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Non-pancreatic cancer tumors in the pancreatic region

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Abstract
Most of tumors found in the pancreas are adenocarcinoma of the pancreas. A small number of tumors in the pancreas, such as islet cell tumors or neuroendocrine tumors, papillary cystic neoplasms, lymphoma, acinar cell tumors, metastatic tumors to the pancreas often, have a far better prognosis, and the majority of these tumors are non-malignant or benign. The author reviewed the recent literatures, and summarized where the tumor comes originally in the pancreas, what is the type of the tumor, and how to treat the tumor.

Keywords: Pancreas, adenocarcinoma, exocrine pancreatic neoplasms, metastases, non-pancreatic cancer.

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Very rare exocrine pancreatic neoplasms
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 was significantly better than that for matched controls, 8 months. There was no difference in the survival of patients with stage 4 disease between cases, 8 months and controls, 7 months [1].

Metastases to the pancreas
Tumors metastasizing to the pancreas are rare, and published series are limited by few patients treated for extended periods of time. Renal cell cancer (RCC) is the most common primary tumor metastasizing to the pancreas. Our aim was to describe the clinicopathologic characteristics and patient outcomes in a modern series of patients who underwent metastasectomy, with an emphasis on RCC. It was made a retrospective review of all pancreatic resections between 1993 and 2009. It was identified 40 patients with a median age of 62 years; 55 percent were female. Patients most commonly presented with abdominal pain (48 %). Operations performed included 10 pancreaticoduodenectomies, 1 middle, 23 distal, 3 total pancreatectomies, and 3 enucleations. Primary cancers were RCC (n=20), ovarian (n=6), sarcoma (n=3), colon (n=3), melanoma (n=2), and others (n=6). Median survival for all patients after metastasectomy was 4 years. Median survival after metastasectomy for RCC was 9 years, and the 5-year actuarial survival was 61 percent. For RCCs, pancreas was the first site of an extrarenal recurrence in 85 percent and was synchronous with the primary in 5 percent of patients. There was no survival difference if the time interval to metastasis was shorter than the median (9 years), if tumor nodules were multiple or bigger than the median (3 cm), or if the pancreas was not the first site of metastases. It was concluded than an aggressive approach to lesions metastatic to the pancreas is often warranted if the patient can be rendered free of disease. Although patients with RCC can experience long-term survival after metastasectomy, survival is less favorable for other primary tumors [2].

Cystic pancreatic lesions NUD

Overview

Cystic pancreatic lesions are often discovered incidentally as an asymptomatic finding, at a rate which is increasing considerably. In recent years the understanding of such tumors has become clearly differentiated. The spectrum of relevant lesions includes in particular the intraductal papillary mucinous neoplasm (IPMN), serous cystic neoplasm (SCN) and mucinous cystic neoplasm (MCN). With certain knowledge of their histological and radiomorphological structure as well as their distribution in terms of location, age and sex, such tumors are easy to differentiate and demarcate from common pancreatic pseudocysts. This also implies the fundamental understanding of complementary endoscopic procedures such as endosonography, which enables aspiration of the content of the cyst. A number of cystic pancreatic lesions have the potential to undergo malignant transformation along the adenoma-carcinoma sequence and therefore necessitate a differentiated approach to their radiological management. One review aimed to develop a broad understanding of the pathological and radiomorphological characteristics of cystic pancreatic lesions and provides advice regarding procedures, particularly with respect to incidentally detected lesions [3].

Radiology

To identify clinical, radiographic, and histopathologic characteristics associated with cancer in cystic pancreatic neoplasms and to evaluate the preoperative diagnostic accuracy to predict cancer in such cysts. Retrospective case series of 114 patients with cystic lesions of the pancreas underwent resection between 1992 and 2006. Eighty-nine patients (78 %) had benign or premalignant cysts; 25 patients (22 %) had malignant cysts (carcinoma in situ and/or an invasive cancer). The factors most predictive of malignancy were age, presence of symptoms, and a dilated pancreatic duct. Of the symptoms recorded, weight loss and jaundice had the strongest correlation with malignancy. It was correctly predicted the pathological diagnosis (benign vs. malignant) for only 39 (67 %) of the 58 patients where a preoperative diagnosis was clearly evident. Endoscopic ultrasound did not seem to improve our ability to preoperatively differentiate benign from malignant cysts. This series confirms that age, the presence of symptoms, and a dilated pancreatic duct on imaging are significantly associated with cancer in pancreatic cysts, and it highlights our inability to consistently make the preoperative diagnosis of cancer. Until more accurate markers of malignancy are available, an aggressive approach to management seems justified [4].

MRI versus EUS

The purpose of one study was to compare the diagnostic performance of MRI and endoscopic ultrasound (EUS) for the characterization of cystic pancreatic lesions and prediction of malignancy. Fifty patients (24 women and 26 men; average age, 57 years) underwent both MRI and EUS. All pancreatic lesions (21 cystic and 29 solid lesions) were proven by histopathologic analysis. Two radiologists retrospectively examined MR images, and a single gastroenterologist reviewed EUS images. The MRI and EUS characterizations of morphologic features of the cystic lesions and predictions of malignancy were evaluated. The prediction of malignancy was done by receiver operating characteristic (ROC) curve analysis. There was no difference between the ability of MRI and EUS to correctly classify lesions as cystic or solid (accuracy, 90-98 % vs. 88 %). There was no difference between the sensitivity of MRI and EUS for the characterization of septa (94 % for MRI vs. 79 % for EUS), mural nodule (67-58 % for MRI vs. 58 % for EUS), main pancreatic duct dilatation (93-86 % for MRI vs. 85.7% for EUS), and communication with main pancreatic duct (100% for MRI vs. 89 % for EUS). The area under ROC curve values for predicting malignancy showed no statistical significance (0.755-0.774 for MRI vs. 0.769 for EUS). It was concluded that MRI and EUS are comparable in the characterization of cystic pancreatic lesions and prediction of malignancy [5].

CEA

The objective of one study was to evaluate and validate cyst fluid carcinoembyronic antigen (CEA) and amylase in differentiating nonmucinous from mucinous pancreatic cystic lesions (PCLs), benign mucinous from malignant mucinous PCLs, and pseudocysts from nonpseudocysts (amylase only). A retrospective analysis of patients with histologically confirmed PCLs from 1996 to 2007 was performed. Cyst fluid CEA (n=124) and/or amylase (n= 91) were measured and correlated to cyst type. Carcinoembyronic antigen levels, but not amylase, were significantly higher in mucinous versus nonmucinous cysts. The sensitivity, specificity, and diagnostic accuracy of CEA 200 ng/mL or greater for the diagnosis of mucinous PCLs were 60 percent, 93 percent, and 72 percent, respectively. Carcino-embyronic antigen levels did not differentiate benign from malignant mucinous cysts. Whereas amylase levels were significantly higher in pseudocysts than nonpseudocysts, 54 percent of noninflammatory PCLs had a level greater than 250 IU/L, including mucinous cystic neoplasms (median, 6800 IU/L; interquartile range, 70Y25, 295 IU/L). Malignant mucinous cysts had significantly lower amylase levels than benign mucinous cysts. It was concluded that cyst fluid CEA and amylase levels are suggestive but not diagnostic in differentiating PCLs. Unlike CEA, amylase may help differentiate benign from malignant mucinous cysts [6].

FNA-based cytology

Preoperative diagnosis of malignancy in pancreatic cystic lesions (PCLs) remains challenging. Most non-mucinous cystic lesions (NMCLs) are benign, but mucinous cystic lesions (MCLs) are more likely to be premalignant or malignant. The aim of one study was to assess the sensitivity, specificity, and positive and negative likelihood ratios (LRs) of EUS-FNA-based cytology in differentiating MCLs from non-mucinous PCLs. It was conducted a comprehensive search of MEDLINE, SCOPUS, Cochrane, and "CINAHL Plus" databases to identify studies, in which

the results of EUS-FNA-based cytology of PCLs were compared with those of surgical biopsy or surgical excision histopathology. A DerSimonian-Laird random effect model was used to estimate the pooled sensitivity, specificity, and LRs, and a summary receiver-operating characteristic (SROC) curve was constructed. It was included 376 patients from 11 distinct studies who underwent EUS-FNA-based cytology and also had histopathological diagnosis. The pooled sensitivity and specificity in diagnosing MCLs were 0.63 (95 % confidence interval 0.56 to 0.70) and 0.88 (95 % confidence interval 0.83 to 0.93), respectively. The positive and negative LRs in diagnosing MCLs were 4.46 (95 % confidence interval 1.21 to 16.43) and 0.46 (95 % confidence interval 0.25 to 0.86), respectively. The area under the curve (AUC) was 0.89. It was concluded that EUS-FNA-based cytology has overall low sensitivity but good specificity in differentiating MCLs from NMCLs [7].

CEA and cytology

Differentiation between the various pathologies presenting as a cystic pancreatic lesion is clinically important but often challenging. It has previously been advocated the performance of endoscopic ultrasound (EUS) with aspiration and determination of mucin and carcinoembryonic antigen (CEA) content. I was reported the results of an ongoing protocol and determine the relative importance of cyst fluid mucin and CEA for the diagnostic process. The institutions prospectively maintained pancreatic cyst database was accessed to identify patients who had undergone pancreatic EUS and cyst aspiration as part of their evaluation. Only those patients who had subsequently undergone resection were selected, with histopathology being the gold standard for comparison. From 2000 to 2009, 174 patients with pancreatic cystic disease underwent surgery, 121 of whom had an EUS with aspiration attempted at our institution with specimens sent for mucin and CEA. Based on histopathology, 86 mucinous lesions were identified, including 44 cystadenomas, 34 intraductal papillary mucinous neoplasms, 7 mucinous adenocarcinomas, and 1 intraductal oncocytic papillary neoplasm; 42 were nonmucinous lesions. The median cyst CEA levels were significantly higher in the mucinous lesions group at 850 versus 2 ng/mL.

It was concluded that assessment of cyst mucin and CEA are complementary, with the best profile obtained when both markers are determined along with cytology. This combination provides a good sensitivity, PPV, and NDLR, as well as reasonable PPV and PDNR [8].

Immunohistochemistry

Serous and mucinous cystic neoplasms (SCNs/MCNs) are the most common true cystic neoplasms of the pancreas and occur more frequently in women. The aim of one study was to characterize the stroma of SCNs to compare its phenotype with that of MCNs. A total of 12 SCNs and 5 MCNs were analyzed immunohistochemically using the following antisera: progesterone receptor (PR), estrogen receptor (ER), inhibin, CD10, and vimentin. Normal pancreatic tissue (17 cases) and ductal adenocarcinomas of the pancreas (3 cases) were used as controls. Eight of 12 patients with SCNs and all 5 patients with MCNs were women. For SCNs, the stroma was sclerotic and paucicellular and showed focal moderate to strong reactivity for PR. Estrogen receptor, CD10, and inhibin were virtually negative. For MCNs, the stroma was more cellular and ovarianlike and showed a larger number of PR-positive cells with focal expression of ER and inhibin. Vimentin was expressed in all stromal cells in both groups. It was concluded that both SCNs and MCNs contain PR-positive stromal cells. In view of the aforementioned clinical and immunophenotypical similarities, it was suggested that in SCNs and MCNs, the stromal framework is similar in origin and/or differentiation [9].

Intraductal papillary mucinous neoplasm

Intraductal papillary mucinous neoplasm is characterized by cystically dilated main and/or branch pancreatic duct with mucus. According to the degree of atypia, intraductal papillary mucinous neoplasm is classified into 3 groups: adenoma, borderline, and carcinoma. Furthermore, intraductal papillary mucinous neoplasm is considered to progress through an adenoma-carcinoma sequence like colorectal carcinoma. Programmed cell death 4 is a recently identified tumor suppressor that was found to inhibit translation. Programmed cell death 4 has been reported to inhibit tumorigenesis, tumor progression, proliferation, invasion, and metastasis in several human malignancies. It was examined 108 cases of intraductal papillary mucinous neoplasm by immunohistochemistry and revealed that programmed cell death 4 expression was recognized in both the nucleus and cytoplasm in intraductal papillary mucinous neoplasm. The positive rate of programmed cell death 4 was 79 percent, 43 percent and 10 percent in adenoma, borderline, and carcinoma, respectively. The positive rate of programmed cell death 4 significantly decreased from adenoma to carcinoma, indicating that programmed cell death 4 might inhibit tumor progression in intraductal papillary mucinous neoplasm. Programmed cell death 4 expression had a strong relationship with p21 expression and an inverse correlation with Ki-67 labeling index. Thus, programmed cell death 4 might inhibit the proliferation of intraductal papillary mucinous neoplasm; and its inhibition might partly result from cell cycle arrest caused by the up-regulation of p21. In conclusion, programmed cell death 4 may inhibit tumor progression in intraductal papillary mucinous neoplasm; and the loss of programmed cell death 4 expression is representative of the malignant potential of intraductal papillary mucinous neoplasm including the proliferative activity. Therefore, programmed cell death 4 can be an important biomarker for intraductal papillary mucinous neoplasm [10].

Molecular overview

Over the last 3 decades, there have been substantial improvements in diagnostic imaging and sampling

techniques to evaluate pancreatic diseases. The modern technology has helped us to recognize premalignant conditions of pancreas including mucinous cystic neoplasms and intraductal papillary mucinous neoplasms (IPMNs). Differentiation between benign and malignant lesions and early detection of any malignant transformation in premalignant lesion are extremely important for further management decisions. Diagnostic cytology has limited sensitivity to further differentiate between benign, premalignant, and malignant lesions of the pancreas. There is limited information about the epidemiological risk factors and molecular mechanisms leading to development and further progression to malignancy of IPMNs. Several studies have shown that pancreatic juice and pancreatic tissue from the lesion can be tested for molecular markers including K-ras, p53, and p16 to differentiate between cancer and chronic inflammatory process. We review cellular signaling pathways that contribute to pathogenesis of IPMNs of the pancreas to further identify potential biomarkers and molecular targets [11].

Risk of recurrence

The risk factors correlated with the post-operative recurrence of intraductal papillary mucinous neoplasms (IPMNs) of the pancreas are not well established. The aim was to determine the risk factors of recurrence. It was reviewed retrospectively the differences of clinicopathologic features between the recurrence and nonrecurrence groups of patients with IPMN who underwent surgical resection and analyzed the recurrence-related factors. A total of 103 patients were confirmed to have IPMNs. The mean postoperative follow-up was 3.2 years, and the recurrence rate was 13 percent. Recurrent cases (n=13) had the following pathologic grades: adenoma, 1; and invasive carcinoma, 12. The mean postoperative survival was 17 months in the recurrence group and 41 months in the nonrecurrence group. The independent risk factors of recurrence were invasive carcinoma (hazard ratio = 72; 95 % confidence interval 2.13 to 2417), elevated carbohydrate antigen 19-9 (hazard ratio = 38, 95 % confidence interval 2. to 542), and main location in the pancreatic head (hazard ratio = 0.16, 95 % confidence interval 0.03 to 0.90). It was concluded that the risk factors associated with recurrence of IPMNs were invasive pathology, elevated carbohydrate antigen 19-9, and main location in the pancreatic head. A more careful follow-up is needed for such patients [12].

CD24

CD24 is a molecule involved in cell adhesion and tumor metastasis. The aims of this study were to evaluate the association between CD24 expression and the progression of intraductal papillary mucinous neoplasms of the pancreas and to investigate the association between CD24 expression in pancreatic cancer and the prognosis of patients who underwent curative pancreatectomy. Immunohistochemical analysis of CD24 was performed for 95 intraductal papillary mucinous neoplasms of the pancreas and 83 pancreatic cancers. We investigated the association between CD24 expression and the histologic grade of intraductal papillary mucinous neoplasms of the pancreas, the clinicopathologic parameters of pancreatic cancers, and the survival time of pancreatic cancer patients who underwent pancreatectomy. The positive rates of CD24 expression in intraductal papillary mucinous adenoma, borderline intraductal papillary mucinous neoplasm, noninvasive intraductal papillary mucinous carcinoma, and invasive intraductal papillary mucinous carcinoma were 5 (20 %) of 24, 12 (48 %) of 25, 10 (43 %) of 23, and 15 (65 %) of 23, respectively. The CD24-positive rates were significantly higher in borderline intraductal papillary mucinous neoplasm and intraductal papillary mucinous carcinoma compared with intraductal papillary mucinous adenoma. The staining scores, which were determined from the percentage of stained cells and the staining intensity, were significantly higher in invasive intraductal papillary mucinous carcinoma than in noninvasive intraductal papillary mucinous carcinoma. In the pancreatic cancers, higher tumor stage, nodal metastasis, and higher-grade tumors were more frequent in the CD24-positive group compared with the CD24-negative group. CD24 expression was associated with shorter survival in univariate analysis. However, based on the multivariate analysis, the CD24 expression was not associated with survival. In conclusion, CD24 is involved in the progression of intraductal papillary mucinous neoplasms of the pancreas and in the malignant behavior of pancreatic cancers [13].

Mucinous cystic neoplasms

The aim of this study was to elucidate the clinicopathologicalnfeatures and prognosis of mucinous cystic neoplasms (MCNs). It was performed a multi-institutional, retrospective study on a collected series of patients with MCN pathologically defined by ovarian-type stroma. Mucinous cystic neoplasm was confirmed in 156 cases, including 129 adenomas (82 %) and 21 noninvasive (13 %) and 6 invasive carcinomas (4 %). Patients with MCN were exclusively women (98 %) with the mean age of 48 years. All but one MCN were in the pancreatic body/tail region with a mean size of 65 mm. Communication between the cyst and the pancreatic duct was found in 18 %. The 3-, 5-, and 10-year survival rates were 98 percent, 97 percent, and 97 percent, respectively. A significant difference in the survival rates was observed between adenomas and carcinomas and between minimally invasive carcinomas and invasive carcinomas. Cyst diameter and presence of mural nodule were predictive of malignant MCN. It was concluded that mucinous cystic neoplasm is a rare but distinctive pancreatic cystic neoplasm with a favorable overall prognosis. All MCNs should be resected to prevent malignant changes but can be observed for an appropriate time when the lesion is small without the presence of mural nodules [14].

Solid pseudopapillary neoplasm

It was reported 3 cases of a hitherto undescribed ovarian tumor histologically and immunohistochemically identical

to pancreatic solid pseudopapillary neoplasms. The patients were aged 17, 21, and 57 years of age. Two tumors involved the left ovary and 1 the right ovary. They ranged from 3 to 25.5 cm and were confined to the ovary. Radiologic investigations did not show an alternative primary site. Grossly the neoplasms were solid and cystic. On microscopic examination they had mostly diffuse and pseudopapillary growth patterns. Other patterns included nested and microcystic, including cysts filled with colloid-like material. The tumor cells were monotonous and the nuclei were round to oval with pale chromatin and occasional longitudinal nuclear grooves. Clear intracytoplasmic vacuoles were noted in 2 cases, and all 3 cases showed eosinophilic globules. Mitoses and atypia were virtually absent. Immunohistochemically, all 3 neoplasms showed intranuclear positivity for β-catenin and loss of E-cadherin reactivity. All 3 tumors were negative for chromogranin, inhibin, and calretinin, although both cases evaluated for thyroglobulin were found negative. One patient has been followed for 6 years and is free of disease. The other 2 cases are recent. The tumors likely to enter into the differential diagnosis include sex-cord stromal tumors, steroid cell tumors, and struma ovarii. The morphologic and immunohistochemical similarity to pancreatic solid pseudopapillary neoplasm facilitates the accurate diagnosis of this rare ovarian neoplasm [15].

To analyze the imaging features of small (≤3 cm) solid pseudopapillary tumors (SPTs) seen at multiphasic multidetector computed tomography (CT) in comparison with those of larger SPTs. A retrospective study was approved by the institutional review board, and the requirement for informed consent was waived. CT images of 42 histopathologically proven SPTs in the pancreas were retrospectively reviewed. Two radiologists in consensus analyzed the CT findings for the shape, location, diameter, ratio of solid-to-cystic components, border and margin, enhancement pattern, and enhancement grade of the tumors, as well as the presence of calcification, dilatation of the pancreatic duct, and parenchymal atrophy. Then, according to the feature analysis results, the reviewers classified all SPTs as typical or atypical; they also subdivided all SPTs into small (≤3 cm) and large SPTs (>3 cm) depending on the tumor size. There were 20 typical SPTs and 22 atypical SPTs. Of the 22 atypical SPTs, 12 (54 %) were 3 cm or smaller in diameter and 10 (45 %) were larger than 3 cm in diameter. Small atypical SPTs usually appeared as solid tumors with a sharp margin and without accompanying pancreatic duct dilatation or parenchymal atrophy. They also showed weak enhancement during the pancreatic phase and a gradually increasing enhancement pattern. All typical SPTs were larger than 3 cm and appeared as well-defined cystic and solid masses with heterogeneous enhancement, while all large atypical SPTs appeared as calcified solid masses or large cystic masses. The imaging features of small SPTs are different from those of large SPTs, and small SPTs frequently appear as purely solid tumors with a sharp margin and gradual enhancement [16].

Acinar cell carcinoma

A 55-year-old man underwent a pylorus-preserving pancreatoduodenectomy in 2006 because of acinar cell carcinoma of the head of the pancreas. Since abdominal CT revealed multiple liver metastases, it was started systemic chemotherapy with gemcitabine (1,400 mg/body, day 1, 8, 15/q4w). At the beginning of this treatment, it seemed to be a stable disease, but CT revealed tumor progression after five months. Despite the change to oral chemotherapy with S-1 (100 mg/body, day 1-14/q3w), tumors were markedly enlarged. Therefore, we selected combination chemotherapy with oral S-1 and hepatic arterial infusion of CDDP (50 mg/body) as third-line. After 6 months of treatment, abdominal CT revealed marked shrinkage of tumors, accompanied by a decrease in AFP level. Though the patient died of hepatic failure in July 2009 (33 months after recurrence), he spent most of his time at home and worked as usual [17].

Pancreatic lymphoma

To investigate the clinical feature and treatment strategy of primary pancreatic lymphoma 39 cases of primary pancreatic lymphoma reported in China were reviewed retrospectively with their clinical characters, treatment, and outcome, as well as a literature review of worldwide reports. The major clinical presentations included discomfort or pain in the upper abdomen and jaundice without specificity. Only 2 cases were identified correctly by computed tomography, and 5 cases obtained positive finding in a biopsy before operation. Thirty-two patients accepted operation; 13 pancreatoduodenectomy and 6 distal pancreatectomy were performed. Thirty-one patients accepted postoperative chemotherapy. Until now, 26 patients are still alive at a range of 3 to 72 months; 5 patients died at 5 to 24 months after operation. The literature review revealed 85 additional cases of pancreatic lymphoma in English reports. Their diagnosis and treatment methods varied. It was concluded that primary pancreatic lymphoma was misdiagnosed as pancreatic adenocarcinoma frequently. Fine needle aspiration biopsy is the most valuable method in preoperative diagnosis. The value of surgery and radiotherapy remains controversial; an operation combining chemotherapy seems to be an appropriate method of treatment for a patient in whom malignancy cannot be ruled out [18].

Cytology

The diagnosis subtyping of lymphoma on specimens collected by endoscopic ultrasound fine-needle aspiration (EUS-FNA) can be extremely difficult. When a cytopathologist is available for the on-site evaluation, the diagnosis may be achieved by applying flow cytometric techniques. We describe our experience with immunocytochemistry (ICC) and molecular biology studies applied on EUS-FNA specimens processed with a liquid-based cytologic (LBC) preparation for the diagnosis of primary pancreatic lymphoma (PPL). Three patients with a pancreatic mass underwent EUS-FNA. The collected specimens were processed with the ThinPrep method for

the cytologic diagnosis and eventual additional investigations. A morphologic picture consistent with PPL was found on the LBC specimens of the 3 patients. Subsequent ICC and molecular biology studies for immunoglobulin heavy chain gene rearrangement established the diagnosis of pancreatic large B-cell non-Hodgkin lymphoma in 2 patients and a non-Hodgkin lymphoma with plasmoblastic/immunoblastic differentiation in the remaining one. It was concluded that an LBC preparation can be used to diagnose and subtype PPL by applying ICC and molecular biology techniques to specimens collected with EUS-FNA. This method can be an additional processing method for EUS-FNA specimens in centers where on-site cytopathologist expertise is not available [19].

Primary pancreatic leiomyosarcomas

Primary pancreatic leiomyosarcomas are rare lesions and not well described, yet they are the most common primary pancreatic sarcoma. English-language medical literature reports 29 cases as single cases or small series. A systematized nomenclature of medicine (SNOMED) search of Mayo Clinic surgical pathology files from 1994 to 2006 identified 22 primary pancreatic leiomyosarcomas. Nine patients with pancreatic leiomyosarcoma were diagnosed and treated at our institution (5 males and 4 females; mean age at diagnosis, 63 y; range, 39 to 87 y) are described, with a literature review. In situ hybridization for Epstein-Barr virus (EBV)-encoded RNA (EBER) was conducted in all cases to exclude EBV-associated smooth muscle tumor (EBV-SMT). Seven of the 9 patients presented with abdominal pain, weight loss, and jaundice. Seven tumors (mean, 10.7 cm; range, 1.0 to 30 cm) were located in the pancreatic head and 2 in the tail. Histologic findings of primary pancreatic leiomyosarcomas (7 spindle and 2 epithelioid) were similar to leiomyosarcomas of other sites. All tumors stained positive for smooth muscle actin and desmin and negative for KIT. No case showed EBER positivity. Pancreaticoduodenectomy was done in 4 patients; 3 patients had palliative procedures, and 2 had biopsy only. No lymph node metastasis was identified in 4 resected tumors, but liver metastases were present in 4 patients. All patients died; 5 deaths were known to be disease related (overall mean survival, 31 months; range, 5 to 98 mo). Historical cases showed similar clinicopathologic findings. These pancreatic leiomyosarcoma lesions have the same morphologic features as their counterparts of other sites. EBER testing should be conducted – especially for pediatric patients – to rule out EBV-SMT. The tumor is likely to metastasize to liver but not regional lymph nodes. Extensive surgical resection should be advocated, even when morphologic results show a low-grade lesion [20].

Multiple myeloma

A pancreatic head mass of unusual etiology was discussed: multiple myeloma diagnosed by endoscopic ultrasound-guided fine needle aspiration [21].

Burkitt lymphoma

A 10-year-old boy was referred to our clinic for tonsillectomy and was found to have a large mass within his oropharynx. Intraoperative biopsies confirmed Burkitt lymphoma. Further imaging and biopsy revealed pancreatic involvement. He was treated with multiagent chemotherapy. He remains disease-free 6 years later. Review of the literature demonstrates other cases of non-Hodgkin lymphoma with pancreatic involvement with good outcomes. Pancreatic involvement is a relatively rare occurrence in childhood lymphoma [22].

Tumor of the papilla of Vater

There has been no uniform terminology for systematic analysis of mass-forming preinvasive neoplasms (which usually are termed tumoral intraepithelial neoplasia) that occur specifically within the ampulla. It was now provided a detailed analysis of these neoplasms, which was proposed to be referred to as intra-ampullary papillary-tubular neoplasm (IAPN). Three hundred and seventeen glandular neoplasms involving the ampulla were identified through a review of 1469 pancreatoduodenectomies and 11 ampullectomies. Eighty-two neoplasms characterized by substantial preinvasive exophytic component that grew almost exclusively (>75 %) within the ampulla (in the ampullary channel or intra-ampullary portions of the very distal segments of the common bile duct or pancreatic duct) were analyzed. The mean age was 64 years, male/female ratio was 2.4, and mean tumor size was 2.7 cm. The tumors had a mixture of both papillary and tubular growth (each constituting at least 25 % of the lesion) in 57 percent; predominantly (>75 %) papillary in 23percent, and predominantly (>75 %) tubular in 20 percent. High-grade dysplasia was present in 94 percent of cases, of which 39 percent showed focal (<25 % of the lesion), 28 percent showed substantial (25 % to 75 %), and 27 percent showed extensive (>75 %) high-grade dysplasia. In terms of cell-lineage morphology, 45 percent had a mixture of patterns. However, when evaluated with a forced-binary approach as intestinal versus gastric/pancreatobiliary based on the predominant pattern, 74 percent were classified as intestinal and 26 percent as gastric/pancreatobiliary. Percent sensitivity/specificity of cell-lineage markers were, for intestinal phenotype: MUC2 85/78 and CDX2 94/61; and for gastric/biliarypancreatic: MUC1 89/79, MUC5AC 95/69, and MUC6 83/76, respectively. Cytokeratin 7 and 20 were coexpressed in more than half. In 64 cases (78 %), there was an associated invasive carcinoma. Size of the tumor and amount of dysplasia correlated with the incidence of invasion. Invasive carcinoma was of intestinal-type in 58 percent and of pancreatobiliary-type in 42 percent. Cell lineage in the invasive component was the same as that of the preinvasive component in 84 percent. All discrepant cases were pancreatobiliary-type invasions, which occurred in intestinal-type preinvasive lesions. The overall survival of invasive cases were significantly worse than that of noninvasive ones (57 % vs. 93 %); and 3 years,

69 percent versus 100 percent; and 5 years, 45 percent versus 100 percent, respectively. When compared with 166 conventional invasive carcinomas of the ampullary region, invasive IAPNs had significantly better prognosis with a mean survival of 51 versus 31 months and the 3-year survival of 69 percent versus 44 percent. It was concluded that tumoral intraepithelial neoplasia occurring within the ampulla are highly analogous to pancreatic or biliary intraductal papillary and tubular neoplasms as evidenced by their papillary and/or tubular growth, variable cell lineage, and spectrum of dysplastic change (adenoma-carcinoma sequence), and thus it was proposed to refer to these as IAPN. IAPNs are biologically indolent; noninvasive examples show an excellent prognosis, whereas those with invasion exhibit a malignant but nevertheless significantly better prognosis than typical invasive ampullary carcinomas unaccompanied by IAPNs. Twenty eight percent (64 of 230) of invasive carcinomas within the ampulla arise in association with IAPNs [23].

To define the differential imaging features of pancreatobiliary- and intestinal-type ampullary carcinomas at magnetic resonance (MR) imaging and to correlate these features with pathologic findings 50 patients with surgically confirmed ampullary carcinoma and preoperative MR results were studied. Two radiologists, blinded to histologic type of cancer, evaluated imaging findings in consensus. Univariate and multiple logistic regression analysis were performed to define imaging findings that were useful for differentiation of the two types of carcinomas. On the basis of hematoxylin-eosin and immunohistochemical staining, 35 patients were classified as having pancreatobiliary type; and 15 patients, intestinal type. At MR, all of 15 intestinal carcinomas were nodular, whereas 16 (46 %) of 35 pancreatobiliary carcinomas were infiltrative. Intestinal carcinomas were isointense (13 [87 %] of 15) to hyperintense (two [13 %] of 15), whereas 34 percent (12 of 35) of pancreatobiliary carcinomas manifested as hypointense compared with the duodenum on T2-weighted MR images, which was a significant difference. Intestinal carcinoma commonly manifested with an oval filling defect at the distal end of the bile duct on MR cholangiopancreatographic (MRCP) images (11 [73 %] of 15 vs. four [11 %] of 35 in pancreatobiliary type). At endoscopy, intestinal carcinoma manifested with an extramural protruding mass (n = 15, 100 %) with a papillary surface (n=11, 73 %), whereas pancreatobiliary carcinoma manifested with intramural protruding (n=5, 28 %) or ulcerating (n=1, 6 %) gross morphologic features with a nonpapillary surface (n=17, 94 %). Multiple logistic regression analysis showed that an oval filling defect at the distal end of the bile duct was the only independent finding for differentiating intestinal from pancreatobiliary carcinoma. An oval filling defect at the distal end of the bile duct on MRCP images and an extramural protruding appearance with a papillary surface at endoscopy are likely to suggest intestinal ampullary carcinoma [24].

Retroperitoneal fibrosis

It was reported one of few cases of idiopathic retroperitoneal fibrosis of the pancreas, which is different from the classical retroperitoneal fibrosis that affects ureters and vessels that mimicking locally advanced pancreatic carcinoma at presentation [25].

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