

REVIEW

Use of Endoscopic Ultrasound in Diagnosing Plasmacytoma of the Pancreas

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ABSTRACT

Context An extramedullary plasmacytoma is a discrete collection of monoclonal plasmocytes arising in tissues other than the bone. Gastrointestinal involvement has been reported in approximately 10% of cases and usually involves the liver; however, there have been a number of cases involving the pancreas. **Discussion** Although helical CT can be used to diagnose pancreatic plasmacytomas based on a typical radiological appearance, there are a number of pitfalls with CT including similar radiologic appearances of other pancreatic tumors, malignant seeding induced by CT biopsy, and creation of multiple secondary plasmacytomas precipitated by CT biopsy. Tissue diagnosis is critical to management in pancreatic lesions as the decision to pursue surgery (pancreatic adenocarcinoma) versus chemotherapy (lymphoma) or radiation (extramedullary plasmacytoma) is dependent on a correct tissue diagnosis. Tissue diagnosis can change morbidity and mortality with respect to specific treatment of pancreatic lesions in the milieu of pancreatic tumor variance. In the confirmed tissue diagnosis of pancreatic plasmacytoma, radiation and chemotherapy can be preferentially chosen over high risk surgery. EUS-FNA has a lower risk of malignant seeding, complications, and a high sensitivity in the diagnosis of pancreatic plasmacytomas, especially with an increased number of passes and bedside cytopathologists. **Conclusion** It is important for physicians to have a high index of suspicion for diagnosing pancreatic plasmacytomas in the appropriate clinical setting (i.e., a previously diagnosed multiple myeloma, extramedullary plasmacytoma or any other plasma cell neoplasm). EUS-FNA is now an indispensable imaging modality to achieve the diagnosis of pancreatic extramedullary plasmacytomas with an inherently lower rate of complications, and should be the first choice for tissue evaluation.

INTRODUCTION

Plasma cell neoplasms are clonal diseases of terminally differentiated B-cells (monoclonal immunoglobulin-secreting plasmocytes) that exist on a spectrum from the asymptomatic monoclonal gammopathy of undetermined significance (MGUS) to full-blown plasma cell neoplasms, or multiple myeloma [1].

Extramedullary plasmacytoma, one of the diseases on this spectrum, is a discrete collection of monoclonal plasmocytes arising in tissues other than the bone. Extramedullary plasmacytomas (i.e., extraskeletal plasmacytomas) are uncommon plasma cell tumors that represent 3-4% of all plasma cell neoplasms [2]. They occur most commonly in the sixth and seventh decades

of life and have a male predominance with a 3-5 times likelihood than females [2]. Extramedullary plasmacytomas can occur either as an uncommon manifestation of multiple myeloma, in approximately 4-7% of patients [3, 4], or as an even less common primary lesion. The latter has no systemic manifestations and a high propensity for involvement of the upper respiratory tract, but can also occur in other sites and systems, including the gastrointestinal tract [5]. The predominance of plasmacytomas in the head and neck is related to the pathophysiology of plasmacytomas. There is a predominance of lymph nodes and the reticuloendothelial system in the head and neck, which explains the increased incidence in this region [2]. Gastrointestinal involvement has been reported in approximately 10% of cases and usually involves the liver [6]. The pancreas, on the other hand, is rarely involved and the diagnosis is often made postmortem with an incidence rate of 2.3% based on autopsy studies [7]. The most common presenting symptoms of extramedullary plasmacytomas of the pancreas are abdominal pain and obstructive jaundice [8]. The objective of this review is to explicate the various diagnostic modalities for pancreatic plasma-

Received November 23rd, 2011 - Accepted December 1st, 2011

Key words Diagnosis; Endosonography; Multiple Myeloma; Pancreas; Plasmacytoma; Tomography

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cytomas and elaborate the role of endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) diagnosis of pancreatic plasmacytomas in comparison to other diagnostic strategies.

COMPUTED TOMOGRAPHY (CT)

Extramedullary plasmacytomas of the pancreas, both primary and secondary, are exceedingly rare, with only 50 cases reported to date [9]. In the first published case of a pancreatic plasmacytoma in a patient with no known history of multiple myeloma, a laparotomy had to be performed to make the diagnosis of what is now called secondary extramedullary plasmacytoma [10]. Since then, high-resolution dual-phase (arterial and portal) contrast-enhanced computed tomography (CT) has become the primary modality for discovering and evaluating pancreatic malignancies, mainly due to its non-invasiveness and relative ease. However, due to the anatomical position of the pancreas, laparotomy has frequently been performed for biopsy and final diagnosis [11] despite CT evaluation. Furthermore, seeding of malignant cells through the track of percutaneous needle insertion and the creation of multiple secondary extramedullary plasmacytomas has been reported in patients with multiple myeloma [12]. A similar event happening during a CT-guided biopsy of a suspected pancreatic extramedullary plasmacytoma is a distinct possibility, particularly considering the track length necessary to reach the retroperitoneum. Despite the aforementioned, helical CT is still the first imaging choice in patients with any suspected pancreatic tumor. However, there are some more pitfalls with the use of CT in addition to the risks of CT-guided biopsy. Although the CT appearance of pancreatic plasmacytoma is well established and is typically described as a multilobular homogenous solid tumor that is hypodense as compared to the pancreatic parenchyma, these CT features are not specific. Despite the well defined characteristics, these findings still resemble typical findings in other pancreatic neoplasms, including carcinoma, islet cell tumors, lymphoma, and metastases, which have very different management algorithms. Thus, tissue diagnosis is critical to management in these lesions as the decision to pursue surgery (pancreatic adenocarcinoma) versus chemotherapy (lymphoma) or radiation (extramedullary plasmacytoma) is dependent on a correct tissue diagnosis. Tissue diagnosis can change morbidity and mortality with respect to specific treatment of pancreatic lesions in the milieu of pancreatic tumor variance [13]. In confirmed tissue diagnosis of pancreatic plasmacytoma, radiation and chemotherapy can be preferentially chosen over high risk surgery [14]. The advent of interventional endoscopic ultrasound, i.e., endoscopic ultrasound-guided fine needle aspiration (EUS-FNA), has made it possible to approach the sensitivity of a high-resolution helical CT, while at the same time, improving specificity and reducing the risk of malignant seeding.

ENDOSONOGRAPHY

Endoscopic ultrasonography or endosonography (EUS) is a combination of endoscopy and intraluminal ultrasonography. Due to the short imaging distance between the high-frequency 5-20 MHz transducer and the target lesion, it is now a widely accepted modality for diagnosing gastrointestinal and pancreatobiliary diseases. Since 1992 and the publication of the first report of EUS-FNA of a pancreatic lesion [15], the field of interventional EUS has expanded to include various types of lesions at different anatomical sites. The advent of EUS-guided fine needle injection has provided some opportunity for uses in various treatment modalities. Interventional EUS techniques now include EUS-FNA, intratumoral drug delivery of chemotherapeutic agents, biliary drainage and anastomosis, celiac neurolysis, and brachytherapy [16].

Indications, Contraindications and Complications

EUS enables the feasibility of inserting a biopsy needle into lesions too small to be identified by CT or abdominal ultrasound, or that are too close to vascular structures to allow a percutaneous biopsy. Even then, the information obtained should have the potential to affect patient management, and EUS-FNA should not be utilized if alteration of patient management scenarios is not implicit [17]. The procedure is contraindicated if its risks outweigh the benefits of the information that could possibly be obtained. This includes lesions that cannot be clearly visualized by EUS, a tumor mass or vessel existing in the needle path and the presence of bleeding diathesis [17]. The procedure increases this risk of acute pancreatitis and tumor seeding, which are the two major complications. However, in comparison to percutaneous biopsy guided by CT or transabdominal ultrasound, the risk of seeding was shown to be low (16.3 vs. 2.2%) [18]. Of note, while a case of an intraductal papillary mucinous tumor being disseminated during the procedure does exist [19], any seeding of a pancreatic extramedullary plasmacytoma during EUS-FNA is yet to be reported. Severe complications do occur, and include uncontrolled bleeding due to pancreatic pseudoaneurysm rupture [20] and acute portal vein obstruction [21]. It is important to remember, therefore, that even though the complication rate is approximately 2%, the mortality of EUS-FNA is not completely nonexistent [22].

Technique

Three main areas of concern when performing EUS-FNA of a pancreatic lesion are needle size and type, number of passes necessary to obtain adequate sample size, and the presence of an on-site pathologist. Several studies compared the performance of 19, 22 and 25 G Trucut needles, with 19 G needles having the highest diagnostic yield, but with very low success rate for head and uncinata lesions; 25 G needles not providing

good specimens for histological evaluation but being advantageous in uncinate lesions; and 22 G lesions lying somewhere in-between, with sample quality worse than that of 25 G needles, but performing well in all lesion sites [22].

In general, four to six passes are recommended, with more passes giving a better yield, but in theory increasing the rate of complications [23]. On-site histopathological evaluation decreases the necessary number of passes and overall procedure time, while increasing the rate of definitive cytological diagnosis [24, 25]. However, more recent studies have shown that the absence of on-site cytopathology does not significantly alter diagnostic accuracy in a high-volume practice with a dedicated endosonographer [26].

Diagnosis

For diagnosing pancreatic solid masses, EUS-FNA was reported to have a sensitivity of 78-95%, a specificity of 75-100%, a positive predictive value of 98-100%, a negative predictive value of 46-80%, and an accuracy of 78-95% [22].

Due to the rarity of pancreatic extramedullary plasmacytoma, it is difficult to establish the exact sensitivity and specificity of EUS-FNA in its diagnosis. The three cases reported so far all had the culprit lesion presenting as an irregular, predominantly hypo-echogenic heterogeneous mass [27, 28, 29]. In all three cases, histological examination revealed a predominantly monomorphic population of light-chain producing plasma cells, with flow cytometry showing CD38 positivity. Two of the patients had previously been diagnosed with multiple myeloma, had already undergone chemotherapy and were referred to radiation therapy. The third patient had a solitary right shoulder plasmacytoma treated with local radiotherapy, with chemotherapy being started after the new diagnosis.

OTHER IMAGING MODALITIES

Transcutaneous ultrasonography, multisection contrast-enhanced CT, magnetic resonance imaging (MRI) and hybrid nuclear imaging techniques (single photon emission computed tomography/CT and positron emission tomography/CT) have all been used to characterize solid pancreatic lesions using their morphologic, hemodynamic and metabolic characteristics.

Transcutaneous ultrasonography is a very useful screening test in patients presenting with possible obstructive jaundice. Similar to the EUS imaging characteristics, pancreatic extramedullary plasmacytomas have been described as heterogeneous focal masses, most often located in the head of the pancreas [30]. The pancreas is often obscured by overlying gas from the gastrointestinal tract and the depth of the organ limits imaging to 2-5 MHz, which allows only lower-resolution images to be obtained. Therefore, only 60-70% of pancreatic masses are usually detected, and more than 40% of lesions smaller than 3 cm are missed [9].

Pancreatic extramedullary plasmacytomas typically appear as multilobular homogenous solid tumors hypodense to the surrounding parenchyma, with contrast enhancement being described as both homogenous and heterogeneous [11, 14]. As in transcutaneous ultrasonography, lesions smaller than 3 cm are often not detected [31]. CT scanning has so far been the most often used method of FNA guidance.

MRI has been far less studied than CT scanning in evaluating pancreatic lesions. The imaging features pancreatic enlargement and a lobulated contour [31]. Unlike CT, it is not commonly used for guiding the needle during FNA.

The role of PET/CT scanning in diagnosing extramedullary plasmacytomas of any localization, including the pancreas, is yet to be established. It can be effectively used for evaluating patients with known multiple myeloma, and can thus detect asymptomatic extramedullary plasmacytomas at any site [32]. While detection of pancreatic extramedullary plasmacytoma by PET/CT is possible in theory, this particular use of positron emission tomography has never been reported in the literature.

CONCLUSION

It is important for physicians to have a high index of suspicion for diagnosing pancreatic plasmacytoma in the appropriate clinical setting (i.e., a previously diagnosed multiple myeloma, extramedullary plasmacytoma or any other plasma cell neoplasm). EUS-FNA is now an indispensable imaging modality for pancreatic disease. It is a safe, relatively non-invasive method to achieve the diagnosis of pancreatic extramedullary plasmacytoma with an inherently low rate of complications, and should be the first choice for tissue evaluation.

Conflict of interest The authors have no potential conflict of interest

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