Original Article

Imprint Cytology: A Diagnostic Aid in Interpretation of Endoscopic Esophageal Biopsies

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Abstract

Background: Although there has been a lot of advancement in the cytological evaluation of many organ diseases, gastrointestinal (GI) cytology has not gained much recognition and is very seldom used with methods like brushings and washings. Smear cytology is a valuable complement to histopathology in UGI endoscopic biopsies. Therefore, a study demonstrating a relationship between IC and conventional histopathology will enable the process to be carried out regularly as a supplement to histopathology. The aim is to compare the findings of histology and imprinting from esophageal biopsies in the event of suspected esophageal lesions. **Material and Methods:** Included in the study were 22 endoscopic esophageal biopsies. From the biopsies, touch impressions were created, stained, and analysed. The same tissue was processed histopathologically by immersing it in 10% formalin. IC results were contrasted with histopathological results. Statistical Analysis Used: The significance of the study parameters was determined using the Fisher exact test and chi square test. **Results:** For esophageal lesions, the IC's sensitivity and specificity were 100% and 80%, respectively. **Conclusion:** When diagnosing esophageal lesions, IC is a useful diagnostic technique that is frequently used as an adjunct to histological testing.

Keywords: Imprint Cytology, Histopathological Examination, Gastrointestinal Endoscopy.

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Introduction

According to Global Cancer Statistics 2022, gastrointestinal tract (GIT) cancers are among top ten in cancer related deaths worldwide. Esophagus is number seven with 445,391.[1] The diagnostic assessment of gastrointestinal malignancies is dependent on a comprehensive evaluation involving clinical history, physical examination, endoscopic procedures, radiological imaging, and laboratory analyses. Within the realm of anatomic pathology, the definitive tissue diagnosis is regarded as the benchmark and is predicated upon the discernment of particular histological patterns, cellular components, secretory products, and causative agents.[2] An integral component of assessing GI tract diseases is gastrointestinal (GI) endoscopy. Significant advancements in the early detection and treatment of GIT lesions have been made possible by the ease, convenience, and safety of contemporary endoscopy[3].

Cytology has come up as a valuable diagnostic modality and an adjunct to histopathology. Gastrointestinal cytology is performed on specimens obtained using the following techniques: brush cytology, crush preparation, and endoscopic fine needle aspiration.[2]

Touch or imprint preparation of endoscopically obtained biopsies can also serve as an adjunct in the prompt diagnosis of GIT lesions.[4]

The use of imprint cytological preparations in the diagnosis of GIT cancers has the capacity for major cost savings.[5]

The implementation of imprint cytological methodologies in the diagnostic evaluation of gastrointestinal tract malignancies presents significant opportunities for substantial economic efficiencies.

The upper gastrointestinal pathology seen in clinical practice is largely composed of a wide variety of esophageal lesions, both neoplastic and non-neoplastic. Tissue samples procured from these lesions facilitate precise diagnostic outcomes in a majority of instances. In the evaluation of esophageal neoplasms, histopathological examination (HPE) is regarded as the gold standard; however, it is notably more time-intensive in comparison to cytological assessment. A lot of gastroenterologists and patients want to know right away if the biopsy was adequate and if the lesion is malignant or benign. Even though biopsy touch imprint cytology (IC) is not often used in practice, it is a simple, quick, and affordable diagnostic method.[6]

Therefore, a study was carried out to demonstrate the association between the outcomes of endoscopic biopsies from esophageal lesions using IC and standard HPE.

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Aims and objective

- To assess imprint smear cytology in lesions of the esophagus.
- To establish a correlation between imprint cytology and histopathology results in order to detect cancer early.

Materials and Methods

Type of study: This prospective study was conducted in the department of Pathology, in collaboration with the Department of Medical Gastroenterology Teerthanker Mahaveer Medical College & Research Centre over a period of one and a half year from July 2018 to Dec 2019

Data collection and analysis: Following institutional ethical committee approval, informed written consent was obtained from all participants after explaining the procedure in detail. Clinical information including age, gender, presenting complaints, and relevant medical history was systematically recorded for each patient.

After obtaining biopsies imprint smears were made and analysed. The diagnosis of lesions was made on imprint smears and histopathological sections separately according to the cytopathological and histopathological findings and typing & grading of malignant lesions on histopathology was done according to WHO classification (5th edition).

Statistical analysis was performed by using SPSS version 23.0 software (SPSS, Inc., Chicago, IL, USA). A 2x2 contingency table was used to determine the sensitivity, specificity, Negative Predictive Values, Positive Predictive Values, and the overall accuracy of imprint cytology compared to histology. Kappa statistics test was used to calculate the degree of agreement between the two diagnostic methods

Inclusion criteria: Participants in the study included 22 patients who had endoscopic biopsies taken from their esophagus and had symptoms suggestive of esophageal disease.

Exclusion criteria: Slides displaying crush artefacts and biopsies with insufficient material were not included in the study. The study did not include patients with lesions limited to the pharynx and oral cavity.

Methods

Recruitment of subjects into the study was done over a period of 1.5 years.

Endoscope biopsies were taken from suspicious area and then transferred from the forceps to two slides with a fine needle, and the biopsies touch imprints were created by gently rolling the tissue over glass slides and exerting little pressure periodically. After being preserved in 95% ethyl alcohol, imprint smears were stained using H&E stain, 2-3 smears of each kept air dried for Romanowsky staining and special stain as required.

The same tissue after imprint smear preparation was collected for histopathological examination. Tissue was transferred to a container containing 10% formalin with proper tagging and was kept for overnight fixation. Routine tissue processing with paraffin impregnation was done and Haematoxylin and Eosin were used to stain the 5 µm-thick sections. The imprint smears and the biopsies were seen by the same pathologist, though blinded to cytology report while interpreting the biopsy to avoid bias. All slides were reviewed by a second pathologist also.

On cytology, lesions were categorized as-

1. Positive for malignancy,
2. Suspicious of malignancy,
3. Negative for malignancy
4. Material unsatisfactory for interpretation

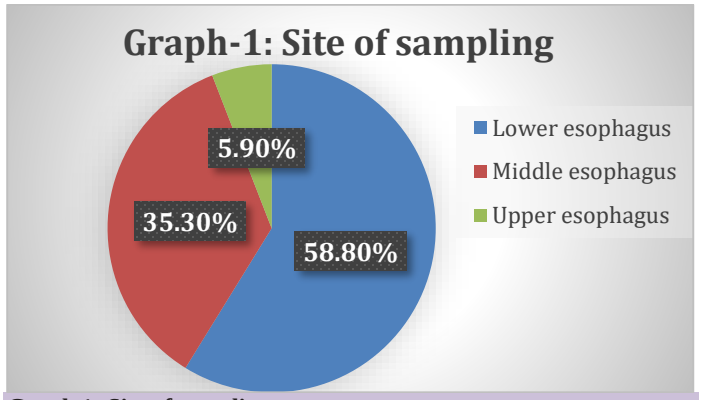
On histopathology, lesions were categorized as-

- Normal
- Inflammatory
- Dysplasia
- Positive for malignancy.

Results

To investigate the range of IC and HPE results in the same patients, as well as aberrant findings in esophageal endoscopic biopsies, were compared in prospective research with 22 patients.

The study cohort comprised 10 males (45.4%) and 12 females (54.5%), yielding a male-to-female ratio of 1:1.5. Patient age ranged from 22 to 75 years, with a mean age of 48.5 years. The most common age group affected was 60-69 years, accounting for 08 cases (36.4%), followed by the 50–59-year age group with 07 cases (31.8%).



Graph 1: Site of sampling

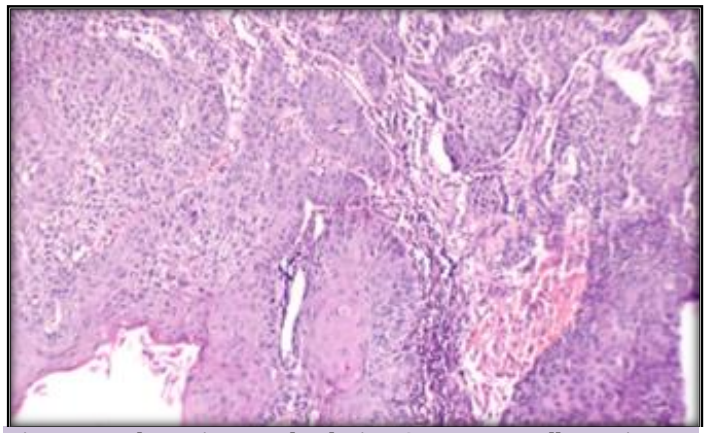


Figure-1: Photomicrograph depicts-Squamous cell carcinoma, esophagus (200x, H &E)

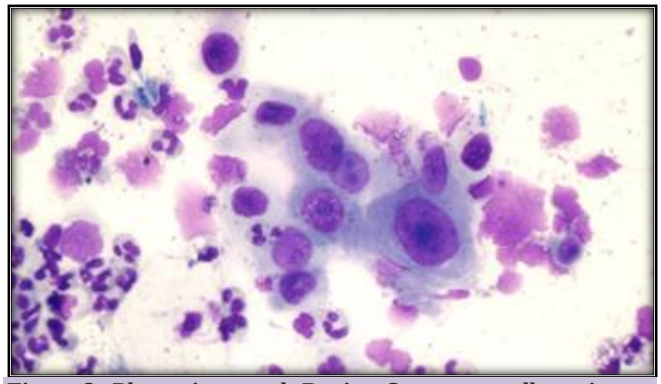


Figure 2: Photomicrograph Depicts-Squamous cell carcinoma (400x, MGG-imprint smear)

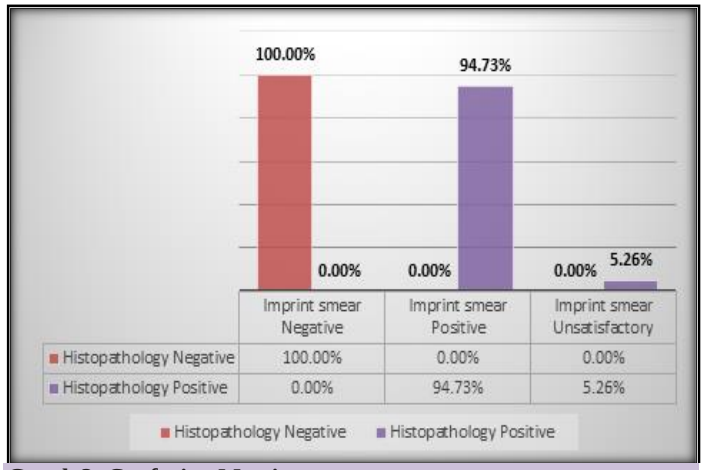
Diagnoses categories of lesions given on histopathology: On HPE, lesions were classified as either neoplastic or non-neoplastic. On histology, they were further subdivided into normal and inflammatory under the non-neoplastic group, and squamous cell carcinoma, adenosquamous carcinoma, poorly differentiated cancer and dysplasia that falls within the neoplastic category. [shown in Table 2]

[Table 2] also shows that study included 4(18.2%) non neoplastic lesions, 18 (81.8%) neoplastic lesions out of which 17(77.3%) lesions were positive for malignancy and 1(4.5%) lesion showed dysplasia.

There were no benign neoplasms found. Esophageal squamous cell carcinoma (61.8%) was the most prevalent neoplastic lesion. [**Figure 1 &2**]

According to [Figure 2], the lower third of the esophagus had the highest prevalence of malignant lesions (58.8%), followed by the middle third (35.3%) and upper third (5.9%). The most frequent reason for endoscopic examination of esophageal lesions was dysphagia. In the majority of patients, radiographic studies revealed malignancies as ulceroproliferative lesions.

Diagnoses categories of lesions given on imprint cytology: Suspicious, positive or negative for malignancy, and unsatisfactory were the types of categories given to lesions on imprint smears. [**shown in Table 1**]



Graph 2: Confusion Matrix.

Table 1: Distribution of diagnoses given on imprint cytology

Imprint Cytology	No. of Cases	%age
Positive for malignancy	17	72.27%
Negative for malignancy	4	18.18%
Unsatisfactory	1	4.54%
Total	22	100%

Table 2: Distribution of diagnoses given on HPE

Histopathology	No. of Cases	%age
Total non-neoplastic	04	18.2
Non specific Inflammation	03	13.6
Normal	01	4.5
Total neoplastic	18	81.8
Squamous cell carcinoma	15	68.2
Adenosquamous carcinoma	01	4.5
Poorly differentiated carcinoma	01	4.5
Dysplasia	01	4.5
Total	22	100%

Table 3: Correlation of diagnoses on IC and HPE

	Histopathology			Total
Imprint smear	**Negative**	**Positive**	**Dysplasia**	
Negative	4	0	0	4
	100.00%	0.00%	0%	20.83%
Positive	0	16	1	17
	0.00%	94.11%	100%	75.00%
Unsatisfactory	0	1	0	1
	0.00%	5.88%	0%	4.16%
Total	4	17	1	22
	100.00%	100.00%		100.00%

Table 4: Confusion Matrix

Confusion Matrix	Imprint smear			
	True Positive	False positive	True Negative	False negative
No. of cases	16	1	4	0

Chi−square = 21
The p-value is 2.7536E-5. Significant at p<0.01

Table 5: Results Statistics

Statistic	Value
Sensitivity	100
Specificity	80
Positive likelihood ratio Negative likelihood ratio	5 0
Accuracy	95.24
Positive predictive value (PPV) Negative predictive value (NPV)	94.12 100

Imprint cytology findings correlation with the corresponding HPE report:

Table 3 -show concordance and discordance between imprint cytology and histopathology diagnoses in terms of percentages.

Table 4 & Graph-2-show confusion matrix with true and false positive and negative results.considering HP results as gold standard

Table 5-shows various key statistical parameters where 100%, 80%, 94.12%, 100%, and 95.24 were the respective values for the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy.

The p-value of imprint smears cytology with standard histopathology was 2.7536E-5.

Discussion

The management and follow-up of esophageal lesions heavily depend on endoscopic examination. Depending on the nature and location of the cancer, cytological methods can be used for prognosis, primary diagnosis, and behaviour prediction[7].

Every effort should be made to provide the most conclusive diagnosis achievable. In instances where a precise diagnosis cannot be established, it is imperative to employ a differential or more generalized category, and the rationale for this approach should be documented. The lack of positive findings indicative of a malignant process does not necessarily negate the possibility of malignancy, given that the sensitivity of the procedure is not absolute. In addition to repeat sampling for suboptimal specimens or for further auxiliary studies, it is imperative to guarantee clinical and radiological correlation.[8]

The proficiency in obtaining, processing, and assessing the cytological specimens is crucial for the cytomorphological assessment of gastrointestinal cancers. In 100 percent of cases, a cytopathologist present in the endoscopic room to supervise an instant assessment of the sufficiency of biopsies collected produced an appropriate specimen[9]

The current study's IC and HPE results and how they relate to one another are:

Imprint Cytology:

On IC, 17 smears were marked as "positive for malignancy." The majority of smears displayed good cellularity. The presence of pleomorphic squamoid cells, primarily in sheets, hyperchromatic nuclei,necrotic background were used to identify squamous cell cancer. Using Pap stain, orangeophilia may be seen. The majority of patients displayed tumour diathesis together with inflammatory cells and necrosis. In 14 cases, corresponding HPE slides revealed squamous cell carcinoma, with one case displaying its basaloid subtype, poorly differentiated carcinoma in one case and adenosquamous carcinoma in one case. In one instance where the initial smear screening revealed cancer, dysplasia was noted on HPE. In view of presence of atypical glandular component repeat biopsy from representative area was advised. One case was reported to be malignant because of the presence of malignant squamous cells and atypical columnar cells in both scattered and clustered form on IC. On the matching HPE slides, adenosquamous cancer was visible.

Four cases with squamous cells that seemed normal and had no atypia, either with or without inflammation, were reported as "negative for malignancy" on IC. Three of these had chronic inflammation that was non-specific, and one instance had no pathology on HPE. Candida was also noted in one such case with PAS positivity.

Imprint cytology revealed that one sample had minimal cellularity, disintegrated cells and necrosis, making it "unsatisfactory." This instance displayed squamous cell carcinoma on HPE.

Histopathology:

Four non-neoplastic lesions were found, one of which had normal histology.

Three cases of non-specific esophagitis were recorded, and all three were in females. This is consistent with a research by Lu et al,[10] that found a small female prevalence.

Among 18 neoplastic lesions, squamous cell carcinoma was the most common, followed by poorly differentiated carcinoma and adenosquamous carcinoma. Further immunohistochemistry work up was advised in case of poorly differentiated carcinoma. In one instance (4.5%) with high grade dysplasia, invasion could not be ruled out due to insufficient subepithelial tissue, and a repeat biopsy was recommended.

The findings of research done by Sharma et al,[11] who found sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic

accuracy 96%, 88%, 92%, 80%, and 95% respectively,were in line with the IC's 100% sensitivity, 80% specificity, 94.12% positive predictive value (PPV), 100% negative predictive value (NPV), and 95.24% diagnostic accuracy (DA) in this study.Young et al,[13] and Mysorekar et al,[12] reported 100% sensitivity.which is comparable to the current research.

Taking several biopsies will increase the accuracy of the diagnosis. GIST, lymphoma, carcinoid, and metastatic cancers are examples of sub-epithelial lesions for which imprint cytology has poor sensitivity[6]. Report of one false positive case was made. The cause of false positive cases may be reactive atypia. In the context of inflammation, atypia should be reported with caution.

Limitations: Small number of cases limit generalizability of study findings. Few biopsies were lacking adequate depth hence did not provide accurate HP diagnosis.

Conclusion

Because it is quick and easy, imprint cytology can be used as a standard approach for evaluating esophageal lesions. If necessary, the doctor can collect more biopsies during the same session thanks to IC's quick assessment of the biopsies' adequacy. Imprints from several biopsies should be obtained in order to increase sensitivity, and cellular yield. Necrotic areas should be carefully inspected for tumour cells. Strict criteria should be used to distinguish reactive atypia from cancer in order to prevent false positive results. It is important to never interpret poor smears as negative for cancer in order to prevent false negatives. Even though impression smears are a reliable method of identifying cancer, they need to be associated with HPE in order to determine the extent of invasion and to type tumours.

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Conflicts of interest

There are no conflicts of interest.

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