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ORIGINAL ARTICLE

Endoscopic ultrasound-guided fine-needle aspiration biopsy of autoimmune pancreatitis: diagnostic clues and pitfalls

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Introduction Autoimmune pancreatitis (AIP) is an inflammatory process that has characteristic clinical, radiographic, and pathologic features but may mimic pancreatic malignancy. In this study, we reviewed our experience in the endoscopic ultrasound-guided fine-needle aspiration evaluation of pancreatic lesions in patients with AIP.

Materials and methods We searched the cytopathology archives and identified a total of 6 cases that had endoscopic ultrasound-guided fine-needle aspiration evaluation and subsequent tissue biopsy or resection with a diagnosis of AIP. The clinical, cytologic, and histopathologic features were reviewed.

Results The original cytologic diagnoses included negative, atypical, and suspicious for malignancy in 2 cases each. On retrospective review, these cases were characterized cytologically by the presence of mixed epithelial cells, mixed lymphocytes, and plasma cells, as well as cellular stromal fragments. Cytologic atypia of epithelial cells was observed in 4 of 6 cases, including mild (3 cases) and moderate (1 case) atypia. *KRAS* mutation analysis was performed in 4 cases with an indeterminate cytology diagnosis, which was negative in all cases.

Conclusions Our results demonstrate that the presence of trilineage epithelial, lymphoplasmacytic, and stromal elements may be suggestive but not definitive for a diagnosis of AIP. The role of *KRAS* mutation analysis in AIP remains inconclusive and may warrant further evaluation.

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Introduction

Autoimmune pancreatitis (AIP) is a chronic inflammatory disease of the pancreas with characteristic clinical, radiologic, and histopathologic features.[1-6] There are 2 forms of the disease: (1) type 1 AIP, the pancreatic manifestation of a multiorgan immunoglobulin G (IgG) 4-related disease, characterized by storiform-type fibrosis, obliterate phlebitis, and increased IgG4-positive plasma cells; and (2) type 2 AIP, a pancreas-specific disorder, characterized by granulocytic epithelial lesions and occasional IgG4-bearing plasma cells. AIP uniformly displays a high response to steroid treatment with a tendency to relapse, particularly in type 1 AIP.[6-8] Clinically and radiographically, the patients with AIP show pancreas enlargement or mass-like lesion and pancreatic duct stricture, thus mimicking pancreatic malignancy and potentially leading to an unnecessary surgical intervention.[9]

Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) or endoscopic ultrasound-guided fine-needle biopsy (EUS-FNB) is the method of choice for evaluating pancreatic lesions, especially pancreatic adenocarcinoma. EUS-FNA/EUS-FNB has also been employed for the diagnosis of AIP.[10-19] Acquisition of core tissue using a larger gauge needle (19 to 22 gauge) is preferential because core tissue suits better for the evaluation of pathologic features such as granulocytic epithelial lesions, fibrosis, IgG4 plasmacytic infiltrates, and venulitis.[12,15,18-20] There are rare reports of diagnosing AIP based on the cytomorphologic features of FNA specimens with variable accuracy.[10,11,14,16] In fact, cytomorphologic analysis of EUS-FNA is primarily used to rule out malignancy rather than to render a definite diagnosis of AIP. In this study, we retrospectively reviewed our experience in the EUS-FNA diagnosis of AIP that was confirmed by follow-up histopathologic evaluation. The cytologic diagnostic clues and pitfalls of AIP were analyzed.

Materials and methods

Case selection

The surgical pathology archives were searched for the cases with histopathologic diagnosis of AIP at Yale–New Haven Hospital from January 1, 2006 to December 31, 2013. We then searched the cytopathology archives to see whether there were preoperative EUS-FNA evaluations for those cases. Only the cases with paired cytologic and histopathologic evaluations, 6 cases in total, were included in this study. Patients' demographic information, clinical presentations, imaging findings, serum IgG4 level if available, cytologic interpretation and histopathologic diagnosis were reviewed. This study was approved by the Internal Review Board at our institution.

Fine-needle aspiration and cytologic evaluation

EUS-FNA was performed at the endoscopy suite using 25- or 22-gauge needles. The aspirates were expelled onto slides, smeared, and air-dried or fixed in 95% alcohol. Air-dried slides were stained with Diff-Quik technique (Thermo Fisher Scientific, Kalamazoo, MI) and used for rapid on-site evaluation. Alcohol-fixed slides were stained with Papanicolaou technique. The remaining aspirates or needle-rinsed material were saved in CytoRich Red fixative (Thermo Fisher Scientific, Kalamazoo, MI) and processed for a cell block. Diff-Quik-stained and Papanicolaou-stained slides as well as hematoxylin-eosin–stained cell block sections were used for evaluation to render a final cytologic diagnosis. The cytologic diagnoses included nondiagnostic, negative for malignant cells (negative), atypical cells present (atypical), suspicious for malignancy (suspicious), or positive for malignancy (positive). These cases were then retrospectively evaluated for 3 components: (1) epithelial cells: cellularity, cell types, and atypia; (2) inflammatory cells: cellularity, and cell type; and (3) fibrotic tissue fragment: present or absent. The cytologic atypia was classified as mild, moderate, and severe based on the criteria modified from Deshpande et al.[10] Atypia was considered mild if only mild nuclear enlargement was seen with or without nucleoli and nuclear overlapping. Severe atypia was defined by the presence of 3-dimensional epithelial clusters, marked nuclear anisonucleosis, nuclear membrane irregularities, abnormal chromatin, single atypical cells, and necrosis. Moderate atypia was used for the cases with only 1 or a few feature(s) of severe atypia.

KRAS mutation analysis

At our institution, cases with an indeterminate diagnosis (atypical or suspicious) for pancreatic lesions are routinely subjected to reflex *KRAS* mutation analysis. *KRAS* mutation was analyzed by polymerase chain reaction followed by single-strand conformational polymorphism analysis using available material, either fixed aspirates or cell block sections.[21]

Surgical follow-up

Based on clinical presentations and cytologic diagnoses, the patients were further subjected to core needle biopsies due to indeterminate diagnoses or surgical excisions of the pancreatic lesions due to concern for malignancy. Our surgical specimens included core biopsy (2 cases), pancreaticoduodenectomy (2 cases), and distal partial pancreatectomy (2 cases). The specimens were fixed in 10% formalin, processed and embedded in paraffin blocks. Hematoxylin-eosin–stained sections of paraffin-embedded tissue blocks were available for histopathologic evaluation. In selective cases, immunohistochemical studies were performed to substantiate final diagnosis.