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Original Article

Histological pattern of esophageal cancer at BP Koirala memorial cancer hospital in Nepal: a three year retrospective study

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ABSTRACT

Background: The incidence of esophageal adenocarcinoma is increasing in trends. Squamous cell carcinoma is associated with tobacco and alcohol consumption. Adenocarcinoma is often associated with a history of gastroesophageal reflux disease and Barrett's esophagus. The aim of this study was to find out the histological pattern of esophageal cancer in one of the largest Cancer center in Nepal.

Materials and Methods: Between January 2008 and December 2011, a total of 106 cases of esophageal cancer were received in the department of pathology, BP Koirala Memorial Cancer Hospital. Relevant clinical data were retrieved from computer database of the hospital.

Results: A total of 106 cases of esophageal carcinomas were diagnosed during a three years period. There were 68 (64.15%) cases of squamous cell carcinoma, 33 (31.13%) cases of adenocarcinoma including signet ring cell carcinoma, 4 (3.76%) cases of undifferentiated carcinoma and 1 (0.94%) case of small cell carcinoma. The esophageal cancer was most common in the age group of 61-70 years of age. Distal third of esophagus was the most common site for esophageal carcinoma, followed by middle esophagus and proximal esophagus.

Conclusion: The most frequent type of esophageal carcinoma is squamous cell carcinoma followed by adenocarcinoma. Distal esophagus is the most common site with male preponderance.

INTRODUCTION

Esophageal cancer is the 6th most common cause of cancer death worldwide with about 386,000 deaths in 2002.[1] The Incidence of esophageal cancer has been increasing, with a shift from squamous cell carcinoma (SQC) arising in upper/ middle third of esophagus to adenocarcinoma arising in distal esophagus.[2] The rates of esophageal adenocarcinoma in United States of America have increased over the past 30 years, while the rates of esophageal SQC have decreased.[3-5]

Predisposing factors for SQC include a high alcohol intake and heavy use of tobacco.[6] The other risk factor is consumption of burning hot beverage which causes thermal injury leading to chronic esophagitis and then

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to precancerous lesion. Esophageal adenocarcinoma arises most frequently in Barrett's epithelium through a series of progressive degrees of dysplasia; from intestinal metaplasia, to low grade dysplasia, high grade dysplasia and subsequently to cancer.[7,8] Infrequently adenocarcinoma originates from heterotrophic gastric mucosa in the upper esophagus or from submucosal glands.

Small cell carcinoma (SCC) represents 1% of esophageal tumors. It usually affect male over 50 years of age. The common site is lower esophagus. It appears to arise from same multipotent epithelial basal cells that produce SQC; both tumors often intermingle.[9] Immunohistochemical reaction for neurone-specific enolase, synaptophysin and chromogranin usually are positive and represent diagnostic marker for SCC.[10]

Undifferentiated carcinoma of the esophagus is rare but highly malignant tumor.

In the WHO classification, undifferentiated carcinoma is defined as a tumor that has no ductal or squamous epithelial structure to indicate definite differentiation. It does not include SCC.[11]

The aim of this study was to find out the histological pattern of esophageal cancer in one of the largest cancer center in Nepal.

MATERIALS AND METHODS

This was a retrospective study conducted in the department of pathology, BP Koirala Memorial Cancer Hospital in Bharatpur, Chitwan between January 2008 and December 2011. The study consisted of 106 (endoscopic biopsies=57, radical esophagectomy specimens=49)) cases of esophageal carcinoma. The Hematoxylin and Eosin stained sections in all cases were reviewed by the authors and diagnosis was confirmed. Immunohistochemical staining for synaptophysin and chromogranin A was performed by the avidin-biotin-peroxidase technique, using ABC staining kits (Vector Laboratories, CA), following vendor's instructions. Relevant clinical data were retrieved from computer database of the hospital. The distribution of age, sex, and location of tumors were analyzed. Statistical analysis was done by using SPSS version 17.0 for windows.

RESULTS

There were a total of 106 cases of esophageal carcinoma. Out of 106 cases, 57 (53.8) were males and 49 (46.2%) were females. The male to female ratio was1.2:1. The esophageal cancer was most common in the age group of 61-70 years, comprising 34% of total cases. The esophageal cancer was uncommon in less than 30 years or more than 80 years of age. The age distribution of esophageal carcinoma is shown in Table 1.

Histopathological findings

Gross findings

The gross findings in SQC were either exophytic or ulcerative lesion with deep irregular ulcers (fig. 1). The

Table 1: Age distribution of esophageal Cancer

Age group (yrs)	Number of cases	Percentage (%)
≤30	3	2.8
31-40	5	4.7
41-50	16	15.1
51-60	31	29.2
61-70	36	34.0
71-80	11	10.4
≥81	4	3.8
Total	**106**	**100**

Figure1: *Macroscopic appearance of SQC showing ulcerative growth pattern with elevated ulcer edges.*

Table 2: Location of esophageal tumors

Histological type	Proximal esophagus		Middle esophagus		Distal esophagus		Site not mentioned		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%
SQC	14	13.21	22	20.75	21	19.81	11	10.38	68	64.15
Adenocarcinoma	0	0	2	1.89	27	25.47	4	3.77	33	31.13
Undifferentiated carcinoma	0	0	2	1.89	0	0	2	1.89	4	3.78
SCC	0	0	1	0.94	0	0	0	0	1	0.94
Total	**14**	**13.21**	**27**	**25.47**	**48**	**45.28**	**17**	**16.04**	**106**	**100**

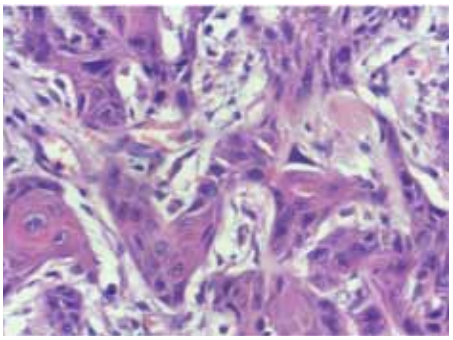

Figure 2A: *Moderately differentiated SQC. The tumor shows focal area of keratinization (HE stain, X200)*

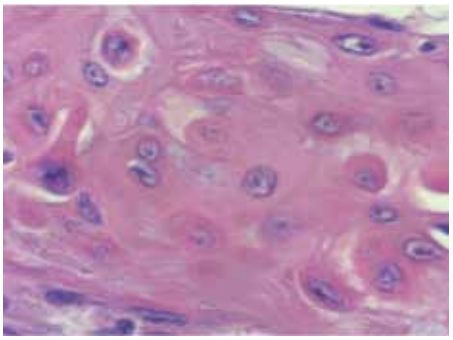

Figure 2B: *SQC with prominent individual cell keratinization (HE stain, X400)*

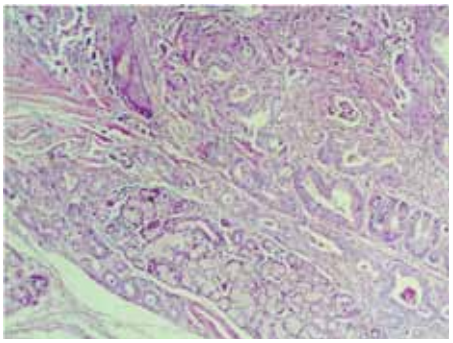

Figure 3A: *Infiltrating sheets of adenocarcinoma in inflammatory stroma. The submucosal glands are surrounded by tumor nests at the bottom (HE stain, X200).*

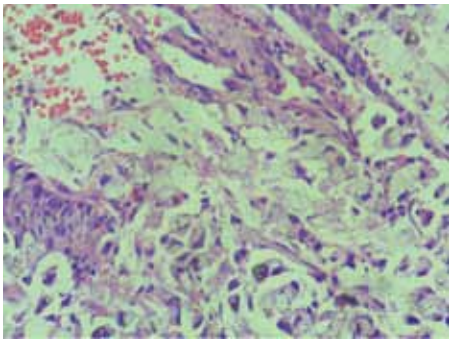

Figure 3B: *Poorly differentiated adenocarcinoma with signet ring cell differentiation (HE stain, X200).*

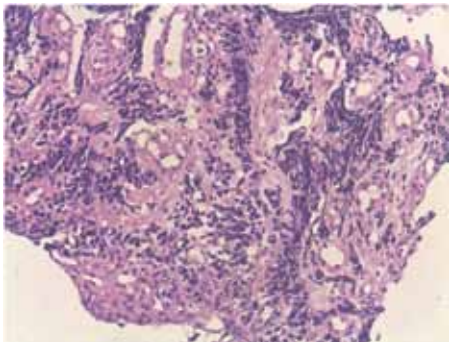

Figure 4A: D*iffuse infiltrating sheets and nests of small, round to oval cells with densely hyperchromatic nuclei with fine and granular chromatin and scant cytoplasm. Crush artifact is evi****dent*** *(HE stain, X100)*

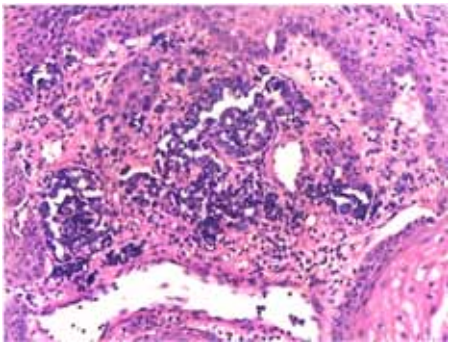

Figure 4B: *Small cell carcinoma with focal glandular component (HE stain, X100).*

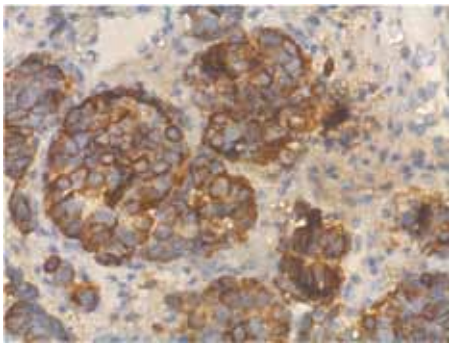

Figure 4C: *Diffuse cytoplasmic staining of tumor cells for Chromogranin A (Original magnification, X200)*

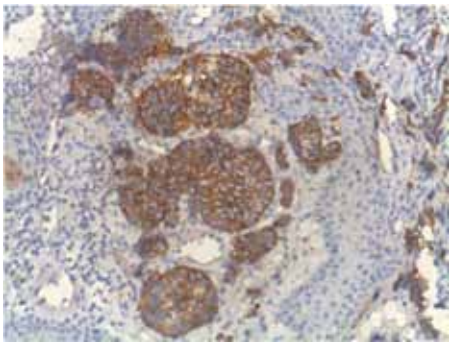

Figure 4D: *Diffuse cytoplasmic staining of tumor cells for synaptophysin (Original magnification, X100)*

adenocarcinoma in distal esophagus showed flat patches to nodular masses. All the tumors were solitary type. The location of esophageal carcinoma is shown in Table 2.

Distal third of esophagus was the most common site for esophageal carcinoma, followed by middle esophagus and proximal esophagus. The maximum number of SQC was seen in middle esophagus (n=22) followed by distal (n=21) and proximal esophagus (n=14). Similarly the maximum number of adenocarcinoma was seen in distal esophagus (n=27) followed by middle esophagus (n=2).

Microscopic findings

Out of 106 cases, there were 68 (64.15%) cases of SQC (fig. 2A and 2B), 33 (31.13%) cases of adenocarcinoma (fig. 3A) including 6 cases of signet ring cell carcinoma (fig. 3B), 4 (3.76%) cases of undifferentiated carcinoma and 1 (0.94%) case of SCC (fig. 4A and 4B).

Out of 68 cases of SQC, 25 (23.58%) were well differentiated, 37 (34.91%) were moderately differentiated and 6 (6.58%) cases were poorly differentiated SQC.

Out of 33 cases of adenocarcinoma, 11 (10.35%) cases were well differentiated, 9 (8.47%) were moderately differentiated and 7 (6.58%) cases were poorly differentiated. There were 6 (5.64%) cases of signet ring cell carcinoma. None of the adenocarcinoma showed adjacent Barrett's mucosa with high grade dysplasia.

The SCC showed diffuse infiltrating sheets and nests of small round/oval cells with minimal cytoplasm and hyperchromatic nuclei with fine granular chromatin. The tumor cells were positive for chromogranin and synaptophysin (fig. 4C and 4D). The highest TNM stage grouping recorded in resected specimens was pT2N1MX (stage IIB).

DISCUSSION

In our study, there were 68(64.15%) cases of SQC, 33(31.13%) cases of adenocarcinoma including signet ring cell carcinoma, 4(3.76%) cases of undifferentiated carcinoma and 1(0.94%) case of SCC. The global histological pattern of disease has changed recently. The two major histological types, SQC and adenocarcinoma differ substantially in their underlying patterns of incidence and key etiologic factors. Data from USA showed a 30% drop in incidence of SQC between 1973 and 2002. Incidence of adenocarcinoma has increased 4-fold over the same period.[2] Cancer of the esophagus shows an increasing occurrence of adenocarcinoma in the lower third of the esophagus and is frequently associated with Barrett's esophagus.[12,13] Thus the Incidence of esophageal adenocarcinoma arising in distal esophagus is increasing in trends. In contrast to those findings, we found SQC as the most common esophageal cancer. The most common site for SQC was middle esophagus followed by distal and proximal esophagus. It is likely that HPV infection plays a much more significant role in SQC carcinogenesis.[14] Distal esophagus was the commonest site for adenocarcinoma.

The single case of SCC was found in middle esophagus. SCC possibly arises from same multipotent epithelial basal cells that produce SQC and both tumors often intermingle with each other.[9] It is not always possible to differentiate SQC and SCC based on histomorphology only. Immunostaining for CK14 and CD56 help distinguish SCC from SQC.[15]

The area with the highest reported incidence for esophageal cancer is in the belt from eastern Turkey through north-eastern Iran, northern Afghanistan and southern Russia to northern China, where it has been directly linked to the preservation of food using nitrosamines.[16] The ethnicity may influence esophageal cancer histology or ethnic background may place an individual at increased risk for certain types of esophageal cancer.[17] Poor socio-economic status resulting in fewer intakes of fresh fruits, vegetables and fish in addition to heavy hookah smoking are suspected to be the major risk factors for the development of esophageal cancer.[18] Other findings suggest that a diet rich in foods from animal origin and poor in foods containing vitamins and fiber increase esophageal cancer risk.[19] Drinking hot tea, a habit common in Golestan province, northern Iran, was strongly associated with a higher risk of esophageal cancer.[20] It has been demonstrated that polyphenols in green tea have cancer-preventing activities.[21-23]

Early detection of cancer is most important. The superficial esophageal cancer is commonly observed as a slight elevation or shallow depression on the mucosal surface. Macroscopically, the lesion can be flat, polypoidal or ulcerative. Endoscopy utilizing Lugol iodine spray may be of value in detecting early dysplastic lesion.[24] When the tumor is confined to the mucosa or submucosa, the term superficial esophageal carcinoma is used irrespective of the presence of regional lymph node metastasis. Superficial carcinoma accounted for 10-20% of all resected carcinomas in Japan, whereas in Western countries, superficial carcinomas are much less frequently reported.[25] Superficial esophageal carcinoma limited to the mucosa may be treated by endoscopic mucosa resection (EMR). The EMR is also indicated for high grade intraepithelial neoplasia. There is no previous report regarding the incidence of esophageal carcinoma in Nepal. This study possibly reflects the histological pattern of esophageal cancer in our population. It is likely to provide valuable data from which the disease can be tracked and prevention effort may be developed.

Multi-center studies of esophageal cancer including demographic data in different geographical and ethnical background are necessary in the future.

CONCLUSION

The most frequent type of esophageal carcinoma is squamous cell carcinoma followed by adenocarcinoma. Distal esophagus is the most common site. Males are affected more than females.

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