Clinico-Pathological Study of 50 Cases of Tumours of Larynx

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Abstract The larynx serves to protect the lower airways, facilitates respiration and plays a key role in phonation. Based on anatomic location, the larynx is divided into the supraglottic larynx, the glottis or glottic larynx, and the subglottic larynx. The tumours of larynx can be divided into benign or malignant. Laryngeal granulomas, Vocal cord nodules, Vocal cord polyps are tumour-like lesions of larynx. Benign laryngeal tumors include a large number of lesions like papillomas, hemangiomas, fibromas, chondromas, myxomas, and neurofibromas. About 95% of laryngeal carcinomas are typical squamous cell tumours. Rarely adenocarcinomas are seen, presumably arising from mucous glands. The exact cause of laryngeal cancer is still unknown. Diagnosis is based on direct or indirect visualization of the larynx, supplemented by CT scan and confirmed by histopathological examination. Objective: The aim of the present study was to study the clinical aspects, histopathological patterns of tumours of the larynx to study the various predisposing factors of laryngeal tumours. The present study

was undertaken on 50 patients clinically diagnosed as cases of tumour of larynx. These patients were made to undergo direct laryngoscopy and the biopsy taken from the growth in the larynx was sent to the department of pathology for histopathological examination. Smoking played the main role in benign growths (25%). The main predisposing factor (73.2%) for malignant growths was smoking, tobacco chewing and alcohol abuse. The most common benign tumour of larynx was the vocal polyp. Out of the 30 cases of squamous cell carcinoma, 15 (50%) were well differentiated, 8 (26.6%) were moderately differentiated and 3 (10%) were poorly differentiated. The symptoms of laryngeal tumours can vary from mild hoarseness of voice to life threatening respiratory distress. All available methods of study should be utilized to make the diagnosis as early as possible. Early diagnosis of the lesion can lead to effective management.

Keywords Larynx · Laryngeal tumours · Histopathological · Clinicopathological

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Introduction

Only vertebrates with their thoracoabdominal diaphragms are able to use their larynges as flutter valves; altering air flow from their respiratory bellows to produce sound. The production of sound for communication of complex information is limited to the highest orders. Thus, only in humans is the larynx significantly altered for voice production.

The larynx serves three basic functions in humans. In order of functional priority they are

- Protective
- Respiratory and
- Phonatory [14].

The larynx serves to protect the lower airways, facilitates respiration and plays a key role in phonation. The protective function is entirely reflexive and involuntary, whereas the respiratory and phonatory functions are initiated voluntarily but regulated involuntarily [15].

Based on anatomic location, the larynx is divided into the supraglottic larynx, the glottis or glottic larynx, and the subglottic larynx. The supraglottic larynx includes the epiglottis, the preepiglottic space, the laryngeal aspects of the aryepiglottic folds, the false vocal cords, the arytenoids, and the ventricles. The inferior boundary is a horizontal plane drawn through the apex of the ventricle. This corresponds to the area of transition from squamous to respiratory epithelium. The glottis consists of the true vocal cords extending to roughly 1 cm below the true cords, the paraglottic space, and the anterior and posterior commissures extending inferiorly about 1 cm. The subglottic larynx has its superior border at the inferior border of the glottis, that is, approximately 1 cm below the true vocal cords and extending inferiorly to the trachea.

Laryngeal granulomas, vocal cord nodules, vocal cord polyps are tumour-like lesions of larynx. Benign laryngeal tumors include a large number of lesions. They often present with hoarseness, change in voice quality, stridor, globus and dysphagia. Benign laryngeal tumors include juvenile papillomas, hemangiomas, fibromas, chondromas, myxomas, and neurofibromas. They may appear in any part of the larynx.

Adenomas (ectodermal tumours) are rare benign tumours arising from seromucinous glands of larynx. Neurilemmoma (neurogenic tumour) is a benign tumour arising from Schwann cells of axon sheath.

Leiomyomas (myogenic tumours) have been reported in children but they occur more often in adults of all ages. Rhabdomyomas of the true adult type are extremely rare tumours of skeletal muscle in larynx. Granular cell tumours are considered to be mesenchymal in origin. They occur mostly on the true vocal cord. Fibromas are composed of fibrillar connective tissue. Lipomas arise from adipose tissue, especially in the false cords.

About 95% of laryngeal carcinomas are typical squamous cell tumours. Rarely adenocarcinomas are seen, presumably arising from mucous glands.

The exact cause of laryngeal cancer is still unknown. However, several interrelated co-factors (mainly tobacco smoking and alcohol consumption), are clearly associated with an increased incidence in laryngeal cancer. Many ongoing studies are awaited to identify genetic factors and oncogenes that may have an aetiological interest.

Diagnosis is based on direct or indirect visualization of the larynx, supplemented by CT scan.

Currently it is normal to acquire a specimen (biopsy) of the tumour by direct laryngoscopy and this is usually carried out under general anaesthesia (or local anaesthesia) allowing a careful and thorough direct examination of the tumour, biopsy material should include an adequate amount of tissue both from ulcerated areas and elsewhere if practicable. The biopsy material is important on three grounds:

1. Definitive diagnosis of malignancy, some active looking keratoses may not be malignant.
2. Identification of the type of tumour:
3. Often neglected, the degree of differentiation may be significant [13].

The aim of the present study was to study the clinical aspects, histopathological patterns of tumours of the larynx and to study the age and sex incidence, the socioeconomic and occupational differences and various predisposing factors of laryngeal tumours.

Materials and Methods

The present study was undertaken on 50 patients clinically diagnosed as cases of tumour of larynx. The study was conducted in the department of Ear, Nose and Throat (ENT) of the Government Medical College and Rajindra Hospital, Patiala. A complete clinical history of each patient was taken and they were thoroughly examined and investigated.

When the patient spoke the voice was carefully listened to. This gave an idea of the likely location of the tumour. Thorough head and neck examination was done. This included evaluations of neck mobility, neck masses, direct examination of the oropharynx and epiglottic tip without the aid of instrumentation and examination of the cranial nerves.

Patients complaining of these symptoms were clinically examined in the Out Door (OPD) Department of ENT. Out of these 50 patients suspected of having tumour in the larynx after indirect (mirror) laryngoscopy were admitted in the ward.

These patients were made to undergo direct laryngoscopy which was done under local or general anaesthesia. In the cases of apprehensive patients and in children, general anaesthesia was used. The patient was kept fasting overnight. An injection of fortwin and atropine; and viscous oral spray was given 30–45 min before laryngoscopy as pre-medication for local anaesthesia. The findings of indirect laryngoscopy were confirmed, the details regarding extent and type of growth were examined; and the biopsy taken from the growth in the larynx was sent to the department of pathology for histopathological examination.

Tabulation of cases was done on basis of age, sex, socioeconomic status, occupational differences, predisposing factors etc.

Observation and Analysis

50 patients having tumours of larynx were selected for this study. The biopsy specimens were examined in the Department of Pathology, Government Medical College and Rajindra Hospital, Patiala for confirming the diagnosis.

Age

Benign tumours were most common in the third decade (30%) and minimum in the seventh decade (5%). Malignant tumours were reported between the ages of 31–80 years with maximum occurrence between the ages of 40–70 years (Table 1).

Sex

Both benign as well as malignant tumours were more common in males as compared to females. Vocal strain, occupation and habits related to smoking and drinking alcohol in the males may have played a role (Table 2).

Socioeconomic Status

Benign tumours were more in the middle class (65%) whereas malignant tumours were reported more in the lower (46.6%) and middle class (43.3%).

Benign tumours were seen equally in rural and urban areas, while malignant tumours were more common (73%) in rural areas.

Prevalence of benign tumours was more amongst labourers (25%), followed by business community (20%)

Table 1 Age incidence

Age in years	Benign tumours		Malignant tumours	
	No. of cases	Per. of total (%)	No. of cases	Per. of total (%)
0–10	0	0	0	0
11–20	2	10	0	0
21–30	6	30	0	0
31–40	4	20	2	6.6
41–50	2	10	8	26.6
51–60	5	25	10	33.3
61–70	1	5	7	23.3
>70	0	0	3	10
Total cases	20	100	30	100

Table 2 Sex incidence

Sex	Benign tumours		Malignant tumours	
	No. of cases	Per. of total (%)	No. of cases	Per. of total (%)
Male	14	70	29	96.6
Female	6	30	1	3.3
Total	20	100	30	100

and housewives (20%). The business community consisted of shopkeepers or milkmen.

Malignant tumours were highest (36.6%) amongst labourers, followed by farmers (13.3%) and businessmen (10%).

Predisposing Factors

Smoking played the main role in benign growths (25%). Vocal strain (20%) and poor orodental hygiene (20%) were other significant predisposing factors. In 20% cases no predisposing factor could be ascertained (Fig. 1; Table 3).

The main predisposing factor (73.2%) for malignant growths was smoking, tobacco chewing and alcohol abuse.

Symptoms

Hoarseness was the main symptom with which all patients of benign and malignant tumours presented. Most of them had complained of hoarseness for more than 6 months. Five patients of benign tumours and twelve patients of malignant tumours presented with difficulty in breathing (dyspnoea). Nine cases of malignant tumours had emergency tracheostomy done due to respiratory distress and one case of benign tumour had to undergo tracheostomy due to severe respiratory distress. Difficulty in swallowing (dysphagia) was seen in two patients of benign tumours and fifteen patients of malignant tumours. While most of the patients of benign tumours had one or two symptoms, patients with malignant tumours had multiple symptoms.

Five patients of malignant tumours had associated lymph node enlargement in neck. Five cases of malignant tumours complained of blood in sputum (haemoptysis).

Histopathological Classification

The ratio of benign to malignant tumours in the larynx is 2:3. The most common benign tumour of larynx was the vocal polyp. Out of 14 cases of vocal polyp, histopathologically, one case was of myxoid variety, nine were of fibrinoid type and four were vascular. Squamous cell papilloma of larynx was seen in two cases. Chronic

Table 3 Predisposing factors

Predisposing Factors	Benign tumours		Malignant tumours	
	No. of cases	Per. of total (%)	No. of cases	Per. of total (%)
Vocal strain	4	20	2	6.6
Smoking/tobacco and alcohol use	5	25	22	73.2
Alcohol use	3	15	3	10
Poor orodental hygiene	4	20	3	10
Plummer vinson syndrome	0	0	0	0
Asbestos dust exposure	0	0	0	0
No factor found	4	20	0	0
Total	20	100	30	100

Fig. 1 50 Tumours of larynx: predisposing factors

inflammatory infiltrate with hyperplasia and mild dysplasia was seen in two cases (Tables 4, 5).

Out of the 30 cases of squamous cell carcinoma, 15 (50%) were well differentiated, 8 (26.6%) were moderately differentiated and 3 (10%) were poorly differentiated. There were two cases of papillary squamous cell carcinoma, one case of basaloid squamous cell carcinoma and one case of epidermoid carcinoma in situ.

Table 4 Histopathological diagnosis

Benign tumours		
Histopathological diagnosis	No. of cases	Per. of total (%)
Vocal Polyp—Myxoid	1	5
Vocal Polyp—Fibrinoid	9	45
Vocal Polyp—Vascular	4	20
Squamous cell papilloma	4	20
Chronic inflammatory tissue with hyperplasia and mild dysplasia	2	10
Total	20	100

Site of Laryngeal Tumour

The majority of the benign tumours in the larynx arose from the glottic region (70%) followed by that of supra-glottic region (25%). Only in one case benign growth was detected in the subglottic region (Table 6).

Patients with malignant tumours had most of them limited to supraglottic region (50%). Some patients had

Table 5 Histopathological diagnosis

Malignant tumours		
Histopathological diagnosis	No. of cases	Per. of total (%)
Well differentiated SCC	15	50
Moderately differentiated SCC	8	26.6
Poorly differentiated SCC	3	10
Papillary SCC	2	6.6
Basaloid SCC	1	3.3
Epidermoid Ca in situ	1	3.3
Total	30	100

Table 6 Site of laryngeal tumour

Site of growth	Benign tumours		Malignant tumours	
	No. of cases	Per. of total %	No. of cases	Per. of total %
Supraglottic	5	25	15	50
Glottic	14	70	6	20
Subglottic	1	5		0
Transglottic	0	0	9	30
Total cases	20	100	30	100

extensive growths involving more than one region, e.g. supraglottic and pyriform fossae (20%), supraglottic and glottic (6.6%), glottic and subglottic (3.3%).

Discussion

Tumours of the larynx are usually detected early due to dysphonia, i.e. change in voice, but the early and precise diagnosis of cancer of the larynx is still a challenge. Many times it is difficult to determine whether a patient has or does not have cancer of the larynx, but as the disease progresses, the diagnosis can be made more easily and confidently. 50 patients with tumours of larynx were studied at the ENT Department of Government Medical College and Rajindra Hospital, Patiala.

Age

Benign tumours were most common in the third decade (30%) and minimum in the seventh decade (5%) in this study. The cases of malignant tumours were reported between the ages of 31–80 years with maximum occurrence between the ages of 40–70 years. [16] stated that malignant laryngeal tumours tend to increase with age, average age of diagnosis being 66 years [4] stated that cancer of the larynx can occur at any age with mean presentation at 50–60 years for men and a decade younger for women. Thompson et al. [18] in a study of 104 patients including 79 men and 25 women of exophytic and papillary squamous cell carcinoma of larynx; found the mean age to be 61 years (the range being from 27–89 years).

The present findings are more or less consistent with the studies of [16, 4] and [18].

Sex

According to present study the occurrence of both benign as well as malignant tumours was higher in males as compared to females. The male to female ratio was 7:3 (i.e. 2.3:1) in case of benign tumours and 29:1 in case of malignant

tumours. Bakshi et al. [3] in a study of 690 cases of carcinoma larynx found that 647 patients were males and 43 were females. Goiato and Fernandes [7] in a study of 66 cases of laryngeal cancer found that 64 of these were males and they represented 97% of the cases, the rest being females.

Socioeconomic Status

The prevalence of benign tumours was more in the middle class, while malignant tumours were common in both the lower and middle classes. Smith [17] stated that low socioeconomic status is associated with cancers of the larynx. Bakshi et al. [3] in their study found that 60% were from the low socioeconomic status, 25% belonged to the middle class and the remaining 15% belonged to the high class.

Residential Area

According to present study the occurrence of benign tumours was the same for patients belonging to rural as well as urban areas. However, the prevalence of malignant tumours was more in peoples from the rural areas.

Smith [17] stated that tobacco-related cancers like those of the larynx tend to be related to the population living in rural surroundings. Bakshi et al. [3] found that 78% were rural and the remaining 22% were from urban regions.

Occupation

The maximum occurrence of benign tumours was found in labourers (25%), followed by businessmen (20%) and housewives (20%) in present study.

In present study out of 30 cases of malignant tumours of the larynx, 36.6% were labourers, 13.3% farmers and 10% businessmen. Maier et al. [11] in a study of 164 patients of cancer of the larynx found that 90% of the cases were blue collar workers, most of them working in dirty or dusty jobs. Bakshi et al. [3] in their study found that 45% patients were farmers and 39% were labourers.

Predisposing Factors

In present study, smoking turned out to be the most common (25%) predisposing factor, followed by vocal strain (20%) and poor orodental hygiene (20%) in the case of benign tumours. The present study could not correlate any case with human papilloma virus for benign tumours. Maier et al. [11] in a study of 164 cases found that smoking and drinking alcohol increase the dose-dependant risk of laryngeal cancer. Kaufman and Burke [9]; and Adams and Maisel [1] also stated that tobacco and alcohol abuse are associated with increased risk of laryngeal cancer. Bakshi

et al. [3] found that smoking was a predisposing factor in 87.8% of the cases and additionally or otherwise alcohol consumption was in 75% of the cases. Goiato and Fernandes [7] in a study of 66 cases of malignancy of larynx found that tobacco smoking and alcohol use are the highest risk factors for laryngeal cancer. In the present study in case of malignant tumours, smoking and tobacco chewing and alcohol use (73.2%) were the most common predisposing factors.

Symptomatology

Hoarseness was the earliest and main presenting symptom in both benign as well as malignant growths. While most patients with benign tumours had only one symptom, patients with malignant tumours had associated symptoms like dyspnoea, dysphagia, cough, haemoptysis and secondaries in the neck. Bakshi et al. [3] in their study found that hoarseness was the most common complaint. Other complaints were sore throat, neck nodes and haemoptysis.

Histopathological Classification

A vocal polyp is covered with stratified squamous epithelium and may exhibit a variety of changes in the stroma which include oedema fibrosis, increased vascularity, haemorrhages and hyaline changes. Thus, on the basis of differing histological changes, vocal polyps were divided into fibrinoid, vascular and myxoid polyps.

Another type of benign growth detected was squamous cell papilloma which is a benign epithelial neoplasm formed by stratified squamous epithelium. These tumours are usually exophytic. The papilloma is a true neoplasm that grows as a soft succulent, raspberry like friable excrescence; usually on true vocal cords.

Squamous cell carcinoma was the most common malignant tumour detected in the larynx. Out of the 26 cases of squamous cell carcinoma, fifteen were well differentiated, eight were moderately differentiated and three were poorly differentiated. A squamous cell carcinoma is an invasive tumour that shows evidence of squamous differentiation.

In present series there were two cases of papillary squamous cell carcinoma, one case of basaloid squamous cell carcinoma and one case of epidermoid carcinoma in situ. Papillary squamous cell carcinoma shows finger-like projections with fibrovascular cores or broad based bulbous growth with rounded projections and limited fibrovascular cores; overlying squamous epithelium is malignant; usually no/limited surface keratinisation. Basaloid squamous cell carcinoma shows typical areas of squamous cell carcinoma (invasive and in situ) with nests or cords of small crowded cells with minimal cytoplasm, hyperchromatic nuclei,

comedonecrosis, prominent hyalinization and peripheral palisading, small cystic spaces and mitotic activity.

In the present study the ratio of benign to malignant tumours was 2:3. Out of the benign tumours, 70% were vocal polyps, 20% were squamous cell papilloma and 10% were chronic inflammation.

Arnold et al. [2] found that papilloma was the most frequent benign tumour of the larynx with the ratio of benign to malignant tumours being 1:10. Cocks et al. [4] found that the majority of benign laryngeal lesions are vocal cord polyps. Nerurkar et al. [12] reported that recurrent respiratory papilloma (RRP) is the most common benign neoplasm of larynx both in children and in adults.

The present findings showed that in cases of malignant tumours 100% were squamous cell carcinoma (SCC). Out of these 50% were well differentiated SCC, 26.6% were moderately differentiated SCC, 10% were poorly differentiated SCC, 6.6% were papillary SCC and 3.3% were basaloid SCC. There was only one case of epidermoid in situ. Kaufman and Burke [9] stated that SCC of the larynx accounts for over 90% of laryngeal cancers. Kumar et al. [10] stated that 95% of all laryngeal carcinomas are typical SCC. Jaiswal and Hoang [8] stated that out of all primary laryngeal carcinomas, 99% are SCC. Bakshi et al. [3] found that 69% were non-keratinizing SCC and 27% were keratinizing SCC. Greene et al. [6] cited that in the larynx, SCC is the most common malignant tumour. Domanowski [5] cited that 96% of laryngeal carcinomas are SCC. Wang et al. [19] stated that SCC accounts for 99% of all primary laryngeal carcinomas (Fig. 2).

The present study is also in line with the above studies.

Fig. 2 Well differentiated SCC (H&E 40×)

Clinical Classification According to Site

In present study, the majority (70%) of the benign tumours were glottic, 25% were supraglottic and only 5% were subglottic. The present study is consistent with the study of Arnold et al. [2] that the most common site of benign vocal polyps is the glottic area.

In the case of malignant tumours, 50% were supraglottic, 20% glottic, 30% transglottic and none subglottic in present study.

Thompson et al. [18] studied 104 cases of exophytic and papillary SCCs of larynx out of which 30% were supraglottic, 46% glottic, 3% subglottic and 21% transglottic. Bakshi et al. [3] in a study of 690 cases of laryngeal malignancy found that 56% of tumours were supraglottic, 17% glottic, 3.6% subglottic and 13% transglottic tumours.

The malignant tumours of the larynx occur more commonly in the supraglottis which is consistent with the studies of Bakshi et al. [3] but not with that of Thompson et al. [18]. The present study is in line with both the above studies that subglottis is the least common site.

Conclusion

The symptoms of laryngeal tumours can vary from mild hoarseness of voice to life threatening respiratory distress. All available methods of study should be utilized to make the diagnosis as early as possible. When it has been established that a cancer is present in these regions, it must be determined what structures it involves and its precise extent. In this way, a more effective treatment regime can be selected for the patients. Laryngeal lesions can create lot of mental and emotional stress in the patient and the family. Early diagnosis of the lesion can lead to effective management.

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