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Malignant Tumors of the Larynx: A Clinicopathological Study of 30 Cases

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Abstract

Background: Cancer of the larynx is a common cancer of the head and neck. This cancer has an established correlation with smoking tobacco and alcohol as causative agents. This study has been conducted in a tertiary hospital in Northeastern India. Minimal data about laryngeal cancer from this area was published in the literature.

Methods: This prospective study was conducted for a period of two years and enrolled 30 patients. Patients were diagnosed, staged, and treated for the cancer, then followed for 12 months.

Results: This study showed that patients in the sixth decade of life were the most common patients that presented with this cancer. There was a male preponderance. Smoking and alcoholism were the most common associated risk factors. Most patients presented with hoarseness followed by a foreign body sensation in the throat. The majority presented with late stage disease. The most common larynx tumor in this study was glottic carcinoma. All cases were squamous cell carcinoma and most were moderately differentiated. Patients underwent treatment with radiation therapy and chemotherapy.

Conclusion: At the one year follow up, 36.67% of patients were found to be in remission. A total of two patients succumbed to this disease.

Keywords: Laryngeal carcinoma, Smoking, Alcoholism, Treatment

Introduction

The global burden of cancer continues to increase largely because of the aging and growth of the world's population alongside an increasing adoption of cancer-causing behaviors, particularly smoking, in economically developing countries.[1] Rates are increasing for several major cancer sites and subtypes, including human papillomavirus (HPV)-related tumors.[2] Head and neck cancer is a public health problem, accounting for the fifth most common of all human cancers.[3] The larynx is in a unique position because it is a major component of the upper respiratory tract and located just anterior to the upper end of the digestive tract.[4] It is

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therefore vulnerable to exposure to various carcinogens. Globally the incidence of laryngeal cancer was 157,000 persons in 2012 which constituted 1.1% of all cancers.[4] This cancer is the 14th most common cancer among men and the 21st most common in both sexes.[5]

Tobacco use, alcohol consumption, and HPV16 infection are considered to be the major risk factors for this disease. Occupational risk factors that include exposure to asbestos have also been described although dust exposures other than asbestos have been historically understudied.[6]

The larynx is divided into the supraglottic, glottis and subglottis based on anatomical location. Tumors of the larynx can be divided into benign or malignant. Laryngeal granulomas, vocal cord nodules, and vocal cord polyps are tumor-like lesions of the larynx. Benign laryngeal tumors include a large number of lesions such as papillomas, hemangiomas, fibromas, chondromas, myxomas, and neurofibromas. About 95% of laryngeal carcinomas are typical squamous cell tumors. Rarely adenocarcinomas are seen to arise from larynx, presumably arising from mucous glands.[7]

Squamous cell carcinoma is the predominant histologic type; approximately 40% of patients will have stages III or IV disease when first evaluated.[8] Most cases of laryngeal cancer are associated with a history of tobacco and/or alcohol use, so the treatment of patients is complicated by medical co-morbidity and the development of second primary cancers.[9,10]

Management of laryngeal cancer requires a multidisciplinary team comprised of a head and neck surgeon, radiotherapist, clinical nurse specialist, palliative care physician, dieticians, and dedicated speech and swallowing therapists. The work of the multidisciplinary team improves the effectiveness of treatment by optimizing the process of preparation and organization, and finally by contributing knowledge and experience in decision-making. Qualification for the most optimal treatment within the multidisciplinary team should be used in all patients with cancer of the head and neck.[11]

The aim of this study was to determine the clinical features of patients with carcinoma of the larynx; determine the pathogenesis and pathological findings of patients with this cancer; and evaluate the different modalities of management for larynx carcinoma.

Materials and Methods

This was a hospital-based prospective study conducted in the Regional Institute of Medical Sciences (RIMS), Imphal, Manipur, India. The study was conducted for a period of two years from October 2011 to September 2013. The study included any case of laryngeal malignancy irrespective of age, sex, religion and socio-economic status. We recruited 30 patients for the study and informed consent was obtained from all patients. The patients were recruited for a one-year period, and then followed for one year. Patients with growths other than malignant tumors and those with laryngeal malignancies that had incomplete treatment were excluded from the study. Follow up was performed at 1, 3, 6 and 12 months.

The clinical diagnosis of laryngeal malignancy was made on the basis of clinical presentation and included hoarseness, foreign body sensation in the throat, dysphasia, pain or discomfort on swallowing, dyspnea, cough, aspiration, or the presence of a neck mass.

A thorough history and complete otorhino-laryngological examination that included an indirect laryngoscopy, laboratory tests for hematology and biochemistry, an endoscopy, fine needle aspiration cytology (FNAC) in cases with neck edema, and radiological studies were performed for each patient. Any patient with suspected malignant growth in the larynx was admitted to the ENT ward for direct laryngoscopy under general anesthesia where a biopsy was taken from the lesion and sent for histopathological examination. After confirmation of the diagnosis, proper staging was done. The appropriate treatment modality was given to each patient. Necessary investigations were performed routinely at each visit during follow-up.

Results

In this study the patients' ages ranged from 41-80 years. The peak incidence of cancer occurred in the 61-70 (36.6%) year age group followed by the 51-60 (23.3%) year age group (Table 1). Male patients constituted 90% of the study population. The male to female ratio was 9:1. Religion-wise statistics showed that 63.3% were of the Hindu religion, followed by Chirstianity (33.3%) and Islam (3.3%). However, this finding according to religion was insignificant as a fixed population-based study for the different religions was not performed. The majority of individuals in this state are Hindus followed by Christians and Muslims.

Table 2 shows the occupation statistics. Farmers constituted 53.3% of patients. There were 73.3% patients who resided in rural areas followed by urban residents (26.6%). Risk factor exposure showed that 90% of patients used tobacco in the form of smoking, 83.3% were addicted to alcohol, 80% smoked and drank alcohol, and 30% used a smokeless form of tobacco. In the study population, there were 23.3% of patients who smoked tobacco, drank alcohol and consumed the betel nut. Table 3 shows the risk factor exposure.

In our study hoarseness was the most common presenting symptom in 76.67% of patients followed by foreign body or sticky sensation, dysphagia, cough, dyspnea, swelling in the neck, neck pain, otalgia, blood stained sputum, and aspiration. Table 4 shows the cases according to clinical presentation.

A total of 63.3% of patients had carcinoma on the left side of the larynx and 36.6% had carcinoma on the right side. In the patients with bilateral extension the maximum bulk of the tumor was taken as the site of origin. On indirect laryngeal examination, 33.33% patients had exophytic growth followed by proliferative (30%), ulceroproliferative (23.3%) and ulcerative (13.33%) which is shown in table 5. Glottic cancer was the most common in 43.33% followed by supraglottic (33.33%) and glottic with supraglottic extension (23.33%). Even though only 7 patients complained about neck edema, on clinical examination 23 patients had evidence of neck node enlargement. Fine needle aspiration cytology (FNAC) was performed on all patients who had palpable neck nodes. There were 17 patients positive for metastatic squamous cell carcinoma and 6 had non-specific reactive lymphadenitis for which they were prescribed antibiotics. The swelling subsided in these patients, which showed that these 6 patients had lymph node enlargement because of an infection rather than metastasis, even though there might have been micrometastasis present in the lymph nodes. The most common involved lymph node was observed at level III.

All patients underwent a direct laryngoscopic examination under general anesthesia for staging workup and biopsy. Histopathologically all tumor types and differentiation were recorded. As shown in table 6, there were 56.67% of patients diagnosed with moderately differentiated squamous cell carcinoma followed by well (33.33%) and poorly differentiated (10%) squamous cell carcinomas. All patients had squamous cell carcinomas with different differentiations; none of the other types of carcinomas were found in our study. We staged the patients according to TNM staging. There were 40% who presented with stage III and 33.33% with stage IV (Table 7). For the 10 patients who presented with dyspnea a surgical tracheostomy was performed in 60% of those patients and 40% had a medical tracheostomy with steroids.

None of the patients underwent surgery because the majority presented at a late age and poor general condition. These patients were not able to undergo major surgery under general anesthesia. Following an explanation of sequelae and surgical complications, the patients and relatives preferred conservative treatment with voice preservation in the form of radiotherapy and chemotherapy or chemotherapy alone. The majority of patients were from low socioeconomic backgrounds which made it difficult to convince them to undergo surgery.

A total of 66.67% of patients received concurrent chemoradiotherapy (CCRT) followed by radiotherapy alone in 33.33% and neoadjuvant chemotherapy in 16.67%. Chemotherapy drugs

Table 1. Distribution of cases of laryngeal cancer according to age.

Age range (years)	No. of cases	Percentage (%)
41-50	6	20
51-60	7	23.3
61-70	11	36.6
71-80	6	20
Total	30	100

administered were cisplatin or carboplatin and 5-flurouracil based chemotherapeutic regimens. Radiotherapy was given as external beam radiotherapy. All patients received a 70 Gy dose in 35 divided doses over 7 weeks with a weekly two-day rest period for normal tissue repair. Patients had the following radiation therapy induced complications: xerostomia (66.67%), taste alteration (73.33%), dysphagia (63.33%) and mucositis (33.33%). The most frequent chemotherapeutic complications were nausea and vomiting seen in 90% of patients. Renal toxicity was the least common in 15%. At the 12-month follow up, 36.67% patient did not have detectable disease, 40% had residual disease, 5% were removed from the study because they were lost to follow-up after the treatment period for follow-up, and 2 patients expired because of non-responsive disease (Table 8).

Discussion

This was a prospective study of 30 cases of laryngeal cancer conducted in RIMS between October 2011 to September 2013. Patients' mean age at presentation was 60.56 years with an age range of 41-80 years. No cases were found below the age of 40 years. Saedi et al.[12] in their study reported the mean age to be 59.92 years. Lam et al.[13] reported the peak age of presentation of laryngeal carcinoma to be 62 years with only 1.6% of cases who presented below 40 years of age.

In our study 53.3% of the patients were farmers and 73.3% resided in rural areas. This showed that the incidence was higher in people from a lower socioeconomic status and in those with poor nutritional status and environmental hygiene. Jaimanti[14] found 78% of cases from a rural area and 22% of cases from an urban area. They

Table 2. Distribution of cases according to occupation.

Occupation	No. of cases	Percentage (%)
Farmer/agriculture	16	53.3
Service	6	20
Business	2	6.6
Driver	2	6.6
Carpenter	1	3.3
Household	3	10
Total	30	100

determined that 60% had low socio-economic status, 25% belonged to the middle class and 15% had high socio-economic status.

Risk factors in this study were in accordance with other studies which showed that tobacco and alcohol use were the most common risk factors for the development of laryngeal carcinoma.[9,14-17]

The most common presenting symptoms in our study were hoarseness (76.66%) and foreign body or pricking sensation of the throat (73.33%). Difficulty in swallowing was seen in 46.66%, cough in 40% and difficulty in breathing in 30% followed by neck swelling in 23.33%. Dysphagia was either in the form of foreign body sensation, irritation or feeling of hair stuck in the throat. Verma et al.[18] reported hoarseness in 73.92%, difficulty in swallowing in 59.95% and cough with expectoration in 39.04%. Amusa et al.[19] reported hoarseness in all cases, cough in 53.8%, and referred ear pain in 43.6% of cases.

According to this study there was more carcinoma of the larynx on the left side (63.3%) compared to the right side (36.6%). The reason

Table 3. Distribution according to risk factors.

Risk factor	No. of cases	Percentage (%)
Smoking cigarette/bidi	27	90
Alcohol	25	83.3
Alcohol + smoking	24	80
Pan/betel nut	9	30
Alcohol + tobacco + betel nut	7	23.3
Tobacco chewing/ zarda/khaini	6	20
Occupational risk factor /factory exposure	0	0
Non-smoker + non-alcoholic	0	0
Other	0	0

Table 4. Distribution of cases according to clinical presentation and duration of symptoms.

Presenting symptoms	No. of cases	Percentage (%)	Duration of symptoms		
			<1 month	1-3 months	>3 months
Hoarseness	23	76.66	6	12	5
Foreign body/ sticky sensation in the throat	22	73.33	11	5	6
Dysphagia	14	46.66	11	2	0
Cough	12	40	7	4	1
Dyspnea	10	30	10	0	0
Swelling in the neck	7	23.33	5	2	0
Neck pain	5	16.66	4	1	0
Otalgia	3	10	2	1	0
Blood stained sputum	2	6.6	2	0	0
Aspiration	2	6.6	0	2	0
Neurological symptoms	0	0	0	0	0

why the left side was more common was unknown; it could be attributed to one-sided swallowing as one side may be predominant in function. In this study, possibly the majority of patients had a predominantly left-sided swallow. Further, a study that consists of a larger number of patients is required to arrive at a definitive conclusion. In the current study, histopathological findings from FNAC of the neck nodes determined that all cases were metastatic squamous cell carcinoma.

Histopathological study of the larynx tissue showed that all cases were squamous cell carcinoma. The non-squamous variety was not found. Of squamous cell carcinomas, there were 56.66% moderately differentiated, 33.33% well differentiated and 10% poorly differentiated. Suen et al.[8] concluded that squamous cell carcinoma was the predominant histologic type. Wiligen et al.[20] reported that 95% of laryngeal carcinoma were typically squamous cell carcinoma and adenocarcinoma was rarely seen. Lam et al.[13] in their study reported that there were 67.3% of patients with moderately differentiated squamous cell carcinoma. The current study results confirmed the finding of the above authors.

In this study the most common laryngeal malignancy seen in the glottis (43.33%), followed by the supraglottis (33.33%) and glottis with extension to supraglottis (23.33%); there was no subglottic carcinoma observed. Suen et al. reported that approximately 40% of patients would have stages II or IV disease when first evaluated.[8] Dietz et al.[21] reported half of the tumors (50.6%) to be glottic, 17.5% were supraglottic, and in 31.9% of cases a subsite of the tumor could not be clearly determined. Lam et al.[13] found that 30% of patients had tumors which involved both the glottis and supraglottis. In this study it was found that 40% of the patients presented at stage III and 33.33% were stage IV. Ortega et al.[22] also reported that 64% of larynx tumors were locally advanced stages III or IV cancers.

In the current study all patients received a 70 Gy dose of radiation therapy; other authors also used a 67-70 Gy radiation dose in their study.[23] Petrakos et al.[24] observed that patients treated with radiotherapy for stages I and II cancer had a high recurrence rate (60%) with a five-year survival rate of 61.3%. Worden et al.[25] stated that chemo-selection was a feasible organ preservation alternative to total laryngectomy for patients with advanced squamous cell laryngeal cancer and cartilage invasion.

In the present study, at the end of 12 months post-treatment, 30% of patients had survived

Table 5. Type of growth on indirect laryngeal examination.

Type of growth	No. of cases	Percentage (%)
Exophytic	10	33.33
Proliferative	9	30
Ulceroproliferative	7	23.33
Ulcerative	4	13.33
Total	30	100

Table 6. Distribution of cases according to histopathological characteristics.

Histopathological findings	No. of cases	Percentage (%)
Well differentiated squamous cell carcinoma	10	33.33
Moderately differentiated squamous cell carcinoma	17	56.66
Poorly differentiated squamous cell carcinoma	3	10

without evidence of disease and 40% had evidence of disease. There were two deaths and five dropout cases. Among the two deaths, one occurred after 3 months and the other death after 12 months from completion of treatment. The follow up period could not be extended beyond 12 months due to time constraints of the study duration. It would have been better if the follow up period could be prolonged so as to evaluate the correct and exact outcome of the treatment modality for management of laryngeal malignancy.

Spector et al.[26] recommended a follow up period of eight years for metastasis and second primary cancers. They concluded that survival of patients with laryngeal malignancy who were treated with primary radiotherapy and salvage surgery was poor. It would have been better if the follow up period could be prolonged so as to evaluate the correct and exact outcome of the treatment modality for management of laryngeal malignancy. The treatment modality and choice of treatment for malignancy of laryngeal cancer remains controversial. Spector et al.[26] stated that no specific treatment modality produced any survival advantage.

Lund et al.[27] concluded that despite the different treatment modalities there was no definite treatment comparable to those achieved by preventing people from smoking tobacco and avoiding other risk and predisposing factors.

Table 7. Distribution of cases according to TNM staging.

Stages	TNM	No of cases	Percentage
I	T1N0M0	6	20
II	T2N0M0	2	6.66
III	T3N0M0	5	
	T1N1M0	0	
	T2N1M0	2	
	T3N1M0	5	
	Total	12	40
IV	T4N0M0	1	
	T4N1M0	0	
	T4N2M0	0	
	T4N3M0	0	
	T1N2M0	0	
	T1N3M0	4	
	T2N2M0	5	
	T3N2M0	0	
	Any T, any N, M1	0	
	Total	10	33.33
Total		30	100

Conclusion

The disease was higher in the lower socioeconomic group and had a definite relationship with the consumption of tobacco (smoking or smokeless) and alcohol intake. Chewing the betel nut (pan) was a very important risk factor. The most common presenting symptoms included hoarseness and foreign body/sticky sensation in the throat. Carcinoma of the larynx was more common on the left side than the right. Carcinoma of the glottis (43.33%) was more common than supraglottis carcinoma (33.33%). No case of subglottic carcinoma was found. Histopathologically, all cases were of the squamous cell type. Among these, the majority were moderately differentiated followed by well differentiated. The majority of cases were diagnosed at a fairly advanced stage (stages III & IV). Those patients were either treated with radiotherapy and/or CCRT. The follow up period of a minimum of five to eight years is necessary to evaluate the survival rates, morbidity, and the correct, exact outcome of the treatment modality

Table 8. Survival rate after follow up at 12 months.

Survival	No. of cases	Percentage (%)
Surviving without disease	11	36.66
Surviving with disease	12	40
Drop out	5	16.67
Death	2	6.67
Total	30	100

for management of laryngeal malignancy.

Conflict of Interest

No conflict of interest is declared.

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