Review Article

The safety of endoscopic ultrasound-guided fine-needle aspiration of pancreatic cystic lesions

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ABSTRACT

Endoscopic ultrasound (EUS) is widely used in the evaluation of various pancreatic diseases including pancreatic cystic lesions (PCLs). EUS-guided fine-needle aspiration (EUS-FNA) of PCLs provides cyst fluid, which is used for the differentiation of PCLs. EUS-FNA of PCLs is a safe procedure with a low complication rate. Contrary to the concerns expressed by some investigators, preoperative EUS-FNA of mucinous PCLs is unlikely to increase the frequency of postoperative peritoneal seeding.

Key words: Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA), pancreatic cyst, safety

INTRODUCTION

Pancreatic cystic lesions (PCLs) are detected with increasing frequency.[1] The prevalence of PCLs is reported to be between 1.2% and 19.6% in image-based studies.[2-4] It is now considered that up to 60% of all PCLs are pancreatic cystic neoplasms.[5]

Endoscopic ultrasound (EUS) is being widely used to image the pancreas.[6] In the revised international consensus guidelines, EUS is recommended when cysts have worrisome features (pancreatitis, cyst diameter ≥3 cm, thickened/enhancing cyst walls, main duct size 5-9 mm, nonenhancing mural nodule, abrupt change in the caliber of pancreatic duct with distal pancreatic atrophy, and lymphadenopathy).[7]

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EUS-guided fine-needle aspiration (EUS-FNA) of PCLs provides cyst fluid for various analyses such as carcinoembryonic antigen (CEA) concentration, cytology, and DNA analysis.[8] The cyst fluid CEA concentration is known to be the most accurate marker to differentiate mucinous from nonmucinous PCLs.[9,10] Cytology is reported to be the most accurate test for the diagnosis of malignant PCLs.[10] One report concluded that PCLs with no high-risk stigmata/worrisome features as defined in the 2012 international consensus guidelines, and no high-grade atypia on cytology have very low risk of malignancy and can be followed conservatively.[11]

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However, some investigators have expressed concern about the safety of EUS-FNA of PCLs. This review will focus on this issue, with an emphasis on the risk of peritoneal seeding.

COMPLICATIONS OF EUS-FNA OF PCLs

The overall complication rate of EUS-FNA in prospective series ranges from 0% to 2.5%.[12] These complications include pain, infection, bleeding, acute pancreatitis, perforation of the esophagus or duodenum, bile peritonitis, and seeding of tumorous cells along the needle tract.[12,13]

The reported complication rate of EUS-FNA of PCLs is low. In a large scale report involving 603 patients with PCLs who had undergone EUS-FNA, the overall complication rate was 2.2% (13 of 603). The identified complications were pancreatitis (n = 6), abdominal pain (n = 4), retroperitoneal bleeding (n = 1), infection (n = 1), and bradycardia (n = 1). Hospitalization was required in 12 patients with a mean hospital stay of 3.8 days. No predictors of complication could be identified.[14]

Intracystic hemorrhage may occur following EUS-FNA of PCLs. In one report, three out of 50 patients (6%) who had undergone EUS-FNA of PCLs developed intracystic hemorrhage. Of these patients, two experienced transient abdominal pain and one was asymptomatic. All patients were observed as outpatients while treated with a short course of oral antibiotics.[15]

EUS-guided brushing of PCLs was introduced to increase the cellular diagnosis of PCLs. However, this seems to be associated with increased morbidity such as bleeding and pancreatitis.[16,17] In the study by Sendino *et al.*,[16] of the 30 patients who had undergone EUS-guided brushing of PCLs, three patients (10%) developed complications (two bleeding and one pancreatitis). One of the bleeding complications was associated with mortality due to a subacute retroperitoneal hemorrhage in a patient on anticoagulation.[16] In another study involving 37 patients, significant complications developed in three (8%) patients. The reported complications were one case of bleeding and two cases of pancreatitis.[17]

EUS-FNA of PCLs is considered to carry an increased risk of fever and possibly infectious complications, compared to that of solid masses and lymph nodes. Both the American Society for Gastrointestinal Endoscopy (ASGE)[18] and European Society of Gastrointestinal Endoscopy (ESGE)[12] guidelines recommend the prophylactic administration of antibiotics. In addition, we recommend aspirating all cyst fluids to minimize the risk of infection.[19]

PERITONEAL SEEDING AFTER EUS-FNA OF PCLs

Perhaps the most controversial issue regarding the complication of EUS-FNA of PCLs is peritoneal seeding. As even stated in the 2012 international consensus guidelines, some investigators do not recommend cyst fluid analysis for the diagnosis of mucinous-like PCLs, and believe that a cyst of any size with worrisome features should not be aspirated since it may cause leakage of cyst content and possibly result in peritoneal dissemination.[7]

It should be noted that the frequency of tumor seeding after EUS-FNA of pancreatic cancers is low, with only a few number of cases reported.[20-23] A large scale report indicated that preoperative EUS-FNA of pancreatic cancer does not increase the risk of needle-tract seeding.[24]

The concern of peritoneal seeding after EUS-FNA of PCLs seems to have arisen from a very limited number of cases. There is one case report of peritoneal seeding after EUS-FNA of intraductal papillary mucinous neoplasm (IPMN). This patient underwent distal pancreatectomy 10 days after EUS-FNA of the lesion. Tumor cells were identified in the intraoperative peritoneal lavage. The pathology was IPMN with an associated invasive carcinoma. Peritoneal seeding developed 20 months after the surgery, and the patient died approximately 25 months after surgery.[25]

The PIPE study published in 2014 evaluated the frequency of postoperative peritoneal seeding in patients with IPMN who had undergone preoperative EUS-FNA (EUS-FNA group, n = 175) and compared it with that of patients with IPMN who had surgery without preoperative EUS-FNA (no sampling group, n = 68).[26] The two groups were comparable with respect to sex, age, follow-up duration, pancreatic head involvement, involvement of the main pancreatic

duct, grade of dysplasia, and the size of histologically proven branch-duct IPMN. The frequency of postoperative peritoneal seeding was 2.3% (4 out of 175 patients) in the EUS-FNA group and 4.4% (3 out of 68 patients) in the no sampling group ($P = 0.403$). In detail, the four patients who developed postoperative peritoneal seeding in the EUS-FNA group had IPMN with an associated invasive carcinoma. Of the three patients who developed postoperative peritoneal seeding in the no sampling group, two had IPMN with an associated invasive carcinoma and one had IPMN with high-grade dysplasia. The authors concluded that preoperative EUS-FNA of IPMN was not associated with an increased frequency of peritoneal seeding in patients who underwent resection.[26]

Whether this result can be applied to mucinous cystic neoplasm (MCN) of the pancreas remains a question. A multi-institutional study of 156 cases of MCN from Japan reported two cases of peritoneal dissemination. However, the report does not mention whether these patients had undergone EUS-FNA or not.[27] To this date, the authors are unaware of any report on peritoneal seeding associated with EUS-FNA in MCN. We speculate that preoperative EUS-FNA of MCN would not be associated with an increased frequency of peritoneal seeding. The cellularity of the cyst fluid is likely to be low, and the malignant potential of IPMNs and MCNs is likely to be relatively lower than that of pancreatic ductal adenocarcinoma.

CONCLUSIONS

EUS-FNA of PCLs is a safe technique. The reported complication rates of the procedure are comparable to those of EUS-FNA of solid lesions. Preoperative EUS-FNA of IPMNs and MCNs is unlikely to increase the frequency of peritoneal seeding. Therefore, with precisely defined indication and preprocedural preparation, EUS-FNA of PCLs can be safely performed.

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Conflicts of interest
William R. Brugge: Consultant with Boston Scientific.

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