Thyroid Gland Invasion in T3 and T4 Laryngeal Carcinoma

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Abstract

Background: Total or ipsilateral hemithyroidectomy or isthmectomy are performed along with total laryngectomy in many cases of advanced cancer larynx with subglottic or extralaryngeal spread. The need for performance of thyroidec- tomy during TL is controversial.

Aim of Work: To assess factors favoring thyroid gland invasion (TGI), indications of hemithyroidectomy, and post-operative complications.

Patients and Methods: It is a prospective analytical study that included 40 patients who were diagnosed as T3 or T4 laryngeal carcinoma and had total laryngectomy with at least hemithyroidectomy. The incidence of thyroid gland invasion was reported histopathologically in laryngeal carcinoma and correlated with site and stage of the primary tumor vocal cord fixation, subglottic extension, and prior irradiation.

Results: Our study included 40 patients; 37 were males. Four male patients cases (10%) had thyroid gland invasion by laryngeal carcinoma, two cases (5%) had colloidal nodules and one case (2.5%) had follicular adenoma. Thyroid cartilage invasion was evident in all 4 cases (100%) with TGI which was of statistical significance \((p\text{-value}=0.026)\). Of the 4 cases with TGI three cases (75%) were transglottic carcinomas, and one case (25%) was glottic carcinoma. All were T4a staged 100%. All cases (100%) with TGI had unilateral fixed vocal cord, infiltrated anterior commisure, and unilateral subglottic extension >1cm.

Postoperative complications occurred in 28 cases (45%). Three cases with TGI (75%) develop complications.

Conclusion: Histological thyroid gland invasion by advanced tumors must not be underestimated. We suggest that subglottic and transglottic tumors are more prone to TGI. We found Thyroid cartilage invasion and preoperative CT findings of thyroid gland were statistically correlated with TGI.

Key Words: Hemithyroidectomy – Cancer larynx – Thyroid gland invasion.

Introduction

THE anatomical relationship between thyroid gland and the larynx provides an explanation for why laryngeal carcinomas may be associated with thyroid gland metastasis [1].

The isthmus of the thyroid gland is positioned over the second, third, and fourth tracheal rings, and the thyroid lobes are located in close proximity to the thyroid laminae, cricothyroid membrane and cricothyroid space. The lymphatics of the subglottic perforate the cricothyroid membrane and drain to the prelaryngeal and pretracheal nodes anteriorly, and drain to the paratracheal nodes posterolaterally. All of these lymph nodes is in close proximity to the thyroid gland [2].

Laryngeal tumors comprise about 1% of all malignancies and 30% of the head and neck malignancies [3].

Squamous Cell Carcinoma (SCC) is by far the most common malignant tumour of the larynx representing 95-96% of all malignant tumours at this location [4].

Laryngeal cancer involving thyroid gland can be due to either direct extension or lymphatic metastasis or rarely haematogenous. These three types of extension are the basis for the indications for thyroidectomy during laryngectomy for advanced cancer larynx [2].

These are three pathways for direct spread of cancer to the extralaryngeal soft tissue, and the thyroid gland; through thyroid cartilage, through cricothyroid membrane, and through cricoid cartilage [5].

Hypothyroidism following total laryngectomy has been attributed to the dissection of the preserved
thyroid lobe, which damages its vasculature or damage to the vascular pedicles and consequently impairs its ability to compensate for the loss of the opposite lobe [6,7].

Patients and Methods

This is a prospective analytical study that was performed at the otorhinolaryngology Head and Neck Surgery Department, Kasr El-Aini Hospital, Cairo University during the period from October 2012 to August 2014.

Cases presented to the outpatient clinic with the diagnosis of laryngeal mass were properly assessed endoscopically and radiologically to select forty T3 or T4 laryngeal carcinoma patients who were candidate for total laryngectomy with at least hemithyroidectomy.

Clinical staging of the primary tumor as well as neck nodes will be based on physical examination, endoscopic assessment and radiological findings according to the American Joint Committee on Cancer Staging 2002 classification TNM staging.

All the patients in the study were subjected to full history taking, examination of the neck, external examination of the larynx, thyroid gland, and cervical lymph nodes, and endoscopic laryngeal assessment, C.T. scan of the Neck with contrast (coronal and axial cuts, soft tissue and bone windows), MRI (T1, T2 and T1 with contrast) in some cases, and direct laryngoscopy to take biopsy.

Inclusion criteria were:

Patients with laryngeal carcinoma stage T3, and laryngeal carcinoma stage T4 who are candidate for total laryngectomy with or without post-operative radiotherapy.

Exclusion criteria were:

Laryngeal carcinoma stage TI, laryngeal carcinoma stage T2, laryngeal carcinoma stage T4B, cases with previous thyroidectomy, history of primary thyroid cancer, patients candidate for conservative laryngectomy, distant metastasis, comorbidities precluding major surgical intervention.

Total laryngectomy with or without partial pharyngectomy was carried out with ipsilateral hemithyroidectomy or subtotal thyroidectomy or total thyroidectomy with preservation of at least one parathyroid gland Fig. (1).

The following parameters were evaluated intraoperatively:

1- Presence of subglottic extension.
2- Gross lymph node involvement.
3- Gross thyroid gland involvement.

Histopathological examination of the specimens was done by an experienced pathologist.

Patients were followed up by full history taking, complete general examination, external neck examinations, and postoperative CT in suspicious cases every month for the first 6 months then every 3 months to assess nodal or stomal or thyroid gland recurrence and to assess the need of thyroid and parathyroid replacement.

The program SPSS for windows (version 11) was used for statistical analysis. Descriptive statistics were carried out for all variables including obtaining mean, mean deviation, median, variance, standard deviation, standard of error and probability of occurrence. The independent samples student (t)-test was used for statistical analysis for all our parametric variables. p-value of 0.05 or less was considered significant, and a p-value of 0.01 or less was considered highly significant.

Results

This study included 40 patients presented with Laryngeal carcinoma T3 or T4. There were 37 males (92.5%), and 3 females (7.5%), so, results were not studied separately for men and women.

Their age ranged from 45 to 80 years old with the mean 61.1 years. The main presentation was hoarseness of voice.

There were 18 cases T3 (45%), "10 cases (25%) T3a, 8 cases (20%) T3b and 22 cases were T4a (55%).
Thirty six cases (90%) had free thyroid gland by CT scanning of the neck, two cases (5%) had nodular thyroid lesions, and 2 cases (5%) were found to had thyroid gland invasion by the laryngeal carcinoma in CT scan of the neck.

Thirty three cases (82.5%) had been subjected to hemithyroidectomy, 4 cases (10%) had subtotal thyroidectomy, 3 cases (7.5%) had total thyroidectomy. There were 33 cases (82.5%) with thyroid gland free of any pathology. 2 Cases (5%) with colloidal nodules. 1 Cases (2.5%) with follicular adenoma. 4 Cases (10%) with thyroid gland invasion (TGI) by laryngeal carcinoma proved by histopathological examination.

All 4 cases were males (100%). Their mean age was 6.18 years. The mean duration of hoarseness was 22.5 months. Three cases (75%) with TGI had no associated medical comorbidity, while one case had ischemic heart disease.

Two cases with (TGI) had received preoperative radiotherapy or chemoradiotherapy. None of the cases with TGI had preoperative tracheostomy.

Three cases with TGI (75%) were transglottic carcinomas, and one case (25) was originally glottic carcinoma.

All cases (100%) with TGI had unilateral fixed vocal cord. All cases with TGI (100%) had infiltrated anterior commissure. All TGI (100%) cases had unilateral subglottic extension > 1 cm. Table (1).

Three cases with TGI (75%) had infiltrated arytenoids, thyroid cartilage was evident by radiological findings in all 4 cases (100%). Table (1).

Thyroid gland invasion was anticipated by CT scan in 2 cases (50%), and it couldn't be diagnosed radiologically in 2 patients, and both had treated by radiotherapy before.

Two TGI cases had postoperative radiotherapy. The other 2 cases did not because they had already received preoperative radiotherapy.

In our study 2 cases with TGI (50%) develop 1 complication stomal stenosis and wound infection, 1 case developed multiple complications hemorrhage and wound infection. There were no nodal or stomal recurrences in all cases with TGI. Non of these cases needed lifelong hormonal replacement.

Two cases (50%) were grade II moderately differentiated SCC, 1 case was grade III poorly differentiated SCC, and 1 case was adenoidcystic carcinoma.

<table>
<thead>
<tr>
<th>Case in the study</th>
<th>Total TGI thyroid invasion TGI value</th>
</tr>
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<tbody>
<tr>
<td>Anterior comissure invasion</td>
<td>40</td>
</tr>
<tr>
<td>Arytenoid cartilage invasion</td>
<td>35</td>
</tr>
<tr>
<td>Subglottic extension</td>
<td>25</td>
</tr>
<tr>
<td>Fixed vocal cord</td>
<td>28</td>
</tr>
<tr>
<td>Thyroid cartilage invasion</td>
<td>38</td>
</tr>
</tbody>
</table>

Table (1): Tumor extension in TGI cases in the study group.

**Discussion**

Thyroidectomy with total laryngectomy is designed to resect any known or occult direct tumour extension or metastasis in order to ensure local control [2].

Many indications for thyroidectomy associated with laryngectomy have been reported in the literature. Many authors recommend hemithyroidectomy if subglottic extension >10-15mm [8]. Other indications are thyroid cartilage invasion on CT [9,10], fixed vocal folds, extension to the anterior commissure, laryngeal ventricle, cricothyroid membrane [10]. All these indications need to be confirmed and refined.

We performed hemithyroidectomy (at least) with total laryngectomy for T3 & T4 laryngeal carcinoma aiming to assess the incidence and factors favoring thyroid gland invasion by laryngeal carcinoma.

In our study we found 4 cases (10%) with thyroid gland invasion by laryngeal carcinoma. Similiary Nayak, and his team [11] studied retrospectively 45 patients had TL with thyroidectomy for LC and found five cases (11.11 %) out of 45 cases had TG invasion.

Dequanter et al., [7] reported three patients (8%) of 35 patients showed thyroid glandular infiltration due to epidermoid carcinoma in two cases, and thyroid carcinoma in one case. While Sparano et al., [10] found a higher incidence; 7 patients out of 30 cases (23%) had TGI.

Dequanter et al., [7] reported three cases (8%) of 35 patients showed thyroid glandular infiltration due to epidermoid carcinoma in two cases, and thyroid carcinoma in one case. While Sparano et al., [10] found a higher incidence; 7 patients out of 30 cases (23%) had TGI.

Comparably, a lower incidence of TGI was reported by Gurunatnan et al., [12] in their studies, in fifty patients only 2%, and respectively had tumor invasion to the thyroid gland. Histologic evidence of TGI in that study was not found in any of the cases (0%).Similar results were reported by Ceylan et al., [13].

In our study, two cases (50%) of TGI cases had received preoperative radiotherapy. None of the cases with TGI (0%) had preoperative tracheostomy.
On the other side, Nayak et al., [11] reported four cases with TGI (9%) received preoperative radiotherapy. Also Saparano et al., [10] have noted that prior radiation of the larynx did not correlate with an increased risk of TGI and should not influence the decision-making process to do hemithyroidecomy with laryngectomy.

In our study, all cases with TGI were staged T4a 100%. Although it is high incidence, it wasn’t of statistical significant. Similary, Kim et al., [14] reported that among 15 patients with laryngeal cancer. Three cases 20% were stage III, and nine 60% were stage IV. TGI developed only in stage IV cases 100%, although that, the difference was not statistically significance, while, others reported that tumors with TGI were classified as T3 and T4 [15]. Also Sparano’s colleague [10] reported direct extension to the thyroid gland in five cases (15%) T4 stage and two cases (9%) were T3.

True cord fixation indicates infiltration of the vocalis muscle in the paraglottic space (PGS) which contains only loose soft tissues that provide little resistance to neoplastic dissemination inferiorly to invade the extralaryngeal compartment via the cricothyroid space the PGS can therefore be considered a critical route of tumor extension in the anteroinferior direction outside the larynx [16].

In our study all cases (100%) with TGI had unilateral fixed vocal cord. \( p \)-value 0.62 (not significant). Also Sparano et al., [10] found all cases had a fixed ipsilateral vocal cord, but they staed that vocal cord fixation contribute independently as a significant factor for thyroid gland invasion. \( (p=0.003) \).

Although tumors with AC infiltration are more prone to extralaryngeal spread due to deficiency of perichondrium at the insertion of the AC tendon, mere involvement of AC could not be a strong indication for thyroidectomy due to the far distance between the anterior commissure and the thyroid isthmus. In the current study all cases with TGI (100%) had an infiltrated anterior commissure. Similary, Saparano et al., [10], Kim et al., [14] and Dequanter et al., [7] found that anterior commissure invasion was present in all cases with TGI (100%).

Neoplasms with subglottic involvement demonstrate a high risk of extralaryngeal and thyroid gland invasion. Laryngeal tumors exit the larynx through weak points in the laryngeal framework. In the subglottic region, this invasion occurs through invasion topoparaglottic space or cricothyroid membraneor paramedian cricothyroid space, immediately lateral to the cricothyroid ligament [16]. Subglottic extension greater than or equal to the height of the posterior lamina of the cricoid cartilage is associated with an increased risk of histological thyroid gland invasion [2].

In our study all TGI (100%) cases had unilateral subglottic extension > 1 cm. There were only one case (25%) did not have subglottic extension histopathologically, that was statistically insignificant.

Also, Nayak and his team [11] reported 33 cases (74%) of 45 had SG extension. 5 of them had TGI. On the other hand Dequanter et al., [7] and Saparano et al., [10] found that all cases 100% with TGI had a subglottic extension more than 1 cm. That was of statistical significance \( (p=0.003) \).

Gallegos-Hernandez et al., concluded that the best predictor of thyroid gland invasion was the evidence of extra laryngeal cancer extension [15].

In our study, there was a statistical significant relation between thyroid cartilage invasionby CT scan and histopathological thyroid gland invasion \( (p-value=0.026) \).

Gurunatnan et al., [12] recommended to sacrifice the whole thyroid gland during surgery if there were laryngeal cartilage invasion and perithyroidal soft tissue involvement. On the other hand, Mendelson et al., [16] in their meta-analysis found that cartilaginous invasion by laryngeal or hypopharyngeatumour was not a significant predictor of thyroid gland invasion \( (p-value > 0.05) \).

In the present study, thyroid gland invasion by laryngeal carcinoma could be anticipated by CT scan in 2 cases 50% out of four cases with TGI. Thyroid gland invasion couldn't be diagnosed radiologically in 2 patients, and both were treated by radiotherapy before. We found thyroid gland invasion by CT scan was a statistically significant factor for TGI \( p\)-value <0.001.

Similary, Dequanter et al., [7] reported the evidence of radiological invasion of the thyroid gland in all the patients with TGI. However Gaillardin et al., [2] reported four cases of 14 (36%) of histological thyroid gland invasion were not suspected on the preoperative CT.

In our study, two cases with TGI were grade II moderately differentiated SCC, and another 1 was grade III poorly differentiated SCC, and the last one was adenoid cystic carcinoma. The relation between the degree of differentiation and TGI was statistically insignificant.
On the other hand Nayak et al., [11] found the tumour differentiation to be a very important factor determining the mode of TG invasion. Moderately differentiated tumours had a propensity for non-contiguous spread, whereas, well differentiated cancers spread contiguously. The difference between the two was statistically significant (p=0.05).

We founded that arytenoid cartilages were infiltrated in 25 cases (62.5%). 3 cases with TGI (75%) had infiltrated arytenoids. No other study commented on role of arytenoids cartilage invasion.

Authors considered thyroid gland invasion by squamous cell carcinoma of the larynx as a factor of poor prognosis [2]. We found that complications occurred in 28 cases (45%), 3 cases with TGI (75%) develop complications. There were no nodal or sternal recurrences in all cases with TGI (0%).

Similary, Dequanter et al., [7] found that the rate of peristomal recurrence was not different comparing the group of patients with thyroid gland invasion with the group of patients without thyroid gland invasion. On the contrary Kim et al., [14] reported distant metastasis or local recurrence developed in three cases with thyroid invasion. And the prognosis for patients with thyroid invasion was worse than for patients with noninvasive tumors, but the difference was not statistically significant (p=0.659).

Sahin [17] in his study onseventy three patients who were treated surgically for squamous cell carcinoma of larynx found coincident 4 thyroid carcinomas.

Based on this study we recommend a very careful preoperative workup for accurate evaluation of laryngeal carcinoma and state of thyroid gland. In advanced stage laryngeal carcinomas we recommend performing hemithyroidectomy in cases with long history of carcinoma, subglottic extension >1cm, extra-cartilagenous spread evident by CT scan, AC infiltrations, and transglottic carcinomas. We recommend total thyroidectomy if there is CT evidence of thyroid gland infiltration.

Further studies could be performed with more recent modalities such as high resolution CT scan, MRI and PET scan for accurate detection of thyroid gland invasion. Also studies for role of immuno-histochemistry and frozen section could be more useful to detect micrometastasis.

Studies with larger number and longer follow-up duration would be performed for proper evaluation of thyroidectomy outcomes and survival rates.

Conclusion:

Histological thyroid gland invasion by advanced tumours must not be underestimated. We suggest subglottic and transglottic tumors more prone to TGI. We found thyroid cartilage invasion and preoperative CT findings of thyroid gland were statistically significant factors for TGI and good indicators for thyroidectomy.

References


