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Histo Morphological Evaluation of Esophageal Lesions

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Keywords
Adenocarcinoma, Barrett esophagus, Dysphagia, carcinoma, weight loss, inflammatory

Abstract
Background: Esophagus is a tubular structure of the gastrointestinal tract with primary pathological lesions including neoplastic and non-neoplastic conditions. It can secondarily be involved by mediastinal lesions, hence the need to detect and differentiate lesions at an early stage.
This study has been incorporated to emphasize the prevalence of different esophageal lesions with the site-wise distribution along with the comparison of their incidences to age and sex.
Methodology: Our study was done at the department of Pathology, father muller medical college, in Mangalore from January 2020 to January 2021. All the cases were assessed concerning age, chief complaints, site of lesion, and histomorphology. Hematoxylin and eosin staining was performed on paraffin-embedded sections which were microscopically analyzed and categorized into various categories.
Results: The study included a total of 61 cases with various ages ranging from 31 to 80 years and a mean age presentation of 52.5 years. The most common primary chief complaint was dysphagia 70%. Neoplastic conditions constituted 78.7 % with the most common neoplastic condition being Squamous cell carcinoma at 67.7%
Conclusions: In the present study, we demonstrate that there can be different kinds of lesions in the esophagus all presenting with a similar complaint of dysphagia. Hence it is necessary to evaluate the microscopic findings of each case with due diligence. A spectrum of various Inflammatory and neoplastic conditions can be seen to occur in the esophagus.

1. Introduction

The esophagus is a tubular structure of the gastrointestinal tract and various primary pathological lesions may be encountered. Like non-neoplastic inflammatory conditions, viral, fungal esophagitis, and neoplastic conditions.

One of the most prevalent cancers of the gastrointestinal tract is from the esophagus, the seventh most frequent in the world. Esophageal cancer is the third most diagnosed cancer in the gastrointestinal system after colorectal cancer (10.2%) and stomach cancer (5.7%). [1]

Studying the underlying pathology of esophageal lesions is essential to better understand the disease's clinical progression. Sometimes these lesions go undetected or may present with just dysphagia and minor clinical consequences. These lesions may be detected, diagnosed, staged, and treated using endoscopic findings, which are crucial.

.Endoscopic evaluations, radiologic imaging, and better knowledge of the condition will help diagnose these tumors more often since they are tiny and asymptomatic. [3,2]

TNM staging is used for esophageal cancer, which is the generally acknowledged method. It is critical to understand the disease's progression to plan appropriate therapy for each stage. For staging, common imaging modalities are computed tomography scans (CT), endoscopic ultrasonography studies, and positron emission tomography scans (PET). The available methods of management now available include surgery, radiation therapy, and chemotherapy as the pillars of modern therapy. [4]

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It is well known that esophageal cancer spreads by several mechanisms, including the lymphatic and hematogenous spread of the disease. The status of the serosal lining of the esophagus is very critical to determine the extension of malignancy. Because of the lack of anatomical barriers, the tumor has the potential to fast spread throughout the region, including the larynx, and other vital organs.[5]
Hence the necessity to detect any lesion at early stages and differentiate them.

2. Objective

Specimens that included biopsy, as well as surgical resections, were studied to seek

1. The Histo-morphological spectrum of esophageal lesions.
2. Categorize the various sorts of inflammatory and neoplastic lesions of the esophagus.
3. Estimate the frequency of those various esophageal lesions according to age and sex.
4. Site-wise distribution of varied inflammatory and neoplastic lesions.

3. Materials And Methods

- Source of the data:
The study group involved cases of all age groups, and gender, who underwent esophageal surgical resection / endoscopic biopsy in Father Muller Medical College Hospital.

- Method of data collection:
A complete medical history comprising age, symptomology, period of symptoms, and demographic details were attained and then converted into a master chart, which was subjected to statistical analysis.

- Study period:
January 1st, 2020 to January 1st, 2021 (One year prospective study)

- Inclusion criteria:
  - All age groups
  - Male and female patients.
  - Underwent esophageal surgical resection/ endoscopic biopsy in Father Muller Medical College Hospital.
- Exclusion criteria:
  - Inadequate and non-diagnostic samples

Sample size:
The sample size of Sixty cases was arrived at by using the
formula,
$\eta=Z\alpha^2p(1-p)/e^2$
with a Z alpha value of 1.96 at 95% Confidence intervals
and 4.13%power, e = allowable error (5%)
Histologic procedure of biopsy and resected specimens:
The esophageal lesions biopsy specimens were immediately deposited in 10% buffered neutral formalin for histological examination.
The surgical specimens were cut from one end to the other while they were still intact. Observations were made on the tumor's gross appearance.
The mucosa proximal as well as distal to the tumor were examined.
3-5mm sections were taken as well as lymph nodes, which had been preserved in 10% buffered formalin and processed using a Leica tissue processor.

- Histopathologic analysis and staging:
To examine the histopathological characteristics, the sections were stained using hematoxylin and eosin standard staining procedures. Esophageal lesions were then analyzed, characterized, and diagnosed following the published WHO criteria and AJCC 8th edition criteria. The features of esophagitis, dysplastic alterations, Barrett's esophagus with intestinal metaplasia, and benign and malignancies were all documented. Esophageal erosions and nonspecific alterations were also thoroughly investigated. Histochemistry with Mucicarmine and PAS was used in cases where it was appropriate.

- Statistical analysis:
The data collected was then transformed into a master chart, which was subjected to statistical analysis using frequency percentage and Chi-square test.

4. Results

Sixty-one cases have been included in our study, out of which 58 comprised biopsies and three resection specimens, and all of which the morphologic features were analyzed

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AGE PRESENTATION:
Of the 61 cases, the majority were distributed in the age group of 61- 70 (18 cases) followed by 51-60 (17 cases). The median age is 52.5 years. [fig.1]

GENDER DISTRIBUTION: Of the 61 cases, 38 (62.3%) were male and 23 (37.7%) were female. [Fig 2]

SPECIMEN TYPE:
Of the 61 specimens, 58 (95.1%) are endoscopic biopsies and three (4.9%) are resected esophagectomy specimens [Table 1]

PRIMARY CHIEF COMPLAINTS: The most common primary complaint, the patients presented with is dysphagia (43 cases). The other primary complaints were abdominal pain, loss of appetite, heartburn, odynophagia, and abdominal discomfort. [Fig 3]

SECONDARY CHIEF COMPLAINTS:
The most common secondary complaint, the patients presented with is weight loss (30 cases). The other secondary complaints were loss of appetite, dysphagia, abdominal pain, abdominal discomfort, reflux, and heartburn. [Fig 4]

SITE OF BIOPSY:
Of the 61 cases, 31 cases (50.8%) were from the esophageal lower segment, 17 cases (27.9%) were from the mid-segment, and 13 cases (21.3%) were from the upper segment. [Table 2]

DISTRIBUTION OF THE CASES: Of 61 cases in our study, 48 (78.7%) were neoplastic, 9 (14.8%) inflammatory, and four (6.6%) other. [Table 3]

HISTOPATHOLOGICAL SPECTRUM: Of the 61 cases, 37 (67.7%) cases were diagnosed as squamous cell carcinoma, nine (14.8%) cases were diagnosed as adenocarcinoma, four (6.6 %) cases had features of post-chemoradiation response, three (4.9%) cases were diagnosed as esophagitis, two (3.3%) cases were diagnosed as gastroesophageal reflux esophagitis, two (3.3%) cases were diagnosed as Barrett's esophagus, one case each of inflammatory polyp, stricture, and carcinoma in situ and rare case of adenosquamous carcinoma. [Table 4]

DISTRIBUTION OF LESIONS - FEMALES:
Of the 23 cases of female patients, 15 (65%) cases were neoplastic, five (22%) were inflammatory, and three (13%) other. [Fig. 7]

SITE-WISE DISTRIBUTION OF LESIONS - FEMALES:
Of the 23 cases, the upper esophagus was the site of 11 conditions, including, Barrett esophagus, reflux esophagitis, squamous cell carcinoma, and adenocarcinoma, all of which occurred in this region.
Nine cases of esophagitis, squamous cell carcinoma, and post-chemoradiation response were found in the esophageal middle segment.
Carcinoma, stricture, and post-chemoradiation reaction were three of the lower esophageal cases studied. [Table 6]

DISTRIBUTION OF LESIONS - MALES:
Of the 38 cases of male patients, 33 (86%) cases were neoplastic, four (11%) were inflammatory, and one (3%) other [Fig. 8]

SITE-WISE DISTRIBUTION OF LESIONS - MALE:
Of the 38 cases in males, 20 cases were from the lower segment of the esophagus and included Inflammatory polyp, reflux esophagitis, squamous cell carcinoma, adenocarcinoma, adenosquamous carcinoma, and post-chemoradiation response.
10 cases were from the upper segment of the esophagus and included esophagitis and squamous cell carcinoma.
Eight cases were from the esophageal middle segment and included malignancies like squamous cell carcinoma and carcinoma in situ. [Table 7]

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Distribution of cases

TYPE OF LESION	NUMBER	PERCENTAGE
INFLAMMATORY	9	14.8%
NEOPLASTIC	48	78.7%
OTHER	4	6.6%

Table 1: Percentage distribution of cases

Histopathological spectrum

Table 2: Percentage distribution of all Histopathological lesions

HISTOPATHOLOGICAL DIAGNOSIS	NUMBER	PERCENTAGE
ESOPHAGITIS	3	4.9%
GASTROESOPHAGEAL REFLUX ESOPHAGITIS	2	3.3%
INFLAMMATORY POLYP	1	1.6%
STRICTURE	1	1.6%
BARETT'S ESOPHAGUS	2	3.3%
CARCINOMA IN SITU	1	1.6%
SQUAMOUS CELL CARCINOMA	37	67.7%
ADENOCARCINOMA	9	14.8%
ADENOSSQUAMOUS CARCINOMA	1	1.6%
POST CHEMORADIATION RESPONSE	4	6.6%

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Site wise distribution - Male

SEGMENT OF ESOPHAGUS	DIAGNOSIS
Upper (10)	- Esophagitis – 1 - Squamous cell carcinoma – 9
Middle (8)	- Carcinoma in situ – 1 - Squamous cell carcinoma – 7
Lower (20)	- Inflammatory polyp – 1 - Reflux esophagitis – 1 - Barrett's – 1 - Squamous cell carcinoma – 7 - Adenocarcinoma – 8 - Adeno-squamous carcinoma – 1 - Post chemo-radiation response – 1

Table 3: Site-wise distribution - Male

Site wise distribution - Female

SEGMENT OF ESOPHAGUS	DIAGNOSIS
Upper (11)	- Esophagitis – 1 - Barrett's – 1 - Reflux esophagitis – 1 - Squamous cell carcinoma – 7 - Adenocarcinoma – 1
Middle (9)	- Esophagitis – 1 - Squamous cell carcinoma – 6 - Post chemo-radiation response – 2
Lower (3)	- Stricture – 1 - Squamous cell carcinoma – 1 - Post chemo-radiation response – 1

Table 4: Site-wise distribution - Female

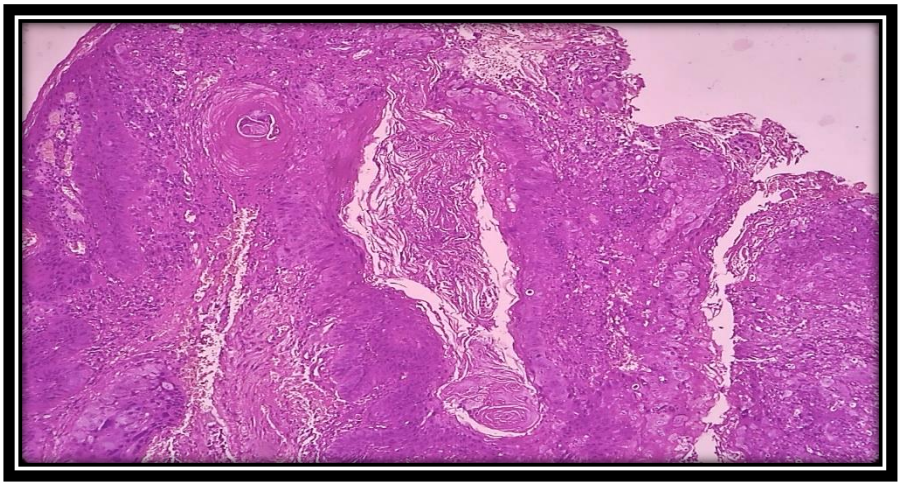

Fig 1 : Photomicrograph of well differentiated squamous cell carcinoma (H&E, x100)

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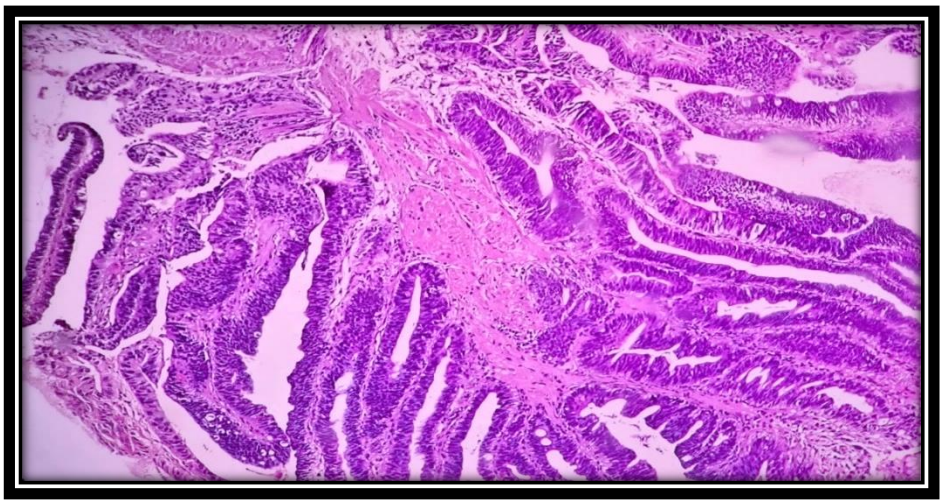

Fig 2 : Photomicrograph of well differentiated Adenocarcinoma (H&E, x100)

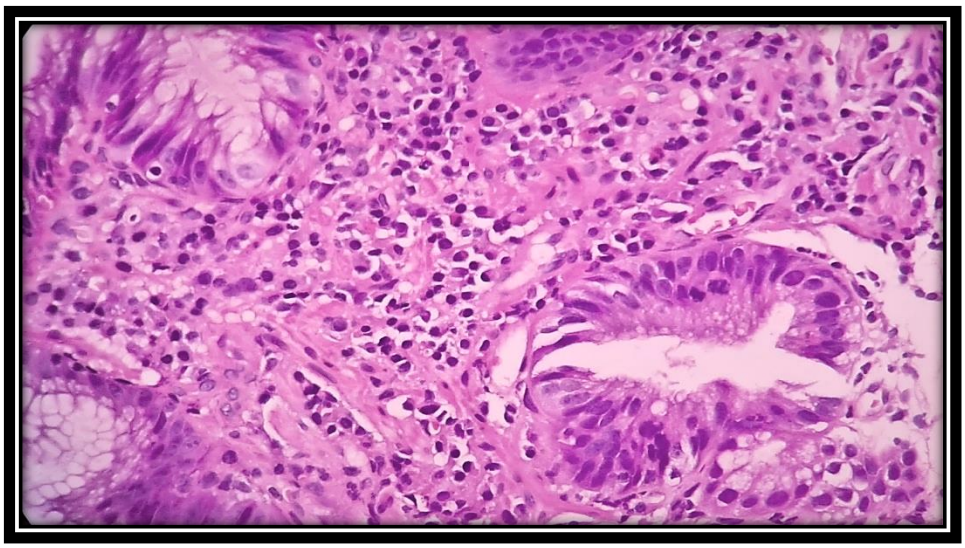

Fig 3: Photomicrograph of inflammatory infiltrate in reflux esophagitis (H&E, x400)

5. Discussion

Our study was conducted from January 2019 to January 2020 and comprised 61 cases which included 58 endoscopic biopsies as well as three resection specimens that were received at the histopathology laboratory of Father Muller Medical College Hospital, Mangalore.

The most common clinical presentation for most of the patients was primarily with the symptom of dysphagia, seen in 70% of the cases followed by the secondary complaint of weight loss in 49% of the cases.

This was similar to other studies done by Orringer et al[6], where dysphagia was seen in 90%, and also the studies by Dhaval Choksi, Bhukari, and Kavitha where dysphagia was seen in most of the cases followed by weight loss. [7,8,9]

But worrisome is the rapidly progressing dysphagia of a very short duration, as it usually ends up being diagnosed as esophageal carcinoma, leading to the progressive decrease in appetite and therefore weight loss[10-11]

Gender distribution in this study: The number of male patients was higher than female counterparts, with a male: female ratio of 1.65. This has

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similarities to the findings of the study by Krishnappa, where the ratio was 2.03:1 [12], and another study by Shilpi with a ratio of 4.7:1 [13].

It is often hypothesized that male preponderance may be attributable to the reason men are more likely to be exposed to behaviors like smoking and drinking.

Distribution of Lesions: The histo-morphological evaluation of esophageal lesions helps pathologists to make a diagnosis of an inflammatory lesion or confirm the diagnosis in the cases suspected of malignancy, having an important role, overall in the management and prognosis.

In our study, the common age group of the cases belonged to the 61 to 70 years range, and the neoplastic lesions were found to be more (78.6%) compared to the non-neoplastic lesions (1.63%) which concordant with the observations in other studies done by Kavitha et al[9], and Bhukari et al[8] but discordant with observations of Krishnappa et al, where the non-neoplastic lesions were more in number compared to the neoplastic lesions. [12]

Site-wise distribution of malignancy: In our study, most of the malignancies were seen in the esophageal lower segment (50.8%) followed by the middle (27.9%), and showed similarity to the observations of studies of Kavitha and Jijo Cherian. [9,14]

This data from the various studies including this study suggest that overall, esophageal malignancies tend to present in the lower and middle segments as compared to the upper segment.

Distribution of malignancy: The most common malignancy was squamous cell carcinoma of the neoplastic lesions in our study, comprised (77%), followed by adenocarcinoma cases (18%) which is similar to the observations of other studies by Jijo cherian et al[14], Dhaval Choksi et al[7], Bhukari et al[8], and Krishnappa et al[12] and Study after study including ours found that squamous cell carcinoma was the most prevalent esophageal tumor.

The gender ratio for malignant lesions:

In this study, we found a high male-to-female ratio (2.2:1) in terms of malignant cases in which males constituted a total of 33 cases including squamous cell carcinoma, adenocarcinoma and other cases of adenosquamous carcinoma and carcinoma in situ. Females were 15 cases.

These findings are concordant with studies by Cherian et al[14], Zhang et al [15], Fernandes et al[16,] and Hansson et al[17].

This could be due to the increased risk factors of tobacco consumption as stated earlier, however, recent studies in other countries, such as Wang et al., show an increase in incidence in females.[18]

Because of the risk factors of alcohol habits and smoking habits. This is a health concern that needs to be identified in the present-day scenario.[19]

Endoscopic presentation of squamous cell carcinoma:

The presentation of esophageal Squamous cell carcinoma endoscopically was a proliferative mass in most 61% of the cases followed by ulcerative growth in 23%, and mucosal irregularity and stricture in 8% of cases each.

Endoscopic presentation of Adenocarcinoma:

Adenocarcinoma of the esophagus endoscopically presented most commonly as ulcerative growth in 62.5% of cases, and as a proliferative mass in 37.5% of cases.

Distribution of non-neoplastic lesions:

Most common of the non-neoplastic lesions were cases of chronic esophagitis, which accounted for 34 percent of the total. Reflux-associated esophagitis and Barrett's esophagitis accounted for 22 percent each.

These findings are similar to the research of Abhilash SC et al[20], Yevoor[21], Khandelia[22], and Hirachand et al.[23] However reflux associated esophagitis were higher compared to other conditions in the study by Somani[24]

6. Conclusion

Patients with esophageal pathology usually display dysphagia and present with the sensation of food sticking in their chest, the reason can be both benign or malignant entities including motility disorders as well as mechanical obstructions and other causes that decrease the lower esophageal sphincter pressures, causing reflux Thus, Endoscopic assessment may detect cancer in many situations and is highly recommended, particularly in elderly patients with dysphagia. The esophageal biopsies, as well as the biopsy location and any associated

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clinical information, should be thoroughly scrutinized for any signs of premalignant diseases. A proliferative mass is a common gross finding of esophageal squamous cell carcinoma, and in 31 of the 64 instances in our research, this was the case.

Statement of ethics: The above study protocol has been approved by Father Muller Medical College's institutional Ethics and Scientific committee.

Disclosure statement: The above authors have no financial conflict of interest to disclose

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