majority of patients will experience long-term survival following resection. The only feature associated with malignant disease was tumor size at presentation. The majority of patients are alive at last follow-up, and a low percentage experienced disease recurrence or death from disease [2].

The aim of one study was to describe the endoscopic ultrasound (EUS) features and utility of EUS-guided fine needle aspiration (FNA) in diagnosing these tumors. A retrospective analysis of SPTs identified in a tertiary institution EUS database between 2002 and 2009 was performed. Medical records, imaging, EUS features, cytology and histology specimens were reviewed. Patients were followed up until 2009. Seven cases of SPTs were indentified out of 2400 EUS performed. All patients were females with a mean age of 41 years (range 22-69). The tumors were solitary with a mean diameter of 2.9 cm (range 2.0-4.3 cm). Five tumors were located in the body and tail of the pancreas and two in the neck. All lesions were hypoechoic, heterogenous and well circumscribed, with five having a cystic component and two having a calcified rim. FNA using a 22-gauge needle was performed in six cases with no complications. A preoperative diagnosis of SPT based on cytology was obtained in 5/6 cases (83 %). Surgical resection was done in six cases with confirmation of SPT and no metastatic disease. The authors concluded that EUS-guided FNA is a minimally invasive, safe and reliable way of diagnosing SPT by providing characteristic cytological specimens. Definitive preoperative diagnosis leads to targeted and minimally invasive surgical resection [3].

To further delineate the clinicopathological and radiological features of solid pseudopapillary tumor (SPT) of the pancreas and summarize the surgical therapy strategy for this tumor a retrospective review of 18 pathologically confirmed cases of SPT was performed and the clinical and pathological features, radiological findings and surgical interventions were analyzed. The patients included 17 females and 1 male with a median age of 23 years. The median diameter of the lesions was 8.0 cm. Abdominal pain was the predominant complaint (8/18). The rest of the patients were asymptomatic and presented with a pancreatic mass detected incidentally. Radiological study revealed a well-demarcated mass which was composed of a solid-cystic portion. On post-contrast CT, the solid portions could be enhanced whereas the cystic parts remained unenhanced. With the preoperative diagnosis of SPT in 11 patients and pancreatic cyst, benign or malignant pancreatic tumor in the rest, pancreatic tumor resection was successfully completed. Surgical exploration findings, pathological characteristics and good prognosis of the patients with SPT, indicated its low-grade malignant potential. It was concluded than in combination with clinical findings, radiological features of SPT may help to make the correct diagnosis and differentiation from other pancreatic neoplasms. Once diagnosed, given the excellent prognosis and low-grade malignancy, less aggressive surgical resection of the primary lesion is proposed [4].

Acinar Cell Adenocarcinoma

Acinar cell carcinoma (ACC) of the pancreas is very rare and usually grows expansively. Recently, a variant of ACC with predominant growth in the pancreatic ducts has been proposed, and is speculated to have potentially less aggressive behavior. The aim of one study was to investigate how the pancreatic duct system is related to the growth and extension of ACC. It was reviewed the detailed gross and histologic features of 13 cases of ACC, of which 7 (54 %) showed intraductal polypoid growth (IPG) of the tumor in the large pancreatic ducts with a mean IPG length of 25 mm. Tumors with IPG were found to spread characteristically along the pancreatic ducts as extending polypoid projections, filling the ducts and destroying the duct walls, although tumors did not tend to extend beyond the pancreatic parenchyma. Comparison of the clinicopathologic characteristics showed that ACC with IPG had less infiltrative features including lymphatic, venous, and neural invasion, formation of tumor thrombus in the portal vein, nodal metastasis, and invasion beyond the pancreas to the surrounding organs; death in only one case (14 %) of ACC with IPG was the result of ACC itself. In contrast, ACC without IPG frequently showed more infiltrative growth, and was the cause of death in 50 percent of patients with this type of tumor. Intraductal dissemination of ACC in pancreatic ducts was proven in one case of ACC with IPG. These findings suggest that a significant proportion of ACC shows IPG, which is potentially linked to less aggressive clinicopathologic characteristics [5].

Adenosquamous Carcinoma

Among exocrine pancreatic tumors, adenosquamous carcinoma (ASC) is a rare, aggressive subtype with a worse prognosis and a higher potential for metastases compared to its more conventional glandular counterpart, adenocarcinoma. The disease distribution shows an approximately 1:1 male/female ratio and a median survival of circa five months. Although such features as central necrosis and hypervascularity are suggestive of pancreatic ASC, more research is necessary to identify other, more specific markers for this tumor subtype. Humoral hypercalcemia of malignancy has also been described with ASC of the pancreas, likely as a result of PTHrP production by the squamous component of the tumor. Similar to the therapeutics of pancreatic adenocarcinoma, adjuvant chemotherapy or chemoradio-therapy is currently indicated for resectable ASC of the pancreas, while gemcitabine or gemcitabine combinations are used for a more advanced disease. Both pathologic and molecular features of pancreatic ASC characterize it as a distinct subtype of pancreatic cancer. As a result, its molecular and genetic makeup could be exploited for both diagnostic and therapeutic quests in the future [6].

Pancreatic Small Cell Carcinoma

It was presented one case of a pancreatic small-cell carcinoma presenting as acute pancreatitis [7].

Lymphoepithelial Cysts

Pancreatic lymphoepithelial cysts (LECs) are rare pancreatic cystic lesions filled with keratinized material, lined by mature, keratinizing squamous epithelium and surrounded by lymphoid tissue containing few lymphoid follicles. It was reported two cases of surgically confirmed pancreatic LECs showing a profound restriction of water molecules on diffusion-weighted (DWI) magnetic resonance imaging (MRI). For pancreatic cystic lesions showing lack of molecular motion on DWI with or without thin marginal enhancement on contrast material-enhanced imaging, LECs consisting of internally keratinized materials with restricted diffusion should be considered in differential diagnoses even though they cannot always be easy to distinguish from other focal pancreatic lesions containing mucin, blood clot, or nonliquefactive necrosis [8].

Metastases to Pancreas

It was reported an ocular melanoma metastatic to the pancreas after a 28-year disease-free interval [9].

Biliary Tract Tumors

Intraductal Tubulopapillary Neoplasm (ITPN)

Intraductal tubulopapillary neoplasm (ITPN) has been recently reported in pancreas. We experienced an unusual intraductal growing bile duct tumor, which showed the same histopathologic and immunostaining profiles as ITPN of pancreas. A 72-year-old female patient visited hospital due to intrahepatic stone. The hilar bile duct tumor was detected and incidental lung mass was found in systemic evaluation. The histopathologic finding of the two biopsy lesions was different. The lung tumor was an adenocarcinoma, and the bile duct tumor showed poorly differentiated carcinoma with eosinophilic cytoplasm. Lung lobectomy and hemihepatectomy were performed under the impression of double primary neoplasms of the lung adenocarcinoma and oncocytic variant of the biliary papillary tumor. However the histopathologic findings and immunostaining profiles of the two resected tumors were the same. Both the lung and bile duct tumors showed a tubulopapillary pattern with high-grade nuclear atypia. Pathologic findings were the same as a recently reported ITPN of the pancreas. Eosinophilic cytoplasm of the bile duct tumor was not oncocytic cytoplasm but pyknotic change due to necrosis. Here, we report the first case of ITPN of the bile duct with lung metastasis. The tumor in this case does not fit with any categories in the current biliary tumor classification. It was speculated that this may be the first case of biliary ITPN [10].

Adjuvants

To analyze the outcome of adjuvant chemo-radiotherapy for patients with distal common bile duct (CBD) cancer who underwent curative surgery, and to identify the prognostic factors for these patients 38 patients with adenocarcinoma of the distal CBD underwent curative resection followed by adjuvant chemo-radiotherapy 1991-2002. There were 27 men and 11 women, and the median age was 60 years (range, 34-73). Adjuvant radiotherapy was delivered to the tumor bed and regional lymph nodes up to 40 Gy at 2 Gy/fraction with a 2-week planned rest. Intravenous 5-fluorouracil (500 mg/m^2/day) was given on day 1 to day 3 of each split course. The median follow-up period was 39 months. The 5-year overall survival rate of all patients was 49 percent. On univariate analysis, only histologic differentiation was significantly associated with overall survival. Tumor size ($\leq$ 2 cm vs. >2 cm) had a marginally significant impact on the treatment outcome. However, there was no difference in overall survival rates between T3 and T4 tumors, for which the main determinants were pancreatic and duodenal invasion, respectively. On multivariate analysis, histologic differentiation and tumor size were independent risk factors for overall survival. It was concluded that long-term survival can be expected in patients with distal CBD cancer undergoing curative surgery and adjuvant chemo-radiotherapy. Histologic differentiation and tumor size were significant prognostic factors predicting overall survival, whereas duodenal invasion was not [11].

Palliative Chemotherapy

A British randomized study of gemcitabine plus cisplatin (GC) combination showed promising results in biliary tract cancer (BTC) patients. In a new study, it was evaluated the efficacy and safety of this combination compared with gemcitabine alone (G) in Japanese BTC patients. Overall, 84 advanced BTC patients were randomized to either cisplatin 25 mg/m^2 plus gemcitabine 1000 mg/m^2 on days 1, 8 of a 21-day cycle (GC-arm), or single-agent gemcitabine 1000 mg/m^2 on days 1, 8 and 15 of a 28-day cycle (G-arm). Treatments were repeated for at least 12 weeks until disease progression or unacceptable toxicity occurred, up to a maximum of 48 weeks. A total of 83 patients were included in the analysis. For the GC and G-arms, respectively, the 1-year survival rate was 39 versus 31 percent, median survival time 11 versus 8 months, median progression-free survival time 6 versus 4 months and overall response rate 20 versus 12 percent. The most common grade 3 or 4 toxicities (GC-arm/G-arm) were neutropenia (56 %/38 %), thrombocytopenia (39 %/7 %), leucopenia (29 %/19 %), hemoglobin decrease (37 %/17 %) and gamma-GTP increase (29 %/36 %). It was concluded that gemcitabine plus cisplatin combination therapy was found to be effective and well tolerated, suggesting that it could also be a standard regimen [12].

Duodenal Tumors

Duodenal Dystrophy

Duodenal dystrophy is a rare disease, characterized by the chronic inflammation of the aberrant pancreatic tissue in the duodenal wall. Two middle-aged men were admitted with upper abdominal pain of several months duration, periodic nausea and vomiting after meals, intermittent

jaundice and weight loss. A diagnosis of cystic dystrophy of the vertical part of the duodenum without chronic inflammation of the orthotopic pancreas was established in both cases by multi-detector computed tomography, magnetic resonance imaging and endosonography. Both patients were successfully treated by two modifications of pancreas-preserving duodenal resections with reimplantation of the bile and pancreatic ducts into the neoduodenum. These cases are a good example of a pancreas-preserving approach to duodenal dystrophy treatment and can be an alternative to the Whipple procedure in cases of mild changes of the orthotopic gland [13].

von Recklinghausen

Gastrointestinal stromal tumor is the most frequent nonepithelial tumor found in the gastrointestinal tract. One important clinical problem is that gastrointestinal stromal tumors, especially the extramural growth type, can be difficult to distinguish from other organ tumors. The case of a patient with an extramural gastrointestinal stromal tumor of the duodenum that mimicked a pancreatic head tumor has previously been reported. It was reported a rare case of a patient with a duodenal gastrointestinal stromal tumor with extramural growth that mimicked a pancreatic neuroendocrine tumor. In this case, the gastrointestinal stromal tumor was also associated with neurofibromatosis type 1 (also known as von Recklinghausen's disease). A 60-year-old Japanese woman with a history of neurofibromatosis type 1 was admitted to our hospital for the treatment of a tumor of her pancreas. She had no symptoms, but an abdominal ultrasonography screening examination had revealed a hypoechoic mass in the head of her pancreas. Laboratory data, including tumor markers, were within the normal ranges, and her insulin and glucagon levels were also within the normal ranges. However, her plasma gastrin level was elevated at 580 pg/mL (30 to 150 pg/mL). A computed tomography examination revealed a hypervascular tumor measuring 14mm in diameter in the head of her pancreas. It was diagnosed the patient as having a pancreatic neuroendocrine tumor and performed a tumor resection with a duodenal wedge resection. Microscopic analysis revealed spindle cell tumors in a trabecular pattern. The patient was finally diagnosed as having a duodenal gastrointestinal stromal tumor of the uncommitted type [14].

Brunner's Duodenal Hemartoma

To describe the computed tomographic (CT) features of Brunner's gland hamartoma with histopathologic correlation the CT images of 9 patients with pathologically proven Brunner's gland hamartoma were reviewed retrospectively. All patients underwent CT performed on multidetector-row CT scanner with various protocols, all of which included portal venous phase. Brunner's gland hamartomas presented as small (mean, 1.9 cm) Yamada type II or III (67 %, 6/9) polyps with frequent internal cyst (33 %, 3/9). They were isoattenuated on unenhanced CT (83 %, 5/6) and hypoattenuated in portal phase (56 %, 5/9) when compared with the pancreas. Peripheral rimlike enhancement in earlier phase was commonly found (6 7%, 6/9) and most of them enhanced homogeneously in the later phase (100 %, 4/4). In a patient with asymptomatic small submucosal mass in the duodenal first or second portion, hypoattenuated mass with peripheral rimlike enhancement or internal cystic change suggests the possibility of Brunner's gland hamartoma [15].

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