THYROID CARCINOMA ASSOCIATED WITH SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK: WHICH POLICY?

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Abstract: Background. Thyroid carcinoma occurring as a second primary associated with head and neck squamous cell carcinoma (HNSCC) is unusual. The clinical management of thyroid cancer in such cases has been debated.

Methods. Between 1975 and 2004, we collected 33 cases. The associated thyroid carcinoma was diagnosed either during or as a consequence of surgery planned as head and neck cancer treatment.

Results. The associated thyroid carcinoma was never seen to recur. Five-year overall survival was 41%. Disease-free survival after 40 and 66 months was 11.1% and 5.6%, respectively.

Conclusions. We consider the treatment of thyroid cancer to be complete when the thyroid gland, either with or without lymph nodes, has been included in the specimen obtained during surgery for HNSCC. In the group of cases in which associated thyroid carcinoma was only found within the neck lymph nodes and the thyroid gland has not been treated, we discourage further surgical treatment or radioactive iodine therapy.

Keywords: thyroid neoplasm; squamous cell carcinoma; head neck neoplasm; neck surgery; thyroid surgery

Thyroid carcinoma occurring as a second primary associated with head and neck squamous cell carcinoma (HNSCC) is unusual and can be discovered as palpable thyroid mass during neck surgery, as an occult carcinoma in the thyroid gland removed during laryngec- tomy or as thyroid cancer that is found in lymph nodes of the neck dissection specimen.

This association, often clinically unsuspected, is especially problematic in terms of management when the primary head and neck disease carries a poorer prognosis than thyroid carcinoma.

Over the past 15 years, few series have been reported in the literature; in 1991 we reported 6 such cases.

To date we collected 27 new cases of head and neck SCC associated with synchronous thyroid carcinoma with various stages at presentation and histologies. Our aim was to clarify and support clinical decision about surgical treatment of the thyroid cancer in such situations.

MATERIALS AND METHODS

Between 1975 and 2004, we reviewed 33 cases of thyroid carcinoma associated with HNSCC from the clinical and pathologic records of Istituto Nazionale Tumori of Milan.
All the patients were admitted to hospital because of head and neck cancer. Surgical resection of the primary along with neck dissection or neck dissection alone was always performed as part of the scheduled treatment for HNSCC. The associated thyroid carcinoma was diagnosed either during or as a consequence of the surgery planned as head and neck cancer treatment.

RESULTS

We reviewed 33 patients (31 men, 2 women), with a mean age of 60 years (range, 44–75 years). All the tumors were staged according to UICC (Union Internationale Contre le Cancer) 2002 TNM classification\(^1\) as shown in Table 1.

All the aerodigestive cancers were diagnosed as SCC of various tumor grades. The histologies of the associated thyroid carcinomas were as follows: 30 cases of papillary carcinoma, 2 of medullary carcinoma, and 1 follicular carcinoma.

Table 2 shows the site of occurrence of HNSCC.

In 2 cases the associated thyroid carcinoma was discovered during neck surgery planned for HNSCC located in the larynx and hypopharynx, respectively. The tumor consisted of a palpable nodule of the thyroid gland that was intraoperatively confirmed by frozen section. Total thyroidectomy was then performed in both patients as part of their surgery.

Thirty-one cases were diagnosed during the postoperative examination of the surgical specimen. Eighteen of these patients did not have the thyroid gland involved in the first surgical treatment planned for HNSCC. In all of them, the associated thyroid carcinoma was found in the lymph nodes.

In these 18 cases, the relation between neck ultrasonography, further thyroid surgery, and histologic examination is shown in Table 3. Eight of these 18 patients underwent reoperation. Seven total thyroidectomies and 1 thyroid lobectomy were performed. In 7 of 8 cases, an associated thyroid carcinoma was found at histologic examination. Ten of 18 patients were never treated on thyroid gland.

Thirteen of 31 patients had the thyroid gland involved in their surgery for HNSCC. Among these 13, 9 patients underwent contemporary thyroid lobectomy. In 5 of 9 cases, associated thyroid carcinoma was found in the gland; in the remaining 4 cases, in the cervical lymph nodes and not in the resected gland (in 3 of these cases, associated thyroid carcinoma and HNSCC metastases were found within the same lymph node).

Four of 13 patients who had a total thyroidectomy. Two had associated thyroid carcinoma in the gland, 1 both in thyroid and lymph nodes and 1 in lymph nodes but not in thyroid gland (in this case associated thyroid carcinoma and HNSCC metastases were found within the same node).

As a result, 15 of 33 patients had synchronous thyroid surgery, while 8 patients were only treated after associated thyroid carcinoma had been confirmed at histologic examination of the lymph nodes.

Globally, 9 cases of associated thyroid carcinoma were found in the thyroid gland, 8 patients had tumor in both the gland and the lymph nodes, and the remaining 16 had associated thyroid carcinoma only in the lymph nodes.

As far as surgical treatment is concerned, thyroid cancer was ultimately treated by total thy-
roidectomy and thyroid lobectomy in 13 and 10 cases, respectively. Ten patients were never treated on thyroid gland. All these patients underwent neck dissection (unilateral level I to V in 28 of 33 cases), and 23 of 33 patients (69.7%) underwent radiotherapy on the neck as part of scheduled treatment for HNSCC. Neither postoperative radioactive iodine therapy nor adjuvant chemotherapy was given.

The patients were followed up for a mean period of 45 months (range, 21–151 months). The associated thyroid carcinoma was never seen to recur. This was true also in the group of patients who did not undergo surgery on the thyroid gland (10 cases). Five-year overall survival was 41%. Disease-free survival after 40 and 66 months was 11.1% and 5.6%, respectively (Figure 1).

DISCUSSION

Surgery alone or combined with radiotherapy–chemotherapy represents the main clinical approach to HNSCC. In tumor stage III and IV, widely recognized schedules suggest that the primary cancer should be treated along with the regional lymph node dissection. In selected stage I and II tumors, elective neck dissection should be a part of the surgical treatment. This policy allowed us to collect this series of patients in whom unsuspected thyroid carcinoma was found at histologic examination of the surgical specimen.

Unexpected pathologic findings may be present in more than 3% of neck dissections,2 and the incidence of thyroid carcinoma incidentally found in the neck dissection specimen performed for HNSCC ranged between 0.5% and 5%.3,4

Moreover, in the study by Mortensen5 performed on autopsies, the incidence of unknown thyroid carcinoma was 5% reaching to 17% in the cases reported by Sampson.6

These data seem to suggest that indolent and clinically unsuspected thyroid carcinoma is not so rare. Associated thyroid carcinoma can be discovered as palpable thyroid mass during neck surgery, as an occult carcinoma in the thyroid gland removed, i.e., during laryngectomy or as thyroid cancer that is found in lymph nodes of the neck dissection specimen. In this latter pathologic instance, the clinical significance of abnormal thyroid inclusion in the cervical lymph nodes has been largely debated over the past years.3,4,7–9 We consider that benign inclusions are extremely rare and agree with other authors on considering such inclusions, usually, as expression of metastatic thyroid cancer. So it has been in the 24 cases presented in this series.

When histologically confirmed, the clinical implication mainly concerns the indication whether to treat or not, following the standard protocols, the incidental thyroid cancer in case it should be associated with HNSCC.

There are few data in the literature regarding the clinical significance, outcome, and treatment of such unexpected findings.

Ninety-four percent of our patients were men, with a mean age of 60 years. Similar figures were reported by Pacheco-Ojeda et al10 and Ansari-Lari et al,9 while in the series from the The University of Texas M. D. Anderson Cancer Center,11 63% of the patients were male with a mean age of 50 years.

Moreover, all the patients in the present series were heavy smokers, and more than 50% of them were also heavy drinkers. We cannot compare these data with those reported in the literature3,8–11 because of lack of information about tobacco and alcohol consumption in the latter.

In our experience and also in the cases reported in the literature,8–11 all the patients initially presented signs and symptoms strictly related to SCC of the upper aerodigestive tract. The associated thyroid carcinoma was always detected as a consequence of the surgical treatment of HNSCC. We never observed the inverse situation in which HNSCC has been detected during the follow-up for thyroid cancer.

These findings allow us to suppose that such patients were “selected” by HNSCC. This seems to be confirmed by the gender distribution of the patients. In fact, thyroid carcinoma is considered 2 to 3 times more frequent among females,12 while in these series few women have been included.
In our series, stage III and IV HNSCC accounted for 76% of cases. Similar figures were reported by Vassilopoulou-Sellin and Weber, Coskun et al, and Resta et al, while in the series of Pitman et al, 4 patients were considered to have stage I–II disease (1 case and 3 cases, respectively) and the remaining 3 patients had stage III–IV (1 case and 2 cases, respectively).

Advanced stages of head and neck cancer usually have a poor prognosis, mainly owing to local and regional recurrences and the onset of a second primary during the follow-up. In the present series, 8 patients had stage I and II head and neck tumors. Six (75%) of these tumors were in the oral cavity (Table 2). In these cases, neck dissection is reserved for selected patients with recognized bad prognostic factors, such as tumor volume, subsite of occurrence or histologic findings. Consequently, we could suppose that also this group of patients, in which associated thyroid carcinoma has been found in the neck, were selected according to the worst prognosis.

All these data suggest that thyroid cancer was more frequently found in patients with HNSCC having an unfavorable outcome. Our results seem to confirm these figures. In fact, the 5-year overall survival was only 41%. Moreover, in our series the disease-free survival after 40 months was 11.1% and dramatically decreased to 5.6% after 66 months (Figure 1). Interestingly, except in 1 case, all the recurrences were attributed to HNSCC and none to the thyroid cancer.

Although the median follow-up ranged between 17 and 66 months, reported data differ from our own in terms of survival but seem to confirm that almost all the patients (28% of cases) had recurrences due to their HNSCC (Table 4).

In our experience, the associated thyroid carcinoma was treated with different approaches. In some patients, thyroid cancer, and occasionally its neck metastases too, were “unexpectedly” treated during the surgery planned for HNSCC. Other patients underwent reoperation after associated thyroid carcinoma had been confirmed at histologic examination of the lymph nodes removed during the neck dissection performed for the same reason. These procedures are largely confirmed in the literature. It is of interest to note that although 10 of our patients did not receive any treatment on thyroid gland, none of them developed a clinically evident thyroid cancer during the follow-up. The same outcome has also been found in 4 cases reported by Vassilopoulou-Sellin and Weber, in 4 cases by Butler et al, in 4 cases by Resta et al, and in 1 case by Ansari-Lari and Westra.

The lower aggressiveness of thyroid carcinoma could explain these figures. A longer follow-up time is probably required to allow the thyroid carcinoma to reach clinical evidence.

In 1991, we reported 6 such cases and concluded that the surgical treatment of primary thyroid cancer after discovering its lymph nodes metastases should be conservative. Vassilopoulou-Sellin and Weber in 1992 agreed with us and suggested that thyroid gland can be followed conservatively if it demonstrates no anomaly on physical examination and on noninvasive imaging. In 2001, Fliegelman et al introduced an interesting algorithm in which incidental metastases of thyroid carcinoma within lymph nodes during head

<table>
<thead>
<tr>
<th>Author</th>
<th>No. of patients, SCC/thyroid</th>
<th>Median follow-up, mo (range)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Butler (1967)</td>
<td>22/17</td>
<td>na (5 mo–8 y)</td>
<td>NED: 8</td>
</tr>
<tr>
<td>Pachedo-Ojeda (1991)</td>
<td>10/10</td>
<td>17 (1 mo–17 y)</td>
<td>DOD: 6*</td>
</tr>
<tr>
<td>Vassilopoulou (1992)</td>
<td>8/8</td>
<td>37 (7 mo–18 y)</td>
<td>AWD: 2</td>
</tr>
<tr>
<td>Pitman (1996)</td>
<td>7/7</td>
<td>24 (12 mo–48 mo)</td>
<td>LFU: 1</td>
</tr>
<tr>
<td>Coskun (2002)</td>
<td>3/3</td>
<td>46 (19 mo–49 mo)</td>
<td></td>
</tr>
<tr>
<td>Ansari-Lari (2003)</td>
<td>21/6</td>
<td>39 (18 mo–81 mo)</td>
<td></td>
</tr>
<tr>
<td>Sheahan (2005)</td>
<td>10/1</td>
<td>3 mo</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>94/64</td>
<td></td>
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</tr>
</tbody>
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Abbreviations: SCC, squamous cell carcinoma; na, not available; NED, no evidence of disease, both SCC and thyroid cancer; DOD, died of disease (SCC); AWD, alive and well; LFU, lost at follow-up.

*1/6 died of other causes.
†1/3 died of thyroid cancer.
‡1/4 died of other causes.
§Died of second primary.
and neck surgery for SCC with a poor prognosis should not be treated by surgery. The same opinion has been reported by Coskun in 2002. This author concluded that occult thyroid cancers usually remain occult cancers and seldom become clinically apparent and that total thyroidectomy may not be mandatory.

All these findings appear in great contrast with the study of Pitman et al., who recommended total thyroidectomy and radio-ablation in selected cases, in an attempt to avoid inadequate therapy for incidental thyroid carcinomas.

Our experience and the studies presented in the literature suggest that eventual prognosis was ultimately determined by the patient's primary aerodigestive tract malignancy. This is particularly true for advanced HNSCC. On this view, we consider the treatment for thyroid cancer to be complete when the thyroid gland (one lobe or the whole gland) with or without lymph nodes has been included in the specimen obtained during surgery for HNSCC. In the group of cases in which associated thyroid carcinoma was only found within the neck lymph nodes and the thyroid gland was not treated, we discourage further surgical treatment or radioactive iodine therapy. In fact, most of these patients underwent radiotherapy on the neck, and this treatment was recently demonstrated to also be effective for the local control of thyroid carcinoma.

In such patients, we suggest lifetime clinical and ultrasound control in order to monitor the possible evolution of the thyroid cancer. 1-Thyroxin suppressive therapy and serum thyroglobulin assay should be considered.

Since data concerning cases of thyroid cancer associated with HNSCC with a good prognosis are scant, both in the medical literature and in our experience, we cannot indicate any standard treatment. These cases, therefore, should be approached on an individualized basis.

An adequate preoperative staging by MRI and ultrasonography is always necessary, reducing the occurrence of “incidental” cancers of the thyroid gland. When this association has been demonstrated preoperatively, standard clinical approach on thyroid cancer should be applied. Of course, surgery on the thyroid, when needed, should be performed in combination with the intervention on HNSCC.

REFERENCES