

Cytohystological discordance on gastrointestinal brushings: Facts unfolded

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ABSTRACT

Introduction: Brush cytology is a rapid, cost-effective, and reliable tool to diagnose gastrointestinal tract (GIT) lesions in low-resource settings. Most of the studies on GIT brushings have focused on upper GI lesions. We have studied the diagnostic accuracy of brush cytology in the entire length of GIT and correlated the cytological diagnosis with histopathology. The aim of this study is to study diagnostic utility of brush cytology of GIT lesions in the context of correlation with biopsy and study the factors responsible for cytohystological discordance. **Materials and Methods:** A retrospective analysis of 101 cases of prebiopsy brush cytology samples of GIT lesions was done over a period of 1 year (June 2014 to May 2015). The cytological diagnosis was compared with histopathological diagnosis and percentage of correlation was calculated. The reasons for discordance were noted and studied. **Results:** The cytological diagnosis of 79 (78.2%) correlated with histopathological diagnosis. There was discordance in cytological and histological diagnosis in 22 cases (21.8%). Inadequacy of cytological sample and overlap of nuclear atypia caused by regenerative changes and malignancy were significant factors for cytohystological discordance. **Conclusion:** The diagnostic accuracy of brush cytology can be improved by taking appropriate measures to eliminate factors responsible for fallacies in cytological diagnosis.

Key words: Brushings, cytology, discordance, gastrointestinal

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INTRODUCTION

Gastrointestinal tract (GIT) is a common site for many neoplastic and nonneoplastic lesions. Technical advances have allowed simultaneous visualization along with procurement of brushings and biopsies from the mucosal and deeper seated lesions of GIT.¹ The diagnostic utility of brush cytology in evaluation of GIT lesions has been widely studied. Some studies have found cytology to be more sensitive than endoscopy-guided biopsy in detecting malignancies while others have found contrasting results.²⁻⁷

Most of the studies have focused on the utility of cytology in upper or lower GIT lesions. To the best of our knowledge, this is the first study on diagnostic utility of cytology in lesions of entire GIT namely esophagus, stomach, small intestine, and large intestine including rectal brushings,

with emphasis on reasons for discordance between cytological and histopathological diagnosis.

MATERIALS AND METHODS

A retrospective analysis of 101 specimens of GIT brushings received in the Department of Pathology at a tertiary care institute during a period of 1 year (June 2014 to May 2015) was performed. Brushings from GIT lesions were smeared on two or three slides by endoscopy team, and the air-dried smears were received in the Department of Pathology where one smear was stained with May-Grunwald-Giemsa. The other smears were rehydrated with normal saline and stained with Papanicolaou stain and hematoxylin and eosin stain after alcohol fixation.

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Inclusion criterion - Only those cases were included whose endoscopy-guided biopsy was also received.

The cytological diagnosis was correlated with histopathology findings, and the sensitivity and specificity of GIT cytology were calculated. The histopathological diagnosis is the gold standard for diagnosing malignancy. The final cytological diagnosis was grouped as positive and negative for malignancy. Cases in which the cytological sample was inadequate for opinion were also grouped as negative for malignancy. The cytohistological correlation was done, and the factors causing discrepancy between the cytological and final diagnosis were studied. The results are summarized in Table 1.

RESULTS

A total of 101 GIT brushings were received for malignant cytology whose histopathology was also available as endoscopy-guided biopsy. Table 2 shows the distribution of GIT brushings according to the site.

In our study, age of the patients ranged between 18 and 85 years. The male-female ratio was 1.8:1. The sensitivity and specificity of cytology were 62.7% and 94%, respectively. The positive predictive value of brush cytology was 91.4% while the negative predictive value was 71.2%. False-positive rate was 6% and false-negative rate was 37.3% [Table 1].

Among 36 esophageal brushings, cytology was false negative while histopathology was positive in 7 cases [Table 1]. Out of these seven discordant cases, the atypia was equivocal in three cases and could not be definitely attributed to neoplasm or reactive atypia. The cells displayed nucleomegaly and mild nuclear pleomorphism. However,

the histopathological diagnosis showed the presence of carcinoma.

There were two cases which were negative on both cytology as well as histopathology where cytology could detect *Candida* while the same was missed on histopathology [Figure 1a]. This can be attributed to superficial nature of *Candida* infection which is limited to just the epithelial cells which are readily detected by brush cytology.

One case showed evidence of malignancy on cytology, but the biopsy was inadequate for opinion.

Among seven specimens of gastric brushings, one case showed equivocal features on both cytology as well as histopathology as the atypical cells could not be attributed definitely as inflammatory or malignant. Two cases which were false negative on cytology showed only inflammatory cells along with columnar epithelial cells while histopathological evaluation showed the presence of lymphoma in one case and signet ring cell carcinoma in another case, thus adding to false-negative cases.

Only 2 out of 16 cases of duodenal brushings showed false-negative cytology in the presence of histopathological evidence of malignancy. One case which was negative both on cytology and histopathology showed *Candida* spores and hyphae on brush cytology.

There were four cases of brush cytology from ileum, all of which were negative for malignancy both on cytology and biopsy. Hence, there was no discordance observed in ileal brushings and biopsy specimens. One of these

Table 1: Comparison of cytological diagnosis with final diagnosis

Cytology	Final diagnosis		Total
	Positive	Negative	
Positive	32	3	35
Negative	19	47	66
Total	51	50	101

Table 2: Distribution of gastrointestinal tract brushings, according to site

Site	Number of cases	Number of discordant cases (%)	Number of cases correlating (%)
Esophagus	36	8	28
Gastric	07	2	5
Duodenum	16	2	14
Ileum	04	0	04
Colon	38	10	28
Total	101	22 (21.8)	79 (78.2)

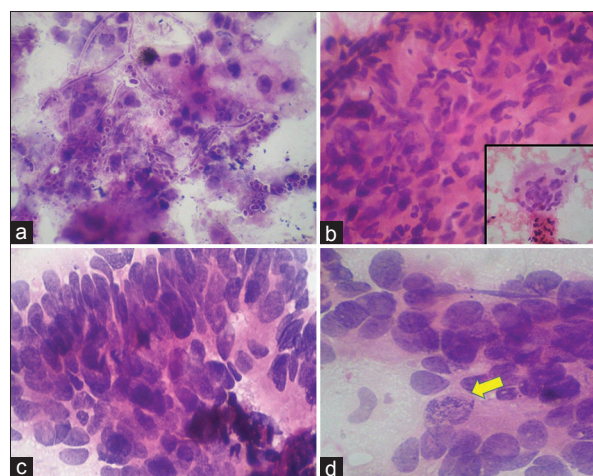


Figure 1: Photomicrograph showing (a) spores and pseudohyphae of *Candida* in esophageal brushings (H and E, x400); (b) epithelioid granuloma in colonic brushing. Inset showing Langhans giant cell (H and E, x400); (c) colonic brushings in a case of adenocarcinoma showing pleomorphic tumor cells with nuclear overlapping (H and E, x400); (d) adenocarcinoma colon with atypical mitotic figure (arrow) (H and E, x400)

cases contained inadequate material on cytology while the biopsy showed only inflammatory granulation tissue with ulceration of the overlying mucosa.

There were 38 cases of colonic brushings. Out of eight cases which had false-negative cytology, three cases had inadequate material on cytology while the biopsy showed carcinoma. In three other cases of false-negative cytology report, it was not possible to identify whether the atypia was due to inflammation or malignancy. The remaining two cases of false-negative cytology report had only inflammatory cells and necrosis on smears with total absence of epithelial cells.

There were two cases where the brush cytology smears showed evidence of malignancy while the biopsy contained insufficient tissue for diagnosis [Figure 1c and d].

Out of 17 cases which were negative for malignancy on both cytology as well as histopathology, one case showed epithelioid granulomas on cytology smears, but the biopsy contained only fibrotic tissue [Figure 1b]. This observation can be explained by the fact that brush cytology can cover larger surface area than biopsy which samples only a focus of tissue. Besides, dyscohesive cells are readily sampled and detected by cytology techniques.

In this study, paucity of diagnostic cells on cytological smears and obscuring by inflammatory cells emerged as significant factors resulting in cytohistological discordance [Table 3].

DISCUSSION

The main purpose of GIT brush cytology is rapid detection of malignancies. With shorter turnaround time, as compared to biopsy, brush cytology is a popular investigation employed to detect the nature of GIT lesions.

There were 22 cases in which cytology was reported as negative while the histopathology report was positive for malignancy. Negative cytology report in the presence of malignancy can be attributed to poor cellularity on cytology smears, making any opinion impossible based on cytological findings alone. Poor cellularity may be attributed to inexperience of the endoscopist taking sample for brush cytology. Even necrosis, excessive inflammation, or fibrosis caused by tumor may also be responsible for inadequate sample collection resulting in

scant cellularity. The brush cytology sample will comprise necrotic fragments and nonviable cells which cannot be categorized further on cytology. Obscuring of cells by excessive inflammatory infiltrate will also lead to negative cytology report. On the other hand, a false-positive cytology report can be caused by over-interpretation of nuclear hyperchromasia of regenerating epithelium of ulcerated mucosa. Reactive atypia may not always be distinguished from atypia due to malignancy on cytology.²

In some studies, cytology proved to be more sensitive than biopsy. The reasons for the same can be the fact that larger mucosal area can be sampled on brush cytology while biopsy targets only a specific area of the lesion.^{1,8} Loosely dyscohesive cells are also more likely to be detected on brush cytology, contributing to increased diagnostic accuracy of this investigation. This can explain finding of granulomas on cytology in a case of colonic brushing while the histopathology showed only evidence of fibrosis. Some workers have suggested combining cytology with histopathology to improve the sensitivity.^{3,9} This is also the routine practice in our tertiary care institute. However, while other studies have only focused on upper GIT lesions, this study has evaluated the utility of brush cytology of the entire GIT. The sensitivity of brush cytology in our study is 62.7%, which is less than that reported in other studies.³⁻⁷ The low sensitivity in our study can be predominantly attributed to lack of representative material and equivocal cytological features of atypical cells.

One drawback of cytology is the inability of this investigation to differentiate between dysplasia and invasive malignancies. Necrosis and extensive inflammation are commonly associated with invasive malignancies, as a part of tumor diathesis. Sometimes, as stated above, these can also be obscuring factors hampering a definitive cytological diagnosis. Hence, cytology and biopsy are complementary modalities used to provide maximum information about the nature of a lesion and help in clinical management.

Cook *et al.* have reported 85% sensitivity of brush cytology in detecting gastric malignancies. However, they recommend cytology only in cases where it is not possible to obtain adequate biopsy. In stenosed areas, where it is not possible to take biopsy, brush cytology can provide diagnostic material which can help to arrive at the correct diagnosis.^{4,10} Besides, singly scattered atypical cells are easily collected by exfoliative method of brush cytology and are more readily detected on cytological smears while the same may be missed while examining the biopsy section which highlights the architectural arrangement of the tissue. Therefore, some studies suggest that biopsy should be repeated in case of obtaining a positive cytology report and negative biopsy on initial endoscopy.^{3,11}

Table 3: Causes of cytohistological discordance

Cause of discrepancy	Number of cases
Atypia? Reactive? Neoplastic	6
Absence of diagnostic cells/inadequate on cytology	13
Positive on cytology	3
Total	22

CONCLUSION

Brush cytology is a reliable investigation which causes minimal discomfort to the patient and also has a rapid turnaround time in a limited resources setting. We have studied the diagnostic accuracy of brush cytology in the entire GIT. Emphasizing the need to collect more material via exfoliative brush and spreading it evenly on the smears can circumvent the issue of false-negative cytology due to inadequate material. Uniform distribution of cytological material on smears can also overcome the diagnostic pitfall arising due to clumping of cells and obscuring by inflammation or necrosis. With comparable sensitivities of both brush cytology and histology, cytology alone can be a reliable diagnostic investigation whenever it is not possible to obtain a biopsy, as in stenosis. By focusing on above-mentioned points, diagnostic accuracy of brush cytology can be improved significantly and provide better results.

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Conflicts of interest

There are no conflicts of interest.

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