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Factors favoring neck metastasis in patients underwent laryngectomy for laryngeal cancer

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Abstract

Background: One third of all head and neck cancers are caused by laryngeal cancer. However, the incidence and prevalence rates have decreased over the past 3 decades. Neck metastasis from cancer larynx is important to be addressed as its presence greatly reduces the probability of survival. However, quality of life should be taken into consideration. Hence, it was important to analyze factors related to neck metastasis from primary laryngeal cancer to detect any change of tumor behavior with time.

Results: One hundred thirty-eight patients underwent concomitant neck dissection with laryngectomy (total or partial). Supraglottic tumors had the greatest share in the neck metastasis with a count of 11 (of 26 neck metastasis), representing 42% and a total value of 11 (of 30 total supraglottic cancer) representing a tendency of spread in 37% of the total case number. Tumor midline crossing was present in 77% cases (20 of 26) with positive nodes, representing a *P* value 0.05.

Conclusion: This study investigated different factors related to lymph node metastasis from primary laryngeal tumor. The most important factors were the site of the tumor and its relation to the midline.

Keywords: Cancer larynx, Neck metastasis, Laryngeal cancer, Neck dissection

Background

In 2017, 210,606 new cases of cancer larynx were recorded worldwide, and the prevalence was 1.09 million cases. However, the incidence and prevalence rates have decreased over the past three decades [1]. Primary laryngeal cancer arises from glottic, supraglottic, subglottic, or transglottic regions [2]. Neck metastasis from cancer larynx is important to be addressed as its presence greatly reduces the probability of survival [3]. Nonetheless, the quality of life should be also taken into consideration. For instance, 70% of patients underwent neck dissection (ND) experience shoulder dysfunction even with keeping the integrity of the spinal accessory nerve [4]. Hence, it was important to analyze factors related to

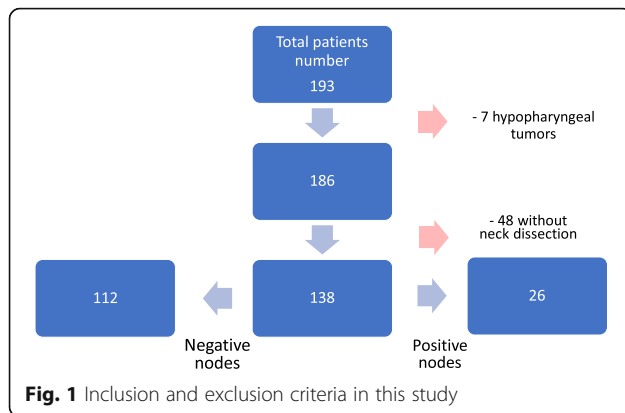
neck metastasis from primary laryngeal cancer to detect any change of tumor behavior with time.

Methods

This study was a retrospective study done in a tertiary care center, from the beginning of 2015 until the end of 2017. The pathological reports for previously untreated patients who underwent laryngectomy were assessed. Patients subjected to laryngectomy with neck dissection were included. Patients who did not undergo neck dissection or those who had laryngectomy for hypopharyngeal cancer were excluded (Fig. 1). Included patients were analyzed for the tumor site, side, size, shape type, differentiation, midline crossing, and lymph node metastasis. Moreover, lymph node metastasis was analyzed in relation to the tumor characters, cartilage invasion, and side of lymph node spread.

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All patients were consented prior their surgeries. Data was anonymized without showing patients' identity. Institutional approval was obtained.

Data were coded and entered using the statistical package SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 20. Data was summarized using mean, standard deviation, median, minimum, and maximum in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. Comparisons between quantitative variables were done using the non-parametric Mann-Whitney test. For comparing categorical data, chi-square test was performed. Exact test was used instead when the expected frequency is less than 5. *P*-values less than 0.05 were considered statistically significant.

Results

One hundred thirty-eight patients underwent concomitant ND with laryngectomy (total or partial). Bilateral ND was performed in 64 patients whilst 74 had unilateral ND. Lymph node (LN) metastasis was detected in 26 patients (19%). The mean age was 59 (9 SD) and male/female ratio was 131/7. Comparison between node negative group and node positive group revealed statistically insignificant *p* values of 0.5 and 0.7 for age and gender, respectively (Table 1). Glottic tumors represented the highest incidence (52/138 cases, 38%) while subglottic tumors had the lowest incidence (7/138 cases, 0.05%). Comparing both groups, glottic tumors remained the highest incidence in node negative group (45/112 cases, 40%) whilst supraglottic tumors were the most common in the node positive group (11/26 cases, 42%) with statistically significant *p* value 0.03. Most of the presenting tumors were T3 stage (103/138 cases, 75%), exophytic (92/138 cases, 67%), mean size 3.6 cm (1.3 SD), crossing midline (83/138 cases, 60%), and infiltrating the thyroid cartilage (82/138 cases, 59%). Histopathologically, 98% (135/138 cases) were squamous cell carcinoma and grade 2 (90%, 124/138 cases) differentiation.

Lymph node metastasis was ipsilateral in 19 cases (73%), contralateral in 5 cases (19%), and bilateral in 2 cases (8%). Supraglottic tumors had the greatest share in the neck metastasis with a count of 11 (of 26 neck metastasis), representing 42% (Table 2) and a total value of 11 (of 30 total supraglottic cancer) representing a tendency of spread in 37% of the total case number (Table 3). Tumor midline crossing was present in 77% cases (20 of 26) with positive nodes, representing a *P* value 0.05.

Discussion

Laryngeal cancer incidence is estimated to be 157,000 cases per year, representing 1.1% of all cancers. Generally, it is classified into supraglottic, glottic, and subglottic cancer. The term transglottic was described by McGavran et al. in 1961 for tumors crossing the ventricle to involve true and false cords [5, 6]. A large retrospective study done in Denmark over 34 years involving 8748 cases showed male predominance (82%) with a median age of 60 years; glottic squamous cell carcinoma (SCC) was the most common tumor [6]. Another study done in China, over 205 patients, also reported predominance of glottic carcinoma 69.8% [7].

Similarly in this study, the authors illustrated data about Egyptian patients who underwent laryngectomy for laryngeal cancer over 3 years in a tertiary care center. The mean age was 59 years (9 years standard deviation), and males were predominantly affected (131 cases, 95%). The most common affected site was the glottis, 52 cases (38%), and the SCC was the major histological type (135 cases 98%) (Table 1). However, some studies showed that supraglottic tumors were the most common [3, 8].

Although the presented tumors were predominantly on one side, in 83 cases (of 138 cases, 60%), the tumor did cross the midline to the other side. Mostly, the presented tumors were masses (92 cases, 67%) invading the thyroid cartilage (82 cases, 59%), and moderately differentiated (124 cases, 90%). These findings were in accordance with Kaur et al. [5] results who also reported predominance of male gender in the sixth decade with moderate differentiated tumors (72% of cases) and exophytic appearance (60% of cases). However, their studied population were majorly affected by transglottic tumor (66%). They admitted that the glottic tumors are more common worldwide. Locatello et al. [9] in their study about advanced cancer larynx reported thyroid cartilage invasion in 26 cases (of 30) which was similar to this study where most of the cases were advanced and had thyroid cartilage invasion.

As certain types of laryngeal cancer have tendency for lymphatic spread [10], neck dissection has become an important tool in its management. Yet, it could add to

Table 1 Analysis of demographic data and tumor factors

	Total cases (n=138)	Negative node group (n=112)	Positive node group (n=26)	P value
Age/years				
Mean (SD)	59(9)	59 (9)	58 (7)	0.5
Gender				
Male	131	106	25	0.7
Female	7	6	1	
Site of tumor				
Subglottic	7	7	0	0.03
Glottic	52	45	7	
Supraglottic	30	19	11	
Transglottic	49	41	8	
T stage				
1	3	1	2	0.1
2	10	7	3	
3	103	86	17	
4	22	18	4	
Side of tumor				
Midline	46	36	10	0.8
Right	51	42	9	
Left	41	34	7	
Midline cross				
No	55	49	6	0.05
Yes	83	63	20	
Size of tumor/cm				
Mean (SD)	3.6 (1.3)	3.6 (1.3)	3.8 (1.2)	0.6
Tumor shape				
Mass	92	74	18	0.8
Ulcer	46	38	8	
Thyroid cartilage infiltration				
No	56	47	9	0.5
Yes	82	65	17	
Tumor type				
Squamous cell carcinoma	135	109	26	1
Mucoepidermoid carcinoma	3	3	0	-
Tumor grade				
Undifferentiated	3	1	2	0.1
Grade 1	4	4	0	
Grade 2	124	102	22	
Grade 3	7	5	2	

SD standard deviation

the morbidity as 70% of patients reported shoulder dysfunction without direct injury to the spinal accessory nerve [4]. Hence, re-evaluation of the tendency of tumor spread and analyzing the corresponding factors is important to minimize overtreatment and to detect any change of tumor's behavior over time.

In this study, neck dissection yielded positive lymph nodes in 26 cases (of 138, 19%). Nineteen cases had ipsilateral LN spread (73%), 5 cases (19) developed contralateral spread, and 2 cases (8%) had bilateral spread (Table 2). Supraglottic tumors were the most common proportion of neck metastasis having 11 cases (42%)

Table 2 Analysis of positive lymph nodes

	Count (n=26)	Percent
Lymph node spread		
Ipsilateral	19	73
Contralateral	5	19
Bilateral	2	8
Tumor origin		
Glottic	7	27
Supraglottic	11	42
Transglottic	8	31

followed by transglottic tumors (8 cases, 31%). In relation to the total supraglottic tumors, it showed 37% of tendency for LN spread (Table 3).

Considering the tumor factors, statistical comparison with the non-metastasized group showed a statistically significant *P*-value of 0.03 regarding the tumor site which was mostly in the supraglottis. In addition, tumors crossing midline had a *P*-value approaching significance of 0.05. Other factors such as tumor size, ulceration, differentiation, and thyroid cartilage invasion were not statistically significant for LN metastasis.

In accordance with this study's results, Tomik et al. [3] described in their study, performed over 1400 patients, 76% unilateral metastasis (348 cases), 5% contralateral metastasis (25 cases), and 19% bilateral metastasis (87 cases). Lim et al. [4] in their study reported 20 cases with positive LN (of 102, 20%). Occult metastasis was 30% ipsilateral and 11% in the contralateral side. Xu et al. [11] in their study mentioned the supraglottic tumors to have the highest incidence of neck metastasis and moderate/poor differentiated tumor were more likely to metastasize than well differentiated ones. They also found that important factors for contralateral metastasis were tumors crossing the midline and presence of ipsilateral metastasis. Locatello et al. [9] in their study mentioned that thyroid cartilage invasion did not affect the overall or disease-specific survival.

Supraglottic cancer tends to metastasize to the regional LN, whether ipsilateral, contralateral, or bilateral, due to its rich lymphatic network [12]. Midline

Table 3 Proportion of cases with lymph node spread in relation to the total number of tumors in the same specified area

	Count	Percent
Subglottic	0/7	0
Glottic	7/52	13
Supraglottic	11/30	37
Transglottic	8/49	16
Total	26/138	19

tumors are prone to spread because of the defect in the inner perichondrium at the insertion of Broyle's ligament [2].

The authors agree with Steuer et al. [13] that any risk of occult metastasis of greater than 20% is an indication for neck dissection. Therefore, for supraglottic tumors, elective neck dissection of the neck is still advised.

Some limitations of this study were encountered such as being a retrospective study which hindered reaching conclusive causality, the duration of the study, and the unavailability of some pathological data such extranodal extension.

Conclusion

This study investigated different factors related to lymph node metastasis from primary laryngeal tumor. The most important factors were the site of the tumor and its relation to the midline. Other factors such as tumor size, ulceration, differentiation, and thyroid cartilage invasion were not statistically significant for LN metastasis.

Abbreviations

LN: Lymph node; ND: Neck dissection; SCC: Squamous cell carcinoma

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Not applicable.

Authors' contributions

MS—Analysis of data and writing. AE—Data collection. All authors have read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. All procedures performed in the study were in accordance with the ethical standards and approved by the ethical committee (Otolaryngology Department of Cairo University- ethical committee reference number is not available). Consent to participate is inapplicable for this retrospective study.

Consent for publication

Not applicable.

Competing interests

The authors have no competing interest.

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