Journal of the American Society of Cytopathology (2015) 4, 282–289

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.jascyto.org/

ORIGINAL ARTICLE

Biliary stent–related alterations can be distinguished from adenocarcinoma on bile duct brushings using a limited number of cytologic features

Jonathon E. Heath, MD, Lindsay B. Goicochea, MD, Paul N. Staats, MD*

Department of Pathology, University of Maryland School of Medicine, 22 South Greene Street, Baltimore, Maryland

Received 29 July 2014; received in revised form 21 June 2015; accepted 22 June 2015

KEYWORDS
Bile ducts;
Bile duct obstruction;
Extrahepatic;
Stents;
Adenocarcinoma;
Cytology

Introduction Although it is widely accepted that cytologic alterations secondary to a biliary stent can be difficult to distinguish from adenocarcinoma in pancreatobiliary exfoliative cytology, no systematic study has been undertaken to identify the cytologic features that best distinguish these entities.

Materials and methods A training set of 29 bile duct brushings (14 with biliary stents, originally classified as atypical or suspicious, with >6 months of benign clinical follow-up; and 15 diagnosed as adenocarcinoma with histologic confirmation) was evaluated for the following: nuclear enlargement, nuclear contour, nuclear overlap, chromatin distribution, nuclear-cytoplasmic ratio, anisonucleosis, macronucleoli, mitoses, acute inflammation, disorganization, necrosis, cell borders, single atypical cells, and 2 distinct cell populations. A distinct validation set of 31 equivocal stented brushings—13 later diagnosed with carcinoma and 18 with ≥6 months of benign follow-up—were similarly evaluated. Cases were categorized as benign or malignant using a scoring algorithm based on statistically significant features.

Results Five features achieved statistical significance: atypical single cells ($P = 0.0001$), 2 distinct cell populations ($P = 0.0007$), and anisonucleosis ($P = 0.0422$) favored malignancy; distinct cell borders ($P = 0.0018$) and acute inflammation ($P = 0.0035$) favored benign. The algorithm correctly classified 12 of 14 benign and 15 of 15 malignant cases in the training set and 16 of 18 benign and 7 of 13 malignant cases in the validation set.

*Corresponding author: Paul N. Staats, MD; Department of Pathology, University of Maryland School of Medicine, 22 South Greene Street, Baltimore, MD 21201; Tel.: (410) 328-5555; Fax: (410) 328-5508.

E-mail address: pstaats@umm.edu (P.N. Staats).

http://dx.doi.org/10.1016/j.jasc.2015.06.006

Conclusions Most bile duct brushings from patients with biliary stents could be definitively and correctly classified as either benign or malignant using 5 morphologic features: single atypical cells, binary cell population, anisonucleosis, distinct cell borders, and acute inflammation.

Introduction

Endoscopy-guided exfoliative cytology has long been considered the most appropriate diagnostic modality for differentiating malignant biliary strictures from benign ones. Although specificity is high (generally >95%), sensitivity has been shown to range from 44% to 72% with most studies reporting around 50%.[1-5] While sampling error may account for up to two-thirds of false negative studies, interpretive error has been shown to be the cause in a significant minority of cases where inflammation, necrosis, and reactive epithelial changes can hinder rendering a definitive diagnosis of malignancy.

In patients with a biliary or pancreatic duct stricture, endoscopic retrograde cholangiopancreatography with cytology brushing followed by placement of a stent is a common diagnostic and therapeutic modality. Repeat biliary brushing cytology at a significant time interval after stent placement is not uncommon, especially considering the fact that a majority of biliary strictures are malignant.[6] Although it is widely accepted that reactive epithelial changes secondary to a biliary stent can be difficult to distinguish from malignancy in pancreatobiliary exfoliative cytology, no systematic study has been undertaken to identify the cytologic features that best distinguish these entities. Herein, we compare the cytologic features of stent-related benign epithelial alterations to those of ductal adenocarcinoma, and we identify a set of features that allow reliable distinction of the two conditions in most cases.

Materials and methods

A retrospective search of the archives at our institution from 2006 to 2009 revealed 14 cases of bile duct brushings from patients with indwelling biliary stents that had been classified as either atypical (n = 12) or suspicious for malignancy (n = 2), each with >6 months of benign clinical follow-up. A comparison set of 15 cases of bile duct brushings classified as positive for malignancy with histologic confirmation of adenocarcinoma was also collected—the latter group of patients did not have indwelling stents. Although it was not possible to confirm the type of stent placed in individual cases based on review of the medical record, given the standard practice in our institution of placing plastic stents until malignancy is definitively diagnosed, it is likely that all or most of the stents were plastic.

The cases had been prepared according to standard laboratory protocol. In each of these cases, materials included ≥1 direct smears that were alcohol fixed and Papanicolaou stained, and 1 liquid-based preparation slide (SurePath, BD Diagnostics, Burlington, NC). The following cytologic features were evaluated: (1) nuclear enlargement: 2-fold or greater increase in nuclear area compared with benign, nonreactive ductal epithelium; (2) irregular nuclear

Table 1 Performance of cytomorphologic features in training set.

Cytomorphologic feature	Benign cases (n = 14)	Malignant cases (n = 15)	Accuracy, %	Sensitivity, %	Specificity, %	*P* value
Atypical single cells	3	14	86	93	79	0.0001
2-cell populations	6	15	79	100	57	0.0007
Distinct cell borders	12	4	79	73	86	0.0018
Acute inflammation	13	6	76	60	93	0.0035
Anisonucleosis	10	15	66	100	29	0.0422
Chromatin clumping	10	14	62	93	29	0.126
Irregular nuclear contours	7	11	62	73	50	0.135
Necrotic debris	11	9	41	60	21	0.182
Macronucleoli	9	12	59	80	36	0.212
Nuclear enlargement	12	15	59	100	14	0.224
Nuclear overlap	14	13	45	87	0	0.259
Chromatin clearing	8	10	55	67	43	0.261
Mitotic figures	2	4	55	27	86	0.262
Increased N/C ratio	11	11	48	73	21	0.318
Nuclear grooves	1	2	52	13	93	0.402
Disordered sheets	14	15	52	100	0	1

Abbreviation: N/C, nuclear-cytoplasmic.