RESEARCH ARTICLE

Diagnosis of Malignant Biliary Strictures: Conventional or Negative Pressure Brush Cytology?

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Abstract

Background/Objective: The aim of this study was to perform a comparative evaluation of the yields of conventional brush cytology and brush cytology with negative pressure in the diagnosis of malignant biliary strictures. **Methods:** A total of 132 consecutive patients undergoing endoscopic were identified. Of these, 88.0 had brush cytology after ERCP and 44 were Brush cytology with negative pressure. Retrograde cholangiopancreatography (ERCP) including brush cytology and brush cytology with negative pressure in patients with biliary strictures between 2012-2015. Endoscopic retrograde cholangiography was performed with a standard videoduodenoscope Olympus TFJ 160-R (Olympus, Hamburg, Germany) and brush cytology with a Cook medical Double Lumen Biliary BrushTM (Cytology). Means and standard frequencies were used to calculate variables. **Results:** Positive results for malignancy were obtained in 22 of 88 patients (25%) by brush cytology and 31 of 44 patients (70.4 %) by brush cytology with negative pressure. **Conclusions:** Sensitivity of cytology sampling could be maximized by negative pressure during ERCP.

Keywords: Cytology- ERCP- EUS-FNA

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Introduction

Biliary strictures can be seen with a wide array of neoplastic and nonneoplastic causes (Eiholm et al., 2013). Management of biliary strictures frequently can pose a significant challenge for both surgeons and endoscopists (Geraci et al., 2008). A definite diagnosis is desirable to the provision of adequate treatment (Brugge et al., 2014).

The tissue specimen collection of the biliary system for diagnostic cytology has been a major development to distinguish malignant strictures from benign ones and is typically performed through cytologic brushings, biopsy forceps, bile aspiration or endoscopic ultrasonography-guided fine-needle aspiration (EUS-FNA) (Kulaksiz et al., 2011; Tapping et al., 2012).

Endoscopic forceps biopsy during ERCP is a safe, simple and convenient technique, and is commonly used in combination with Brush cytology. Brush cytology performed at endoscopic retrograde cholangiopancreatography (ERCP) is the most commonly used method for collecting tissue from the bile duct (Furmanczyk et al., 2005). It was first described in 1975 by Osnes et al. as an effective technique with no complications (Osnes et al., 1974). The diagnostic specificity of biliary brush cytology rates ranging from 80% to 100% (Eiholm et al., 2013). Although highly specific, the major limitation of the technique is its low sensitivity reported in most studies to date (Eiholm et al., 2013). In most published studies, the diagnostic sensitivity is in the 36.0-83.0% range (Furmanczyk et al., 2005).

To improve the sensitivity of brushing cytology during ERCP, we described a new method of biliary biopsy using a negative pressure during brush cytology, which enables a safe and reliable tissue specimen collection within the biliary tract. To evaluate the usefulness of this approach, we prospectively compared its diagnostic yield with brush cytology in the diagnosis of biliary strictures.

Material and Methods

Patients

Patients with biliary strictures undergoing ERCP at "Taleghani hospital", Tehran, Iran, between 2012 and 2015 were included prospectively in this study. In 88.0 patients, brush cytology was performed after ERCP. 44.0 patients with biliary stricture underwent Brush cytology with negative pressure. Exclusion criteria were the following: 1) strictures that would not permit passage of guidewire, brush or dilator, 2) Post-operative strictures, 3) previous brushing or placement of biliary stent. Informed written consent was obtained before the procedure from all patients. The study was approved by the research and ethic committees of the Shaheed Beheshti University of Medical Sciences.

Endoscopic retrograde cholangiography (Osnes et al.) was performed with a standard videoduodenoscope

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Olympus TFJ 160.0-R (Olympus, Hamburg, Germany). Brush cytology was performed with a Cook medical Double Lumen Biliary BrushTM (Cytology). Six cytology smears from each brushing sample were stained with Giemsa and Papanicolaou for routine diagnostic cytology.

The specimens were evaluated by an experienced cytopathologist. Cytological results were classified as: 1) negative for malignancy, 2) presence of atypical cells, 3) insufficient specimen for diagnosis, 4) suspicious for malignancy, or 5) positive for malignancy. For the purpose of statistical analysis, we grouped samples with insufficient material, negative for malignancy and atypical cells as negative, whilst specimens suspicious for malignancy and positive for malignancy were considered together.

The final diagnosis was confirmed following surgery, histopathological diagnosis of the lesion, radiological infiltration of adjacent organs or metastases , or after at least a 6.0- month follow-up.

For analysis, variables were described with means and standard frequency, and Sensitivity, specificity, positive and negative predictive values and diagnostic accuracy were determined for each test. Statistical analysis was performed with SPSS statistical software version 13.0 (SPSS, Inc., Chicago, IL, USA).

Results

The median age of patients was 60 years (range 45-86), and the male: female ratio was 2.14. Among these, 85 Patients were confirmed to have malignant neoplasia: pancreatic head adenocarcinoma (18), cholangiocarcinoma (17), liver hilum tumors (1).

Brush cytology was performed in 88 patients. Malignancy was detected in 22.0 of 88 patients. Brush cytology with negative pressure was performed in 44 patients. Malignancy was detected in 31 cases. Table 1 gives the distributions of true positive and negative results of these two modalities comparing them with the final one. Table 2 summarizes the sensitivity, specificity, positive and negative predictive values, and accuracy percent values for cholangioscopic biopsy, Brush and brush with negative pressure.

Discussion

Biliary strictures can be caused by a wide gamut of conditions including various inflammatory diseases and by benign or malignant bile duct tumors (Eiholm et al., 2013). It accounts for significant morbidity and mortality and remains a major diagnostic challenge (Nanda et al., 2015).

Table 1. Cytological Diagnosis Compared to Follow-up

	Brush (n)	Brush with negative pressure (n)
NO	88	44
True positive	22	23
True negative	34	13
False positive	0	0
False negative	32	8

Table 2. Diagnostic Performance of Brush Biliary Cytology for Diagnosing Malignant Biliary Stricture

	Brush cytology	Brush cytology with negative pressure
sensitivity	40.7 %	74.2 %
specificity	100.0 %	100 %
PPV	100.0%	100%
NPV	51.5%	61.9%
Accuracy		

PPV, Positive Predictive Value; NPV, Negative Predictive value

Endoscopic retrograde cholangiopancreatography (ERCP) and percutaneous transhepatic cholangiography (PTC) are common procedures which allow delineating the site of strictures and may give some information on the nature of the stricture, but only a tissue diagnosis is conclusive (Davidson et al., 1992; Kurzawinski et al., 1993). ERCP offers the advantage of obtaining tissue diagnosis to differentiate benign from malignant causes (Shanbhogue et al., 2011). Brush cytology is the most common sampling technique used in the daily clinic, but the sensitivity is unsatisfactory. low, ranging from 4.0% to 60.0% (Salomao et al., 2015). This prospective study assessed the usefulness of two cytological modalities, which is Brush cytology and brush cytology with negative pressure for the evaluation of biliary strictures.

Brush cytology for biliary strictures is simple to perform, highly specific and adds minimal time, expense and risk; (Alizadeh et al., 2011; Nanda et al., 2015) which was first described in 1975 by Osnes et al. The specificity of brush cytology has been reported to vary between 95% and 100% (Foutch et al., 1990b; Ferrari et al., 1994; Stewart et al., 2001). Stewart et al, also reported three false positives cytological diagnoses among one hundred and sixty patients (specificity 98.1%). Sturm and colleagues also reported specificity of 97.2% with two false positive cytological diagnoses among 74 patients with benign strictures (Sturm et al., 1999). In this study we found the specificity of 100% with no false positive diagnoses.

In our study the sensitivity of brush cytology was found to be 40.7%. However, some published studies have demonstrated higher diagnostic sensitivity of brush cytology (Macken et al., 1999; Urbano et al., 2008; López-Jurado et al., 2009; Kawada et al., 2011). Foutch et al used brush cytology in their study for diagnosis of malignant biliary obstruction in 39.0 patients and found the sensitivity was 54.0% and specificity was 100% (Foutch et al., 1990a). In a study performed by Ferrari et al (Ferrari et al., 1994) including 55.0 bile duct and 19.0 pancreatic duct strictures patients, the performance of brush cytology was evaluated. Brush cytology showed sensitivity of 56.2% and specificity of 100% in the referred study (Ferrari et al., 1994). In a study of 406 consecutive patients evaluated over a 6.5 year period, 246.0 of whom had proven carcinoma, brush cytology was positive in 59.2% of cases (Stewart et al., 2001). Singh et al (Singh et al., 2003) assessed the sensitivity of brush cytology in 30.0 patients with biliary obstruction caused by carcinoma gallbladder (n=16) carcinoma head of pancreas (n=10), or

cholangiocarcinoma (n=4.0). When compared with final diagnosis, Brush cytology was positive for malignancy in 8.0 cases (26.7%) (Singh et al., 2003). This diagnostic disagreement is associated with various factors such as experience, skills, institution type of the pathologists and the pathologic type of the tumor (López-Jurado et al., 2009; Sugimoto et al., 2014).

It has been reported that the limited sensitivity of brush cytology may be due to poor or inadequate cell sampling, difficulties in sample processing, and interobserver variability in interpretation by pathologists (López-Jurado et al., 2009). In our study, 2.0 of 88 cytologies were excluded because of inadequate cellular yield. Inadequacy rates have been previously reported from 0% to 58.3%, with most in the 5% to 10% range (Desa et al., 1991; Ferrari et al., 1994; Lee et al., 1995; de Peralta-Venturina et al., 1996; Kocjan and Smith, 1997; Macken et al., 1999).

Here we described a new method of biliary biopsy using negative pressure during brush cytology, which enables a safe and reliable tissue specimen collection within the biliary tract. In our study brush cytology with negative pressure exhibited the sensitivity of 74.2% and specificity of 100%. In addition, the statistical analysis showed a PPV of 100% and NPV of 61.9% compared to final diagnosis. This finding indicated that negative pressure produces more reliable results than Brush cytology. The material obtained by negative pressure is more abundant than those obtained by brush cytology. An important limitation in our study is the cross-sectional design; we could not increase the specimen.

This study demonstrated a high sensitivity (74.2%) and specificity (100%) for the brush cytology with negative pressure. This sensitivity was higher than brush cytology (40.7%). In addition, this technique is simple, safe, fast and relatively inexpensive for widespread use. However, single evaluation of sensitivity does not provide an objective evaluation of a methodology and further assessment in other institutions is recommended.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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