ORIGINAL ARTICLE

A Comparative Study of Endoscopic Biopsy and Endoscopic FNAC in Gastrointestinal Malignancies

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ABSTRACT

Objectives: Gross description of gastro-intestinal malignancy is facilitated by endoscopy of the upper and lower gastro-intestinal tract and also provides tissue for definitive diagnosis. Currently, direct vision endoscopic forceps biopsy & FNAC are two standard techniques used to establish a preoperative diagnosis in gastro-intestinal malignancies. The objective of our study is to evaluate the diagnostic accuracy of endoscopic findings when combined with fine needle aspiration and endoscopic biopsy in the diagnosis of gastrointestinal malignancies. So, we compare both techniques (endoscopic forceps biopsy & endoscopic FNAC) to each other and how accurately both techniques are diagnosing the lesion in combination with each other. **Material and Method:** In our study, 40 cases of suspected gastro-intestinal malignancies underwent endoscopic biopsy & FNAC in a period of one and half years. **Result:** Out of 40 cases, total malignant lesions were accounting for 32 cases. 27 cases were diagnosed as malignant by biopsy. FNAC showed positive results in 28 cases. The FNAC was found to be 81.82% Sensitive and 85.71% Specific & an accuracy of 82.5%. Biopsy had Sensitivity 81.82% Specificity 100% & Accuracy 85%. The Combined accuracy of both endoscopic FNAC and biopsy was 93.93%. **Conclusion:** The advent of endoscopic biopsy & FNAC have facilitated the detection & diagnosis of gastrointestinal malignancies. Biopsy though is considered to be diagnostic, Fine Needle Aspiration along with Biopsy can help in the detection of additional cases of malignancy. Thus, both procedures applied together can detect more malignant cases & can establish a more definitive diagnosis.

KEY WORDS: Endoscopy, FNAC, Biopsy, Gastrointestinal Malignancies.

Introduction

Cancer is the leading cause of death in economically developed countries and the second leading cause of death in developing countries[1].GI cancers account for 26% of the global cancer incidence and 35% of all cancer-related deaths[2]. In 2020, 935 thousand deaths from colorectal cancer were recorded worldwide, with 1.9 million new cases and a mortality rate of 55% men and 45% women[3]. For the next 20 years, the World Health Organisation (WHO) predicts an average global increase rate of 3% per year[4].

Gastrointestinal cancers collectively are the commonest malignancies worldwide. These cancers increase sharply in incidence in people in their 60s and 70s[5].Malignant lesions of gastrointestinal tract lesions are detected late as the patients are either asymptomatic or present with mild, nonspecific symptoms in the early stages of the disease. Thus, early detection of malignancy greatly improves the survival rate[6].

Video endoscopy has revolutionized the diagnosis of gastrointestinal diseases[7].Endoscopy of the gastrointestinal tract allows a gross description of lesions and permits sampling of tissue for a definitive diagnosis[8].

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A small proportion of these tumors will remain undetected by conventional techniques (i.e. by endoscopic biopsy only) because only surface cells or tissues are sampled. Primarily infiltrative lesions, ulceronecrotic tumors, and submucosal tumors like lymphomas and sarcomas are difficult to diagnose only by biopsy[9], But the availability of flexible needles allows samples to be obtained from lesions lying deep to necrotic debris or to normal mucosa, and which may be hard to diagnose by conventional (biopsy) means [8,9].The ultimate diagnosis of malignancy is based on histologic or cytologic criteria[8]. Currently, direct vision endoscopic biopsy and FNAC are two standard techniques used to establish the preoperative diagnosis of gastroesophageal malignancies.

The purpose of this prospective study is to compare the diagnostic accuracy of endoscopic fine needle cytology and forceps biopsy with macroscopic appearances and site of the tumor in patients who are suspected of having neoplasm of the esophagus, stomach, intestine, etc. at routine endoscopy.

Materials & Method

Inclusion Criteria: All patients suspected of gastrointestinal neoplasm.

Exclusion Criteria: Patients already diagnosed as having gastrointestinal neoplasm.

Endoscopic forceps biopsy specimens and cytological specimens were taken from 40 lesions suspected of being neoplastic at endoscopy over a period of one and half years from December 2011 to May 2013. All examinations were done with a forward-viewing endoscope and the samples were obtained in the following sequence:

- Fine needle aspiration and
- Forceps biopsy

Finally, the results of endoscopic fine needle aspiration cytology were compared with that of endoscopic biopsy.

FNAC Specimen

Fine needle aspirates are obtained using a flexible sclerotherapy injector with an endoscope with a 0.8cm 23 gauge retractable needle at its distal end. A 20 ml disposable syringe is attached to the hub of an injector. After visualizing the lesion to be investigated injector is introduced through the biopsy channel of the endoscope and advanced to the surface of the target lesion. The needle is then pushed out beyond the protective sheath and introduced into the target lesion. Aspiration is performed by the needle moving back and forth under continuous negative pressure created by applying adequate and gentle suction with the syringe. The suction is gently released and the needle is withdrawn from the lesion. The Procedure is repeated at another site. The needle is then retracted back into the protective sheath before its removal from the forceps channel. Lastly, aspirated material is taken on a glass slide for making smears fixed in formalin and stained with PAP-stained H&E.

Biopsy Specimen

Biopsy specimens were taken using forceps with a central spike and fenestrated cup with a diameter of 2mm. The specimens were fixed in 10% formalin and stained with haematoxylin and eosin stain.

Absence of complication

None of the patients experienced severe subjective discomfort, bleeding, or perforation after the biopsy. In patients who underwent surgical treatment after gastric biopsy, there was no evidence of intraabdominal complaints, such as abscess or hematoma.

Results

The present study includes a total of 40 cases. We compared the diagnosis by two techniques (endoscopic biopsy and endoscopic FNAC) with respect to the site and with respect to the endoscopic finding.

Sitewise distribution of all the cases: Out of 40 cases, 25 (62.5%) cases were of the esophagus, 7 (17.5%) of the stomach, 2 (5%) of the small intestine, and 6 (15%) of the colon and rectum.

Number of cases according to the endoscopic finding: In our study Out of 40, 24 (60%) cases were of friable growth; 5 (12.5%) nodular or polypoidal growth; 4 (10%) stricture; 6 (15%) ulcerative lesions and 1 (2.5%) of thickened wall.

Comparative diagnosis of two techniques

Out of total 40 cases 32 cases were malignant. among these 32 cases 22 were squamous cell carcinoma (Figures 2 and 3) and 9 were adenocarcinoma and 1 was leiomyoma.

A comparison of both techniques in gastrointestinal lesions showed 28 cases of malignancy by FNAC and 27 cases by biopsy out of all 40 cases. Both the techniques showed the same diagnosis of malignancy in 23 cases (Table 1).

Table 1 shows cross-tabulation of FNAC vs. Biopsy findings for all cases. There were 9 cases where discrepancies aroused between the diagnosis by two techniques. Of these 9 cases, 4 cases were diagnosed as malignant by biopsy, where FNAC reported either inflammatory in 1, benign in 1, and paucicellular in 2 cases.

In the remaining 5 cases FNAC raised suspicion of being malignant where the biopsy was negative for malignancy. On endoscopic biopsy out of these 5 cases, 3 cases showed dysplastic changes only. In these 3 cases, 2 were friable growth, one at gastroesophageal junction and other at D1D2 junction which was a peripherally located tumor in intestinal wall in the region of ampulla of vater which was difficult to be accessed by biopsy. One was stricture at the lower end of the esophagus (Figure 1). Here biopsy (Figure 2) missed the growth due to the limited access of biopsy probe while on FNA (Figure 3), needle was able to take out the material as needle can penetrate through the stricture and go deeper. On excision, it came out to be squamous cell carcinoma.

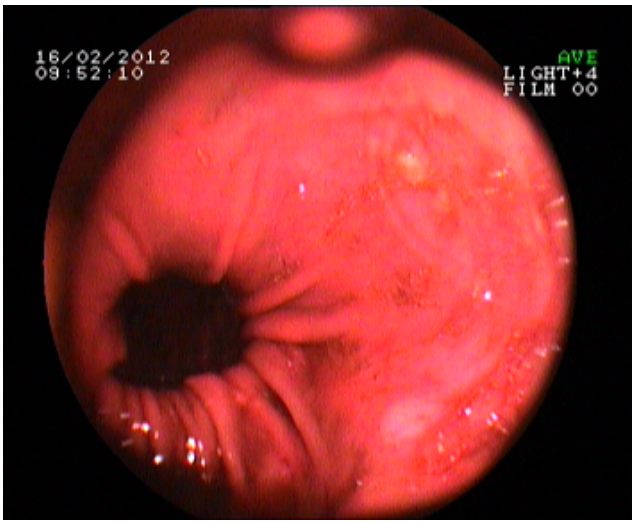

Figure 1: Endoscopy: Presence of stricture at 30 cm

The remaining 2 biopsies out of these five cases showed benign tumors. One of them was stricture at the lower end of the esophagus. On excision, it came out to be squamous cell carcinoma. The other one was a polypoid growth in the stomach (fundus) and was diagnosed as leiomyoma stomach after excision.

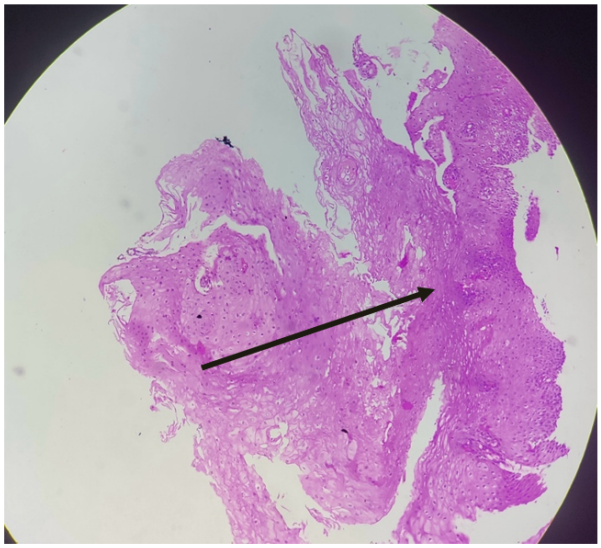

Figure 2: Histopathology: Stratified Squamous epithelium with mild dysplasia. Invasion could not be commented upon (H&E 40X).

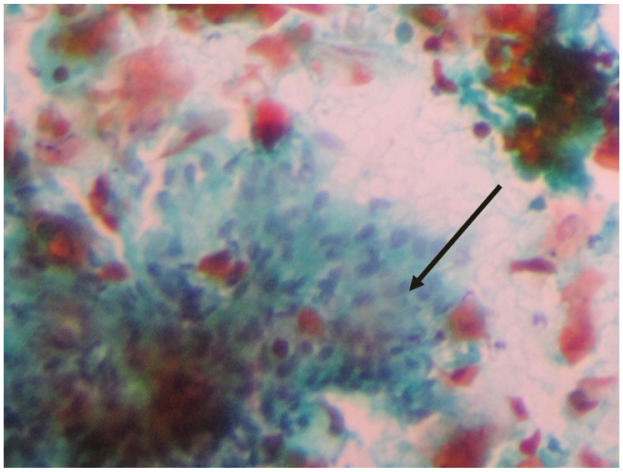

Figure 3: Squamous cell carcinoma: Loose clusters of keratinized malignant cells, hyperchromatic nuclei, very high N/Cs, and cyanophilic cytoplasm are present. (PAP: 40X)

Thus FNAC had a sensitivity of 81.82%, specificity of 85.71%, positive predictive value of 96.42%, negative predictive value of 50%, accuracy of 82.5%, Kappa statistics 0.527; p-value < 0.05, Significant.

Biopsy had sensitivity of 81.82%, specificity of 100%, positive predictive value of 100%, negative predictive

Table 1: FNAC finding Vs Biopsy findings: Cross tabulation of all cases

		Diagnosis of biopsy					
		Malignant	**Benign**	**Dysplastic Epthelum (Adenoma)**	**Inflammatory**	**Inadequate for Opinion**	**Total**
Diagnosis on FNAC	Malignant	23	2	3	-	-	28
	Benign	1	-	-	-	-	1
	Dysplastic	-	-	1	-	-	1
	Inflammatory	1	-	-	4	-	5
	Paucicellular	2	-	1	-	2	5
	Total	27	2	5	4	2	40

value of 53.84%, accuracy of 85%, Kappa statistics 0.612 ; p-value < 0.05, Significant.

The combined accuracy of both endoscopic FNAC and biopsy was 93.93%.

Discussion

Our study included total of 40 cases. We compared the diagnosis by two techniques with respect to the site and with respect to the endoscopic finding.

In our study, for esophageal lesions, FNAC was more sensitive but the combination of the two techniques increased diagnostic accuracy. FNAC showed positive results in 21/25 cases and biopsy in 19/25 cases. Some cases were missed by FNAC & some were missed by biopsy. Particularly cases of strictures and in small peripherally located growth were missed by biopsy and FNAC gave the correct diagnosis. There is a substantial likelihood that a biopsy may miss a growth, particularly in cases of strictures and tiny growths located in the periphery. FNAC may provide the right diagnosis in certain circumstances. Due to the limited access to biopsies, the majority of patients with strictures undergo unsuccessful diagnostic procedures. In these cases, FNA can provide a diagnosis[8,10,11]. Additionally, it has been stated that EUS-FNA/B is a minimally invasive and useful diagnostic technique that is crucial in the identification of gastrointestinal subepithelial tumors[12]. It is emphasized that repeating a biopsy may be necessary for high diagnostic accuracy. A single biopsy may not be sufficient to avoid the possibility of a false negative report.

In our study among cases of gastric malignancies, biopsy was found to be more sensitive as compared to FNAC. Biopsy diagnosed 3 out of 7 cases as malignant while FNAC suggested malignancy in 2/7 cases. However a single-center smaller case series[13] published, reported an accuracy of 83.3% in EUS-FNA of thickened gastric walls and suggested that EUS-FNA/FNB is necessary for patients with a thickened gastric wall and prior negative biopsy on endoscopy.

FNAC gave false positive report in one case which was found to be benign on biopsy. Later on it was found to be leiomyoma after operation. Although in skilled hands, false positive cytology results are uncommon, epithelial cell contamination and pathologic misinterpretation are two common causes of false positive outcomes.

In the present study lesions of the Small Intestine, FNAC (2/2) proved to be better as compared to biopsy (1/2). In one case FNAC gave the diagnosis of adenocarcinoma where biopsy failed to diagnose. This was a peripherally located tumor in the intestinal wall in the region of the ampulla of vater which was difficult to be accessed by biopsy. Similarly, one study reported a mass at the region of the ampulla of Vater partially obstructing the pancreatic duct. The initial punch biopsy yielded only intestinal mucosa. Subsequent endoscopic FNAC suggested the diagnosis of a malignancy, as confirmed by additional punch biopsies[14].

In Colonic & Rectal lesions, the biopsy was found to be more accurate than FNAC. FNAC gave positive results in 3/6 cases and on biopsy 4/6 cases were found to be positive for malignancy. FNAC gave false negative results in one polypoid lesion in the rectum which was found to be adenocarcinoma on biopsy. This is in contrast to a study where Fine needle aspiration cytology has increased the diagnostic yield in oesophageal and colonic lesions[15]. Similarly, biopsy positive in 27/30 (90%) and fine needle

aspiration cytology in 29/30 (96.6%) of rectal lesions was reported by an author [16]. A Sensitivity of 83.6% for biopsy of colonic cancer was also reported in one study [17].

We also compared the results of FNAC and biopsy with respect to endoscopic findings. The most common cases were friable growth (24/40 or 60%) in our study. In friable growth, FNAC had more accuracy as compared to biopsy especially where it is small and/or peripherally located growth. The accuracy of FNAC was 87.5% (21/24) and of biopsy 83.33 % (20/24). The combined accuracy was 95.83% in our study.

It is mentioned in literaturethat fine needle aspiration cytology may sample the fungating growths better [16]. This was in contrast to studies where the accuracy of the biopsy was more than that of FNAC [7,8].

In cases of polypoidal lesions, accuracy of biopsy for malignancy was more (3/3) as compared to FNAC (1/3) in our study. In one case there was a hard growth in the stomach. In that case, we could not aspirate the material and the biopsy also was inconclusive. This may be because of the plugging of the needle or blunting of the needle to penetrate a hard mass.

In our study, FNAC proved to be more sensitive (3/4) as compared to biopsy (1/4) for Strictures. In two cases biopsy was negative whereas cytology was positive for malignancy. Endoscopic FNAC was found to have sensitivity (96%), specificity (90%), and diagnostic accuracy (98%), the efficiency of this technique was better in necrotic, stenotic, and infiltrative gastro-esophageal malignancies. A prospective research comparing the diagnostic accuracy of forceps biopsy with endoscopic fine needle aspiration cytology, aspiration cytology showed significantly better results in cases of infiltrative cancers (95.8% vs. 78.9%) [7]. Similarly, another study also found that all three infiltrative tumors were correctly diagnosed by fine needle aspiration cytology and is likely to have better sensitivity in infiltrative and submucosal tumors, though the number of patients with infiltrative tumors was quite small in their study [12]. This was also true with our study.

Our study showed the overall diagnostic superiority of the conventional technique of forceps biopsy to the endoscopic fine needle aspiration cytology. The cumulative accuracy of biopsy was higher than the cytology; however, significantly better results were obtained when the biopsy was combined with fine needle aspiration cytology. Fine needle aspiration was more sensitive in malignancies as compared to forceps biopsy in lesions like stricture and small peripherally located lesions. Furthermore, this technique yielded positive results in 4/33 (12.12%) malignant lesions with false negative biopsy. Likewise, biopsy yielded positive results in other 4/33 (12.12%) malignant lesions with false negative FNAC in these cases. Thus, adding endoscopic fine needle aspiration to the existing conventional technique of biopsy is an advantage. This was also supported by other studies [18–20]. The absence of any complications adds further value to this technique. Many studies [21–24] have reported that other cytology methods like brush cytology can also increase the diagnostic yield in infiltrative tumors and obstructing lesions that prevent the passage of the endoscope to the desired site. In our study, the combination of biopsy and cytology improved the accuracy, which agrees with the results of others [25–28] and the false negative rates were significantly lower when aspiration cytology was combined with biopsy. Our study is relatively consistent with those of other authors [7,8,29,30] (Table 2).

Table 2: Comparison of Diagnostic Accuracy Of Endoscopic FNAC And Endoscopic Biopsy With Other Studies

	Biopsy	FNAC	FNAC+Biopsy
Zargar et al [7]	87.2%	94%	98.5%
Katti et al [8]	89%	95%	100%
Kochar et al [29]	88.8%	89.1%	100%
Malhotra et al [30]	90%	83.3%	100%
Present study	85%	82.5%	93.9%

When sampling techniques were used in isolation, the diagnostic sensitivity was less but the combination was found to have higher sensitivity, specificity, and diagnostic accuracy.

Conclusion

We conclude that endoscopic fine needle aspiration cytology is a simple, rapid, safe, and accurate method for the diagnosis of endoscopically visualized malignancies and is of particular value in cases of stricture and small and/or peripherally located malignancies. The higher yield of needle aspiration in these lesions is due to its ability to allow adequate cytological

sampling from the deeper layers. Although the numbers with stricture and small and/or peripherally located malignancies were small in our study, consistently gratifying results were obtained with aspiration cytology for such lesions. It is concluded that fine needle aspiration cytology should be routinely combined with conventional techniques (biopsy) in an attempt to increase the yield for the diagnosis of gut malignancies. This would in turn enhance the survival rate tremendously as the malignancy would be diagnosed early and management can be favorably modified. Thus the techniques are complementary and when used in combination will help to achieve better diagnostic accuracy.

Limitation of the study

Though endoscopic FNAC proves to be simple, safe and reliable technique in obtaining higher yield and diagnostic accuracy in necrotic deeply infiltrative stenotic tumor and those located in submucosa, but it has limitation of giving false negative results in pts with ulcerative / friable growth. Numbers with stricture and small and/or peripherally located malignancies were small in our study, although consistently gratifying results were obtained with aspiration cytology for such lesions.

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