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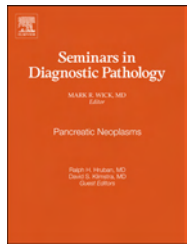

Non-neoplastic pancreatic lesions that may mimic malignancy

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ABSTRACT

The widespread use of abdominal ultrasound (US), computed tomography (CT), and magnetic resonance imaging (MRI) has resulted in an increased identification of asymptomatic pancreatic lesions. Preoperative diagnoses of pancreatic lesions can be difficult. Solid and cystic lesions and anatomic variants of normal can all mimic tumor clinically and radiologically. Newer imaging modalities have increased the likelihood of the accurate diagnosis of non-neoplastic pancreatic disease, however, despite the many advances; it still remains a challenge to differentiate rarer non-neoplastic entities and inflammatory masses from adenocarcinoma, preoperatively. Adding to the challenge is the fact that a variety of inflammatory, solid and cystic non-neoplastic lesions have significant clinical and radiological overlap with malignancies. About 5-10% of pancreatectomies performed with the primary clinical diagnosis of pancreatic carcinoma are later proved to be essentially non-neoplastic lesions. It is vital to include these non-neoplastic entities in the differential diagnosis while working up abnormal clinical and radiological pancreatic findings because it may drastically alter therapeutic options for the patients. The significance of recognizing these lesions preoperatively is to help to guide the clinical decision-making process and the avoidance of an unnecessary pancreatectomy. Examples of such entities include chronic pancreatitis, sarcoidosis, intrapancreatic accessory spleen (IPAS), lymphoid hyperplasia, lipomatous pseudohypertrophy (LPH), lymphangioma, lymphoepithelial cyst (LEC) and endometriosis.

Introduction

The widespread use of abdominal ultrasound (US), computed tomography (CT), and magnetic resonance imaging (MRI) has resulted in an increased identification of asymptomatic pancreatic lesions, the so-called "incidentalomas."[1] Preoperative diagnoses of pancreatic lesions can be difficult. Solid and cystic lesions and anatomic variants of normal can all mimic tumor clinically and radiologically.[2] The addition of fine needle aspiration to endoscopic ultrasound (EUS-FNA) has become a mainstay in the diagnosis of pancreatic lesions, improving our ability to diagnose many lesions; however, due to contamination by gastrointestinal mucosa and a sensitivity and specificity less than 100%, not all lesions can be specifically characterized. Cystic pancreatic lesions are particularly challenging and most cystic pancreatic neoplasms are identified within the pancreatic tail.[3] The increased knowledge of the malignant potential of mucinous cystic pancreatic lesions has made surgery relevant when a cystic pancreatic lesion is identified.[1] Moreover, pancreatic carcinoma identified at an early stage and removed has a significantly improved prognosis, hence the inclination to act

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on these findings.[1] About 5–10% of pancreatectomies performed with the primary clinical diagnosis of pancreatic carcinoma are later proved to be "pseudotumors," essentially non-neoplastic space-occupying lesions.[2,4] This percentage is decreasing with improved radiologic and endoscopic sampling diagnostic capabilities, however, there are a variety of solid and cystic non-neoplastic lesions that have significant clinical and radiological overlap with malignancies and are discussed below.

Inflammatory lesions

Chronic pancreatitis

Chronic pancreatitis of any type can cause scarring of the pancreas and resemble malignancy. The two types of chronic pancreatitis notorious for causing mass-like lesions, which are difficult to distinguish from carcinoma are autoimmune pancreatitis (AIP) and paraduodenal pancreatitis.[2,5]

Autoimmune pancreatitis (AIP)

AIP has been referred to as lymphoplasmacytic sclerosing pancreatitis, non-alcoholic duct-centric or duct-destructive chronic pancreatitis, sclerosing pancreatitis, and primary sclerosing cholangitis of the pancreas.[2,5,6] AIP typically results in a mass or "pseudotumor" focused within the head of the pancreas.[2,5,6] Less commonly, AIP causes a lesion in the body or tail of the pancreas or creates a diffuse, firm enlargement of the pancreas, which would lack a discrete mass.[2,5,6] The duct-centric nature and associated sclerosis of AIP can cause segmental duct stenosis of the main pancreatic and extrapancreatic ducts seen by endoscopic retrograde cholangiopancreatogram (ERCP) and often results in patients presenting with jaundice.[2,5,6] All of these characteristics cause a substantial amount of AIP cases to be diagnosed clinically as pancreatic cancer.[2,5,6] There are two types of AIP—type 1 and type 2.[7] The age range is from the fourth through sixth decades, with type 1 more frequently seen later.[2,5] Type 1 AIP, the classic lymphoplasmacytic sclerosing pancreatitis (LPSP),[7] which ironically, given the postulated autoimmune basis for the etiology, affects males slightly more frequently (M:F = 2:1).[2,5] Type 2 AIP, the idiopathic duct-centric chronic pancreatitis (IDCP) or AIP with granulocytic or prominent neutrophilic epithelial lesions/ductitis[7] tends to affect younger patients in their mid-40s, with no gender predilection.[2,5,6]

An elevated serum IgG4 level can be helpful to distinguish AIP from ductal adenocarcinoma.[2,5,6] Unfortunately, not all patients, with AIP and a mass-forming lesion, have elevated levels of IgG4.[5,6] The IgG4 levels typically range from 136 to 1150 mg/dl (average 600 mg/dl).[5] The IgG4 level has been shown to correlate with disease activity.[6] Identifying this preoperatively can help avoid an unnecessary pancreatectomy.[2,5,6] Other laboratory values that may be abnormal are increased levels of pancreatic enzymes, hypergammaglobulinemia, autoantibodies such as antinuclear antibody (ANA), rheumatoid factor (RF), and others.[6] Another clinical hint is that approximately one-fourth of AIP cases have been shown to be associated with autoimmune and idiopathic inflammatory diseases, such as Sjogren's syndrome, primary sclerosis cholangitis, primary biliary sclerosis, diabetes mellitus (DM), ulcerative colitis (UC), Crohn's disease (CD), and systemic lupus erythematous (SLE).[2,5,6] Even more cases are associated with autoimmune diseases than initially thought, with additional diagnoses identified after the fact during follow-up.[2,5,6] This realization has contributed to the theorized autoimmune explanation for the pathogenesis of AIP, with a subset of AIP cases thought to be caused by autoantibodies directed against pancreatic secretory trypsin inhibitor (PSTI).[6] There is still a significant portion of patients who lack the clinical and serologic stigmata of autoimmune disorders that are affected by AIP.[5]

Recent studies have demonstrated that AIP may be an isolated primary or systemic process, which involves multiple organs potentially linked to sclerosing pancreatitis, cholangitis, sialadenitis, retroperitoneal fibrosis, interstitial nephritis, hepatic inflammatory pseudotumor, and lymphadenopathy.[2,5,6] The pancreatectomy may show a solid, sclerotic tumor-like appearance of the pancreatic parenchyma that appears as a homogenous, milky-white smooth-cut surface versus adenocarcinoma that has been described as gray-green, irregular, and gritty.[5,6] Microscopically, the morphologic hallmarks of classic type 1 AIP are plasma cells and sclerosis,[5] with at least a moderate periductal infiltration of lymphocytes and IgG4-positive plasma cells, a venulitis, and diffuse sclerosis in the advanced stages seen (Fig. 1).[2,5,6] The presence of more than 20 IgG4-positive plasma cells per high power field around ductal areas has been thought to be highly specific for type 1 AIP (Fig. 1).[6] The infiltrate may also have neutrophils,[2] eosinophils, and macrophages.[6] Lymphocytes are predominantly T cells and if germinal centers are present, consist of B cells.[5,6] The plasma cells show a polyclonal pattern, expressing kappa and lambda light chains.[6] The medium-sized to large-sized interlobular ducts are typically affected, resulting in the aforementioned stenosis of the lumens.[2,5,6] The more advanced cases of type 1 AIP may affect the smaller ducts and have more sclerosis or fibrosis.[5,6] The venulitis is seen in 90% of type 1 AIP cases and usually affects small- to medium-sized veins (Fig. 1).[2,5,6] In type 2 AIP, focal invasion and destruction of ductal epithelium by neutrophils and occasionally eosinophils, the so-called "granulocytic epithelial lesions" (GEL), are seen.[6,7] The GELs affect small- and medium-sized ducts and often cause destruction and obliteration of the duct lumen. The number of GELs and their severity varies from case to case.[6]

The clinical, radiologic, and pathologic features of AIP often mimic pancreatic adenocarcinoma, e.g., stenosis of the bile duct, elevated serum levels of carcinoembryonic antigen (CEA), and carbohydrate antigens (CA) 19-9 and DUPAN II. The significance of recognizing AIP preoperatively is the avoidance of an unnecessary pancreatectomy and recognizing an entity that has been documented to improve and regain endocrine and exocrine function spontaneously after biliary drainage and steroid therapy.[6] The long-term prognosis for AIP is thought to be better than non-immune chronic pancreatitis.[6]The recurrence rate is 17% (range: 6–26%).[6]

Paraduodenal pancreatitis or groove pancreatitis

All of the following terminologies are used to denote groove pancreatitis: paraduodenal pancreatitis, cystic dystrophy of