Review

Solid Pancreatic Masses: Not Always Adenocarcinoma

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Primary pancreatic lymphoma (PPL) is a rare disease that comprises 0.5% of pancreatic neoplasms. It is difficult to differentiate PPL from pancreatic adenocarcinoma (PC). As both conditions have similar clinical presentations and radiologic findings, PPL is frequently misdiagnosed as PC. As PPL is associated with a better prognosis than PC, a timely diagnosis may obviate the need for aggressive surgery (with attendant high morbidity) and may lead to early initiation of targeted therapy.

Wallace and colleagues present a typical case of PPL and provide a review of lymphoma diagnosis and management.[1] This case report describes an elderly woman who presented with abdominal pain, jaundice, and weight loss. A computed tomography (CT) scan revealed a pancreatic head mass with intrahepatic and extrahepatic biliary tree dilation. With this classic presentation, there is no doubt that PC must be one of the top differential diagnoses. However, 10% of solid pancreatic neoplasms are not PC. Other differential diagnoses to consider include pancreatic neuroendocrine tumor (PNET), autoimmune pancreatitis (AIP), metastasis from other primary sites, and rare diseases such as pancreatic tuberculosis or pancreatic sarcoidosis. All of these pathologies can masquerade as PC. The typical morphologic appearance of PNET includes well-circumscribed lesions that do not classically cause obstructive jaundice unless they coexist with hepatic metastasis. Functional PNETs may present with a variety of symptoms. A diagnosis of AIP is supported by elevated levels of immunoglobulin G4 in addition to CT findings of diffuse or focal pancreatic enlargement with or without a peripheral gland "halo."[2] Isolated metastatic disease to the pancreas can be seen in a variety of cancers, most commonly in melanoma, renal cell, lung, colon, gastric, breast, and ovarian cancers and rarely in prostate cancer.[3,4]

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In the case report by Wallace and coworkers, prior brushings obtained by endoscopic retrograde cholangiopancreatography (ERCP) and CT-guided biopsies yielded inconclusive findings.[1] Subsequently, fine-needle aspiration (FNA) obtained by endoscopic ultrasound (EUS) as well as analysis of flow cytometry confirmed a B-cell lymphoma. The patient responded well to chemotherapy. An unnecessary major surgical intervention with potential morbidity and/or mortality was avoided.

Diagnosis

Diagnosing PPL remains challenging. This condition must be differentiated from PC as well as from secondary involvement of the pancreas by non-Hodgkin lymphoma. Laboratory tests are nonspecific for the diagnosis of PPL. The most commonly used diagnostic investigations in a symptomatic patient include CT scans and/or magnetic resonance imaging scans. Radiologic studies alone are usually not sufficient for definitively differentiating between PPL and PC. One finding not reported by Wallace and colleagues is the caliber of the pancreatic duct.[1] A large symptomatic pancreatic head mass in the absence of pancreatic duct dilation makes a diagnosis of PC uncertain.[5] Calcifications have not been reported in PPL patients. Diffuse intra-abdominal lymphadenopathy is not commonly a feature of PC. It is also important to note that lymph node metastases from PC generally occur proximal to the level of the renal vein.[6] Therefore, lymph node involvement below the renal veins argues against a diagnosis of PC. ERCP findings in PPL patients may show a spectrum of changes, ranging from a completely normal duct to evidence of strictures without any significant distal dilation. Criteria established by Behrns and associates can help to differentiate PPL from secondary involvement of the pancreas.[7] These criteria include a lymphoma localized to the pancreas with lymph nodes confined to the peripancreatic region, the absence of mediastinal nodal enlargement, no hepatic or splenic involvement, and a normal white blood cell count.

The Role of Endoscopic Ultrasound

Flamenbaum and colleagues reported that EUS findings of PPL patients include a hypoechoic pancreas with a hyperechoic pancreatic duct wall and isoechoic peripancreatic lymph nodes.[8] Although endosonographic features may provide some clues for diagnosing PPL patients, it is imperative to obtain cytopathologic analysis for diagnosis and classification. Tissue may be obtained by CT guidance, EUS-guided FNA, or open biopsy. EUS-guided FNA of pancreatic masses is a safe, accurate, and preferred method because it is dynamic and performed in real time.[9]

O'Toole and associates reported EUS-FNA complication rates of 0% for solid pancreatic lesions and 1.2% for cystic pancreatic lesions.[10] The high sensitivity and specificity of EUS-FNA for PC has been demonstrated in earlier studies.[11-13] If FNA is not diagnostic, then an EUS-guided Tru-Cut biopsy may be useful as a rescue intervention.[14] When used in combination with additional studies such as flow cytometry, tissue sampling is very sensitive for establishing a diagnosis of PPL.[15,16]

Treatment Options

There is still some controversy regarding the treatment of PPL. The study of PPL treatment has been limited by the rarity of the condition and, therefore, a lack of randomized trials and large case series. Chemotherapy is generally accepted as the mainstay of treatment for non-Hodgkin lymphoma patients. The majority of PPL cases are of diffuse large B-cell lineage. The most common chemotherapeutic regimen consists of cyclophosphamide, doxorubicin, vincristine, and prednisone. With this regimen, complete remission has been achieved in a majority of patients. More recently, the addition of rituximab (Rituxan, Genentech) to the regimen has been shown to further improve the response rates of patients with diffuse large B-cell lymphoma.[17] New targeted radioimmunotherapy with 131-I-tositumomab (Bexxar, GlaxoSmithKline) is being used for refractory non-Hodgkin lymphoma.[18,19]

The role of surgery is limited in the management of PPL patients because of the high morbidity and mortality rates associated with traditional pancreatic resections. Surgery is difficult in the setting of PPL because these tumors are generally bulky and are often associated with an otherwise histologically normal pancreas, which carries a high risk of postoperative pancreatic fistulae. However, a few reports have been published on the potential benefits of surgery in patients with PPL. Koniaris and associates reviewed 122 cases of PPL and reported that 58 cases were treated medically (with a 46% cure rate) and 15 patients underwent surgical resection of localized disease (with a 94% cure rate).[20] The researchers argued that technical improvements in pancreatic surgery can lead to reduced perioperative morbidity and mortality and that pancreatectomy should therefore be re-evaluated as a treatment method. Battula and colleagues reported that the 5-year survival rate of PPL patients treated with the current chemotherapy regimens was less than 50%, which was inferior to the rate associated with a combination of surgical intervention and chemotherapy; therefore, the researchers concluded that pancreaticoduodenectomy may have a therapeutic role in association with chemotherapy.[21] However, with recent increases in chemotherapy efficacy, the potential benefit of surgical treatment for PPL patients remains questionable.

The case report by Wallace and coworkers highlights the differential for solid pancreatic lesions and the importance of careful consideration, which may reveal an alternative diagnosis that may obviate the need for invasive surgical intervention.[1]

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