Journal of the American Society of Cytopathology (2016) 5, 116–121

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.jascyto.org/

ORIGINAL ARTICLE

A study to improve the identification of pancreatobiliary adenocarcinoma utilizing fine-needle aspiration cytology and immunohistochemical application for KOC and S100P

Sarah Tinsley, MD, Edward J. Wilkinson, MD*, Larry J. Fowler, MD

Department of Pathology, Immunology and Laboratory Medicine, University of Florida College of Medicine, Gainesville, Florida

Received 19 June 2015; received in revised form 20 October 2015; accepted 23 October 2015

KEYWORDS
Pancreas;
Fine-Needle Aspiration;
Immunohistochemistry;
Malignancy;
Sensitivity;
Specificity

Introduction The identification of pancreatic adenocarcinoma by fine-needle aspiration (FNA) cytology is a difficult, yet critical, task. This study uses a panel of two immunohistochemical (IHC) markers, KOC and S100P, to augment the interpretation of pancreatic adenocarcinoma using cytopathology specimens and to compare these to corresponding surgical specimens.

Materials and methods We retrospectively reviewed 33 surgical specimens with pancreatic adenocarcinoma and 33 corresponding, preceding FNA cytology specimens. IHC studies for KOC and S100P were performed on both the surgical specimens and cytology cell blocks. Three pathologists reviewed the staining intensity and amount of tumor cell staining within these blocks. The findings were then analyzed for sensitivity, specificity, and combined sensitivity and specificity for the 2 markers.

Results KOC performed similarly to S100P in sensitivity for surgical specimens (90.9% for both) and better for FNA specimens (92.3% versus 82.7%, respectively). The specificity of KOC was significantly better than S100P for surgical and FNA specimens (100% for KOC in both specimens versus 72.7% and 89.7% for S100P in both specimens, respectively). The combined sensitivity of the panel of KOC and S100P was 99.2% for surgical specimens and 98.7% for FNA specimens. The combined specificity was 72.7% for surgical specimens and 89.7% for FNA specimens.

*Corresponding author: Edward J. Wilkinson, MD; Department of Pathology, Immunology and Laboratory Medicine, University of Florida College of Medicine, 1600 SW Archer Rd, Gainesville, FL 32610-0275; Tel.: 352-273-9070; fax: 352-627-9242.

E-mail address: wilkinso@pathology.ufl.edu (E.J. Wilkinson).

http://dx.doi.org/10.1016/j.jasc.2015.10.003

Conclusions We found using KOC and S100P on FNA cell block cytology specimens to be a useful adjunct for interpretation when an interpretation of atypical or suspicious for pancreatic ductal adenocarcinoma is being considered and there are atypical epithelial cell groups in the cell block.

Introduction

The identification of pancreatic adenocarcinoma by fine-needle aspiration (FNA) cytology is a difficult, yet critical task. Cytology is often the only diagnostic specimen received before major surgery, such as a Whipple procedure, or chemo-radiation is begun. Although a moderate number of immunohistochemical tests have been studied in pancreatobiliary surgical specimens, including mesothelin, MUC1, MUC2, MUC5AC, CDX2 and others,[1-5] there are currently no widely accepted immunohistochemical (IHC) or molecular tests applicable to FNA specimens for the differentiation of atypical cells due to a reactive process versus adenocarcinoma in this setting. A 2014 study by Ali et al.[6] performed a meta-analysis of immunohistochemical tests to augment the diagnosis of pancreatic adenocarcinoma in surgical specimens and developed a variety of panels, with sensitivities and specificities at different cutoff levels. From these analyses they concluded that significant improvement in sensitivity and specificity was obtained in the diagnosis of pancreatic adenocarcinoma. This study uses one of these panels, KOC (K homology domain containing protein overexpressed in cancer [IMP3]) and S100P, to determine the utility of such testing in the diagnosis of pancreatic adenocarcinoma using FNA cytopathology specimens, and compares these to corresponding surgical specimens.

Pancreatic adenocarcinoma accounts for 85% to 90% of all malignant pancreatic neoplasms and is the fourth leading cause of cancer death in the United States.[7] The 5-year survival rate is dismal, with 90% of patients dying within 1 year.[8] Patients typically present in an advanced stage with approximately 20% having tumors that are judged resectable.[9] FNA is a common method for achieving a tissue diagnosis prior to a surgical procedure, although the interpretation of the cytologic material is often difficult because of overlapping cytologic features between neoplastic and reactive ductal epithelium.[10] To improve the sensitivity and specificity of pancreatic FNA, many tumor markers and IHC targets have been studied. Two promising IHC tests, KOC and S100P, have been recently investigated as a panel for this purpose.[6]

KOC is an oncofetal RNA binding protein that binds to and regulates insulin-like growth factor II transcripts and is involved in the post-transcriptional regulation of cell proliferation during embryogenesis. Its expression appears limited in normal mature tissues, primarily being expressed in the placenta.[11] Normal and reactive pancreatic tissue and duodenal tissue is negative for this marker.[11] Mucinous lesions of the pancreas without dysplasia are negative as well.[11] Malignant neoplasms outside the pancreas that have been found to express KOC include adenocarcinomas of the uterine cervix, ovarian carcinomas, pulmonary non-small cell carcinomas, ampullary carcinomas, colorectal carcinomas, carcinomas of the head and neck, and soft tissue sarcomas.[11] Within the pancreas, other malignant neoplasms including pancreatic endocrine tumors, serous cystadenomas, and solid-pseudopapillary tumors have been reported to be negative.[11] The positivity of KOC in invasive pancreatic ductal adenocarcinoma within surgical specimens is reported to range from 74% to 97% in multiple studies[7,11,12] and expression increases with tumor stage.[11]

S100P belongs to the family of S100 calcium-binding proteins. The reactivity level by IHC has been found to increase during progression from pancreatic intraepithelial neoplasia to invasive adenocarcinoma.[7] Hypomethylation of its gene is suggested to account for the overexpression of S100P protein in pancreatic ductal adenocarcinoma.[7] Non neoplastic pancreatic duct tissues are negative for this marker.[7] In other benign tissues, S100P is expressed in bladder, gallbladder, and gastric epithelium.[10] Other malignant neoplasms found to have S100P reactivity include breast cancer, lung adenocarcinoma, and some colon and prostate carcinoma cell lines that are resistant to therapy.[10] The positivity of S100P in invasive pancreatic ductal adenocarcinoma within surgical specimens is reported to range from 75% to 100% in multiple studies.[6,10]

When KOC and S100P are combined in an IHC panel to identify pancreatic ductal adenocarcinoma in surgical specimens, the resulting sensitivity and specificity are at 98%/96%, respectively, at a cutoff of 10% positivity in tumor cells for both markers.[6]

Materials and methods

With prior institutional review board approval, we retrospectively reviewed pathology reports of 927 cases of pancreatic resection specimens from July 1, 2004, to June 30, 2014. From these we selected cases where the diagnosis on the surgical specimen was pancreatic ductal adenocarcinoma, for which there was a preceding pancreatic FNA case at this institution and the cytologic interpretation was indeterminate, atypical, suspicious, or positive for adenocarcinoma. Case selection required that there was adequate tumor material in the cell block from the FNA. Using these criteria, 33 surgical specimens along with 33 corresponding, preceding FNA cytology specimens were selected (Tables 1 and 2). Of the 33 cytology (FNA) cases selected for staining, the original cytology diagnoses contained 21 that were labeled “positive