INTRODUCTION

Patients with biliary obstruction usually undergo endoscopic retrograde cholangiopancreatography (ERCP) to confirm diagnosis and decompress the biliary tree. Many patients are considered unsuitable for surgery due to locally advanced disease, metastatic neoplasia or high surgical risk. Accurate diagnosis is essential if surgery is to be considered or indeed for placement of self-expandable metallic stent in inoperable situations. Furthermore, for considering patients to palliative chemo or radiotherapy a tissue or cytological diagnosis is often required.

Tissue sampling at the time of ERCP is suboptimal. Ideally, a tissue sampling technique should have high sensitivity and specificity for cancer detection, besides being simple, safe and inexpensive. All methods currently available have high specificity, but low to moderate sensitivity.

Biliary brush cytology has been the most frequently used and studied technique at ERCP. It was first described by OSNES et al. as a simple, safe and effective technique. Even though its specificity is close to 100%, brush cytology sensitivity for cancer detection is modest, ranging from 30% to 70% in most published studies. Many centers perform dilation of biliary strictures on an inconsistent basis. Conceptually, endoscopic stent dilation prior to brushing may increase the number of cells available for diagnosis, enhancing cytology yield.

The aim of the present study was to compare the results of brushings performed before and after dilation of biliary strictures.

PATIENTS AND METHODS

Patients with extra-hepatic biliary stricture undergoing ERCP at “Hospital São Paulo”, São Paulo, SP, Brazil, between April 1999 and January 2002 were included prospectively in this study. Exclusion criteria were the following: 1)
endoscopically visible periampullary tumors, 2) strictures that would not permit passage of guidewire, brush or dilator, 3) post-operative strictures and 4) previous brushing or placement of biliary stent.

Informed written consent was obtained before the procedure from all patients. This study was approved by the “Hospital São Paulo” Federal University of São Paulo Ethical Committee.

Following cannulation of the common bile duct, the stricture was identified and a guidewire was passed through it. Brushing was performed using a Geenen-type brush over the guidewire. Dilation was then performed using a 10 Fr dilating catheter. Immediately following dilation, an identical brush was used to attain repeat cytology. Whenever endoscopic therapy was indicated, a stent was placed after brushing. Biliary sphincterotomy was performed in 18 patients (36%) to facilitate bile duct access or stent placement.

Each brush was immediately smeared on six glass slides in the ERCP suite (three fixed in 95% ethanol and three air dried). Samples were evaluated by an experienced cytopathologist who was blinded to the dilation status of each cytology sample. The specimens were stained with Papanicolaou and Giemsa techniques, and interpreted according to the characteristics established by RABINOVITZ et al.\(^{(22)}\), using standard cytological criteria for malignancy\(^{(1)}\). Cytology samples 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-month follow-up.

Student’s t test or Fisher exact test were used to compare variables between the groups with malignant neoplasia and inflammatory disease. Sensitivity, specificity, positive and negative predictive values and diagnostic accuracy were determined for each test. The results were compared using the McNemar test. A P value of less than 0.05 was considered statistically significant.

**RESULTS**

Fifty consecutive patients with biliary strictures having undergone ERCP and brush cytology were prospectively enrolled. Among these, 40 patients were confirmed to have malignant neoplasia: pancreatic adenocarcinoma (18), cholangiocarcinoma (17), gallbladder cancer (2), metastases (2) and neuroendocrine carcinoma of the pancreas (1). Inflammatory disease was observed after a mean follow-up of 29 months (range 17–39 months) in 10 patients: chronic pancreatitis (6) and inflammatory stenosis secondary to bile duct stones (4).

Patients with malignant neoplasia were significantly (P = 0.02) older (mean age = 64 years, range 42-82 years) than those with inflammatory disease (mean age = 54 years, range 39-68 years).

The results of biliary brush cytology obtained from the 50 patients before and immediately after stricture dilation are shown in Table 1. There was no statistically significant difference between the results obtained before and after dilation (P = 0.18), and those obtained before and combining pre- and post-dilation brushings (P = 0.50).

**TABLE 1 – Results of biliary brush cytology obtained before and/or after stricture dilation in 50 patients (expressed in % and 95% confidence interval)**

<table>
<thead>
<tr>
<th></th>
<th>Predilation</th>
<th>Postdilation</th>
<th>Combined</th>
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<tr>
<td>Sensitivity</td>
<td>40.0 (24.8 – 55.2)</td>
<td>27.5 (13.7 – 41.3)</td>
<td>45.0 (29.6 – 60.4)</td>
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<tr>
<td>Specificity</td>
<td>100.0 (100.0 – 100.0)</td>
<td>100.0 (100.0 – 100.0)</td>
<td>100.0 (100.0 – 100.0)</td>
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<tr>
<td>PPV</td>
<td>100.0 (100.0 – 100.0)</td>
<td>100.0 (100.0 – 100.0)</td>
<td>100.0 (100.0 – 100.0)</td>
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<td>NPV</td>
<td>29.4 (14.1 – 44.7)</td>
<td>25.6 (11.9 – 39.3)</td>
<td>31.3 (15.2 – 47.4)</td>
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<tr>
<td>Accuracy</td>
<td>52.0 (38.2 – 65.8)</td>
<td>42.0 (28.3 – 55.7)</td>
<td>56.0 (42.2 – 69.8)</td>
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**Cytology samples classified as positive and suspicious for malignancy were found in 5 and 11 patients before dilation, 3 and 8 after dilation, 7 and 11 cases when both pre- and post-dilation samples were combined, respectively. Cytology specimens were classified as insufficient for diagnosis in 14 (28%) patients before dilation, 18 (36%) after dilation and in 9 (18%) patients when combined (not significant).**

When the results of pre- and post-dilation brushings were combined, brush cytology was more sensitive for cholangiocarcinoma (52.9%) than pancreatic carcinoma (33.3%), but there was no statistically significant. In view of the small number of patients a type II error can not be excluded.

Complications were observed in six cases: acute pancreatitis (two), early stent occlusion (two), bleeding following precut sphincterotomy (one). One patient with previous Billroth II gastrectomy and advanced cholangiocarcinoma died 4 days after ERCP due to perforation of the afferent loop.

**DISCUSSION**

Imaging studies (CT, MRI and EUS) are able to diagnose biliary obstruction, but they often can not confirm the etiology\(^{(4, 10, 18)}\). Although EUS represents a major advance in the evaluation of biliary strictures, current limitations have to be emphasized such as: technical sophistication, requirement of significant expertise to accurate image interpretation, high cost, potential complications, lack of facility for therapeutic intervention and difficulty in differentiation between benign and malignant stricture\(^{(15)}\).

Reliable differentiation between benign and malignant etiology remains a challenge. Acquiring tissue from such lesions during ERCP is the classical approach since affected patients are commonly evaluated and primarily treated during ERCP\(^{(4)}\).

Features that affect cancer detection rate on cytology samples are adequacy and processing, slides interpretation and tumor type\(^{(1)}\). Some previous studies\(^{(13, 14, 19, 24)}\) excluded patients with insufficient cellularity, so they showed a higher sensitivity for cancer detection than they would have achieved if all cases had been analyzed. If patients with inadequate specimens were
excluded from our data, the sensitivity for cancer before stricture dilation, immediately after and combining pre- and post-dilation would increase to 59.3%, 44% and 56.3%, respectively.

Surprisingly, the present study shows that brushings performed after dilating the biliary epithelium using a 10 Fr dilation catheter have more inadequate samples for cytological analysis, although the difference is not significant. This finding may be explained by the presence of more clots or degenerate cells after duct dilation. Nevertheless, repeated brushings not only decreased the percentage of cases with insufficient samples from 28% to 18%, but also improved cancer detection rate from 40% to 45%.

MOHANDAS et al. (16) demonstrated that dilating a malignant stricture using a 10 Fr catheter before bile aspiration enhanced cancer detection rate in comparison with a non dilation group (63.3% vs. 26.6%). Similarly, FARRELL et al. (4) evaluated the sensitivity for malignancy of brush cytology after aggressive stricture manipulation by combined dilation up to 10 Fr and endoscopic needle aspiration. This sequence of procedures significantly increased cancer detection rate (85%) compared with brushing alone (57%). De BELLIS et al. (3) investigated the sensitivity of brush cytology after dilation in a series of 139 patients with suspected malignant stricture. Cancer detection rate before dilation (34.5%) was similar to post-dilation rate (31%). Subgroup analysis revealed no difference in sensitivity after catheter (34.7%) or balloon (27.7%) dilation. The authors concluded that the diagnostic yield increased from 34.5% to 44% (P<0.01) when the results for the two consecutive brushings were combined.

Some cases of insufficient samples would have been avoided if the brush were not pulled out of its sheath before the specimens were smeared on glass slides. The technique used in this study may result in cellular loss within the sheath, but this is still a point of controversy. We did use such approach in order to maintain access to the proximal bile duct. Cancer detection rate for biliary brush cytology in the present study was higher for cholangiocarcinoma (52.9%) than for pancreatic carcinoma (33.3%), similar to the literature. (3, 8, 14, 19, 21, 25, 26). Pancreatic tumors or metastases, which extrinsically compress the bile duct or manifest submucosal growth, are unlikely to be detected by brushing during early-stage disease. Cholangiocarcinomas, which originate from biliary epithelium, may be more amenable to cytological diagnosis.

In conclusion, sensitivity for malignancy of biliary brushings performed before and after stricture dilation are similar, although combination of results increases sensitivity and diagnostic accuracy.

ACKNOWLEDGMENT

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REFERENCES