HEAD AND NECK

Occult contralateral nodal metastases in supraglottic laryngeal cancer crossing the midline

Sedat Öztürkcan · Hüseyin Katilmiş · Ismail Özdemir ·
Bilge Tuna · Işil Adadan Güvenç · Riza Dündar

Abstract We evaluated the risk of occult contralateral neck involvement according to T stage and ipsilateral neck stage in centrally located supraglottic laryngeal cancer. The side largely involved by the tumor was defined as ipsilateral and the other side was defined as contralateral in terms of the neck dissection side. We retrospectively analyzed clinical and pathologic data from a group of 189 centrally located supraglottic cancer patients in which bilateral neck dissection was part of the primary treatment. Among 378 neck dissection specimens, the rate of bilateral metastasis was 33/189 (17.5%). The rate of occult metastases in the contralateral side were 33/75 (44%) and 6/114 (5.3%), when ipsilateral neck was pN+ and pN−, respectively. Clinically or pathologically positive ipsilateral nodes and the extracapsular spread in the ipsilateral positive nodes displayed significantly higher risk of contralateral metastases. The incidence of occult contralateral metastases did not seem to be affected significantly by T stage of the tumor. Our retrospective study confirmed that the probabilistic criteria of the incidence of contralateral occult metastases in supraglottic laryngeal cancer with tumor largely involving one side and crossing the midline. On the basis of our data, there is a high prevalence of contralateral metastases in tumors with clinically or pathologically positive ipsilateral lymph nodes. The extracapsular spread of the nodes is also an important determinant of the contralateral involvement.

Introduction

Knowledge of the pattern of lymphatic spread in cancer of the larynx is a crucial element to plan a proper management strategy of the neck. Elegant anatomic and embryologic studies [1–3] have demonstrated the laryngeal compartments and spread of laryngeal cancer.

Because of the anatomic distribution of lymphatic drainage in the head and neck areas [4, 5], those lesions that develop in well-lateralized primary sites (vocal cord, ventricle, aryepiglottic fold, etc.) tend to metastasize to the ipsilateral side of the neck. Conversely, in cancer involving structures of the midline larynx, both the sides of the neck are at risk. In fact, any lesion, particularly with ipsilateral neck metastases, creates a risk for contralateral neck involvement, especially if the ipsilateral nodes are multiple and large [4, 6]. The risk of contralateral or bilateral neck involvement in laryngeal cancer seems to be also determined by the site and size of the initial tumor, being higher in supraglottic cancers (from 13 to 50%) and in more advanced lesions [6]. However, the issue whether elective neck treatment should routinely be directed on both the sides of the neck is still controversial.

In this article, we retrospectively analyzed clinical and pathologic data from a group of 189 supraglottic laryngeal cancer patients in which the tumor was largely involving

S. Öztürkcan (✉) · H. Katilmiş · I. Özdemir · B. Tuna · R. Dündar
Department of Otorhinolaryngology and Head and Neck Surgery,
İzmir Atatürk Research and Training Hospital,
Ministry of Health, Izmir, Turkey
e-mail: seralbercan@yahoo.com

I. A. Güvenç
Department of Otorhinolaryngology and Head and Neck Surgery,
Borçka State Hospital, Ministry of Health, Artvin, Turkey

one side and crossing the midline and bilateral neck dissection was part of the primary treatment. The largely involved side by the tumor was termed as ipsilateral and the other side was termed as contralateral in point of neck dissection side. We aimed to evaluate the risk of contralateral neck involvement according to the site and stage of the tumor and ipsilateral neck stage.

Material and methods

The clinical records of 189 patients with supraglottic laryngeal cancer largely involving one side and crossing the midline, who were operated in our clinic between January 1998 and December 2005, were reviewed retrospectively. The study was approved by the Institutional Review Board of İzmir Atatürk Training and Research Hospital.

All the patients fulfilled the following criteria: tumor located in supraglottic larynx and crossing the midline, surgery on the primary tumor and bilateral neck in the same session, clinically negative neck (decided by palpation) on the contralateral side and no previous treatment for the laryngeal tumor. The side largely involved by the tumor was defined as ipsilateral and the other side was defined as contralateral in terms of the neck dissection side.

All patients were treated with either a partial (57) or a total (132) laryngectomy and bilateral (189) neck dissection. Neck dissections were reclassified according to the new classification system endorsed by the Committee for Head and Neck Surgery and Oncology of the American Academy of Otolaryngology—Head and Neck Surgery (AAO—HNS) in 2002 [7]. In total, 378 neck dissections consisted of 8 radical neck dissection, 8 modified radical neck dissection with preservation of the sternocleidomastoid muscle and spinal accessory nerve, 142 selective neck dissection (II–V) and 220 selective neck dissection (II–IV) depending on the extent of the disease. T stage of the tumor and clinical stage of the neck was performed according to the findings of direct laryngoscopy and palpation, respectively. T stages of the tumors were reclassified according to the staging system recommended by the American Joint Committee on Head and Neck Cancer in 2002 [8].

In clinically N0 (cN0) patients, in order to decide on the type of the neck dissection, all the ipsilateral selective neck dissection (II–IV) specimens were studied with frozen sections. When pathologically positive nodes were found in frozen section, the ipsilateral neck dissection was extended to include the lymph nodes at level V. In cN+ patients, radical, modified radical neck dissection or selective neck dissection (II–V) were performed.

In our clinic, the sensitivity and specificity of frozen sections in the detection of occult neck metastases were found to be 89.4 and 100%, respectively.

Postoperative radiotherapy was administered to the pathologically N+ (pN+) patients. Indications for postoperative RT included advanced primary disease, positive margins and at least one positive neck node.

The contralateral metastases rates were analyzed using the Chi-square test and Fisher's exact test. Probability values less than 0.05 were considered statistically significant. Statistical analyses were performed by Epi Info Statcale programs.

Results

Among the 189 tumors, 12 (6.3%) were classified as stage 1, 51 (27%) were classified as stage 2, 79 (41.8%) were classified as stage 3 and 47 (24.9%) as stage 4. In total, 125 (66.1%) patients were staged as ipsilateral cN0, 64 (33.9%) patients were staged as ipsilateral cN+ and 378 neck dissections were carried out.

Clinical N state of the ipsilateral neck

The frequencies of involvement of the contralateral side were statistically higher with cN+ ipsilateral necks compared to the cN0 ipsilateral necks, that is 28/64 (43.7%) and 11/125 (8.8%), respectively ($P = 0.00$). Table 1 shows the risk of occult contralateral neck involvement according to the ipsilateral clinical N state.

Involvement of the ipsilateral neck

We found that overt ipsilateral metastasis was 47/64 (73.4%) and ipsilateral and contralateral occult metastases were 28/125 (22.4%) and 39/189 (20.6%), respectively. The rate of metastases in the contralateral side were 33/75 (44%) and 6/114 (5.3%), when ipsilateral neck was pN+ and pN−, respectively demonstrating a statistically higher rate with pN+ ipsilateral necks ($P = 0.00$). Table 2 shows the risk of nodal metastases in the contralateral side according to the results of ipsilateral neck dissection.

Extracapsular tumor spread

In our series, the risk of bilateral neck involvement increased with extracapsular tumor spread as detected by the histopathologic examination of the ipsilateral positive

Table 1 The risk of occult contralateral neck involvement according to the ipsilateral neck clinical stage

	Contralateral pN+ (%)
Ipsilateral cN0	11/125 (8.8)
Ipsilateral cN+	28/64 (43.7)

Table 2 The risk of nodal metastases on the contralateral side according to the results of ipsilateral neck dissection

	Contralateral pN+ (%)
Ipsilateral pN0	6/114 (5.3)
Ipsilateral pN+	33/75 (44)
Ipsilateral pN+ (ECS−)	13/46 (28.3)
Ipsilateral pN+ (ECS+)	20/29 (69)

neck and this increase was found to be statistically significant. The risk of contralateral neck disease was 69% (20 of 29) in patients with extracapsular tumor spread in the ipsilateral lymph nodes compared with 28.3% (13 of 46) in patients with ipsilateral positive nodes without extranodal invasion. ($P = 0.00$)

T stage of the tumor

In our series, the level of T stage did not show an increased risk of bilateral neck involvement with an advancement in tumor stage. Comparing the risk of contralateral neck metastases in T1–2 and T3–4 cancers, there was no statistically significant difference ($P = 0.49$ and $P = 0.62$ for cN0 and cN+ ipsilateral nodes, respectively). Tables 3 and 4 show the risk of neck involvement according to the tumor stage and ipsilateral clinical stage.

Discussion

Despite the noteworthy attention devoted to the ipsilateral cN0 neck in laryngeal cancer, little is known about the risk of bilateral neck involvement and its therapeutic and clinical implications.

Table 3 The risk of neck involvement according to the tumor T stage (cN0 ipsilateral neck)

cN0	Ipsilateral pN+ (%)	Contralateral pN+ (%)	Bilateral pN+ (%)
T1 ($n = 9$)	11.1	0	0
T2 ($n = 31$)	32.2	12.9	9.6
T3 ($n = 59$)	22	6.7	3.4
T4 ($n = 26$)	15.4	11.5	3.8

Table 4 The risk of neck involvement according to the tumor T stage (cN+ ipsilateral neck)

cN+	Ipsilateral pN+ (%)	Contralateral pN+ (%)	Bilateral pN+ (%)
T1 ($n = 3$)	66.7	66.7	66.7
T2 ($n = 20$)	75	45	40
T3 ($n = 20$)	75	40	40
T4 ($n = 21$)	71.4	42.8	42.8

The anatomical and embryological studies indicate that, as the supraglottis does not form by fusion of two lateral cell masses, but rather is thought of as a midline structure, supraglottic cancer has a high prevalence of bilateral cervical lymph node metastases compared with the other laryngeal sites [9, 10] Treatment of bilateral neck in SCC of the supraglottis is thus necessary.

Weber et al. [11] demonstrated a statistically significant reduction in the incidence of cervical recurrent disease from 20 to 9% in their two different studies. They reported that 38 of 39 recurrences (among 202 patients with supraglottic cancer) had developed in nonsurgically treated necks in their initial study. According to this finding, they performed a routine bilateral neck dissection to all of the supraglottic cancer patients and afterwards they showed the incidence of cervical recurrence had been reduced in their latter study.

Because of the high sensitivity of modern imaging procedures (USG,CT, MRI) the early detection of neck node metastases is nowadays very much facilitated. The MRI and CT seem equal in discriminating abnormal nodes [4]. But we decided on the clinical N stage by palpation, because we were not able to perform these techniques to all of our patients due to financial problems.

In our study, it is noteworthy that contralateral neck metastases in centrally located supraglottic cancer with ipsilateral cN0 neck was only 8.8% compared to a higher rate of contralateral neck metastases with ipsilateral cN+ neck that was 43.7%. Analogs rate (35–50%) of contralateral neck metastases were reported by Gallo et al. [12] and others [6, 13] in supraglottic cancers with ipsilateral cervical overt metastases.

Luca et al. [14] reported that the occurrence of bilateral node metastases associated with central tumors was 20%. Gallo et al. [12] found the frequency of bilateral neck involvement with central tumors in the supraglottis was 43.7%. He also mentioned that tumors reaching the midline larynx from an original unilteral lesion had the same risk of contralateral neck disease as tumors growing in the midline larynx. However, Cağlı et al. [15] reported that, in their study including T2–T4 stage supraglottic carcinomas with cN0 necks, bilateral neck metastasis was 7.7% with central lesions and it was 4% with lesions largely involving one side and crossing the midline. In our series, bilateral neck involvement was 17.5% (33/189) with supraglottic tumor largely involving one side and crossing the midline.

Comparing the risk of contralateral neck metastases in T1–2 and T3–4 cancers, we did not find any statistically significant difference ($P = 0.49$ and $P = 0.62$ for cN0 and cN+ ipsilateral nodes, respectively). Gallo et al. [12] compared stage 1–2 with stage 3–4 cancers, and found an increased, although not significant, risk of contralateral neck metastases. Cağlı et al. [15] reported that the prevalence

of bilateral occult metastasis proportionally increased with T stage from 8.3 to 22.7% and to 31.2%, respectively, for T2, T3 and T4.

Previous studies do demonstrate, however, that in central cancers, if metastases are present on one side, occult metastases on the opposite site are likely and manifest in 40–50% within 2 years [6, 16]. Luca et al. [14] also reported that 48% of the patients with central tumor and node metastases on one side of the neck also had metastases on the opposite side, whereas only 12% of the patients with a lateral lesion and with ipsilateral metastases are initially seen with metastases on the other side. In our series, the frequency of contralateral metastasis in centrally located supraglottic cancers with largely involving one side and crossing the midline was significantly higher in patients with ipsilateral node metastases than patients without ipsilateral metastatic nodes (44 and 5.3%, respectively).

The analysis of the histologic examination of the positive lymph nodes showed that, in our series, the risk of contralateral neck disease was 69% (20 of 29) in patients with extracapsular tumor spread in the ipsilateral lymph nodes compared with 28.3% (13 of 46) in patients with ipsilateral positive nodes without extranodal invasion, and this was statistically significant. Biller et al. [6] and De Santo et al. [13] reported that the increase of ipsilateral neck stage seems to correlate with an overall higher risk of contralateral neck metastases. Besides these reports, Gallo et al. [12] in their series with 127 patients showed that node number, level, size and extracapsular tumor spread in the clinically positive ipsilateral neck were not predictive of the risk of contralateral lymph node involvement. He found contralateral metastases in 40.9 and 36% of the patients with and without ipsilateral extracapsular tumor spread, respectively.

As a result, in our series, the analysis of clinical and histopathologic factors involved in determining the risk of a contralateral neck disease with a supraglottic cancer largely involving one side and crossing the midline showed that, ipsilateral cN+ neck, positive ipsilateral nodes detected intraoperatively, and the extracapsular spread in the ipsilateral positive nodes were apparently associated with increased risk of contralateral occult disease but T stage of the tumor did not seem to be related to the risk of occult contralateral metastasis.

Conclusion

Our retrospective study confirms that the probabilistic criteria of the incidence of contralateral occult metastases in supraglottic cancer with tumor largely involving one side and crossing the midline. On the basis of our data, there is a significantly higher prevalence of contralateral metastases in such tumors with clinically or pathologically positive ipsilateral lymph nodes than with negative ipsilateral lymph nodes. The extracapsular spread of the nodes is also an important determinant of the contralateral involvement. The incidence of occult contralateral metastases does not seem to be affected by T stage of the tumor.

References

1. Kirchner JA, Som ML (1971) Clinical and histological observations on supraglottic cancer. Ann Otol Rhinol Laryngol 80:638–645
2. Olofsson J (1974) Growth and spread of laryngeal carcinoma. Can J Otolaryngol 3:446–459
3. Tucker GF Jr (1963) Some clinical interferences from the study of serial laryngeal sections. Laryngoscope 73:728–748. doi:10.1288/00005537-196306000-00010
4. Adams GL, Maisel RH (2005) Malignant tumors of the larynx and hypopharynx. In: Cummings CW, Flint PW, Harker LA, Haughey BH, Richardson MA, Robbins KT, Schuller DE, Thomas JR (eds) Cummings Otolarngolology Head and Neck Surgery, 4th ed. edn. Mosby, Philadelphia, pp 2222–2284
5. Shah JP, Medina JE, Shaha AR, Schantz SP, Marti JR (1993) Cervical lymph node metastases. Curr Probl Surg 3:273–344
6. Biller H, Davis W, Ogura JH (1971) Delayed contralateral metastases with laryngeal and laryngopharyngeal cancers. Laryngoscope 81:1499–1502. doi:10.1288/00005537-197109000-00014
7. Robbins KT, Clayman G, Levine PA, Medina J, Sessions R, Shaha A, Som P, Wolf GT (2002) Neck dissection classification update: revisions proposed by the American Head and Neck Society and the American Academy of Otolaryngology-Head and Neck Surgery. Arch Otolaryngol Head Neck Surg 128:751–8
8. Grene FL, Balch CM, Fleming ID, Rhit AF, Haller DG, Morrow M, Page DL (2002) editorial board. Larynx. In: American Joint Committee on Cancer: AJCC cancer staging manual, 6th ed. Springer, New York, pp 47–59
9. Lawson W, Biler HF, Suen JY (1989) Cancer of the larynx. In: Myers EN, Suen JY (eds) Cancer of the Head and Neck, 2nd edn. Churchill Livingstone Inc., New York, NY, pp 533–553
10. Bocca E (1991) Surgical Management of supraglottic cancer and its lymph node metastases in a concervative perspective. Ann Otol Rhinol Laryngol 100:261–267
11. Weber PC, Johnson JT, Myers EN (1994) The impact of bilateral neck dissection on pattern of recurrence and survival in supraglottic carcinoma. Arch Otolaryngol Head and Neck Surg 120:703–706
12. Gallo O, Fini-Storchi I, Napolitano L (2000) Treatment of the contralateral negative neck in supraglottic cancer patients with unilateral node metastases (N1-3). Head Neck 22:386–392. doi:10.1002/1097-0347(200007)22:4<386::AID-HED12>3.0.CO;2-5
13. DeSanto LW, Magrina C, O'Fallon WM (1990) The ''second'' side of the neck in supraglottic cancer. Otolaryngol Head Neck Surg 102:351–361
14. Luca O, Redaelli de Z, Piero N, Davide T, Daniela G, Matteo T, Johnny C, Giorgio P, Antonino RA (2002) The distribution of lymph node metastases in supraglottic SCC: therapeutic implications. Head Neck 24:913–920. doi:10.1002/hed.10152
15. Cağlı S, Yüce I, Yiğitbaşı OG, Güney E (2007) Is routine bilateral neck dissection absolutely necessary in the management of N0 neck in patients with supraglottic carcinoma? Eur Arch Otorhinolaryngol 264:1453–57. doi:10.1007/s00405-007-0384-z
16. Feind CR, Cole RM (1969) Contralateral spread of head and neck cancer. Am J Surg 118:660–665. doi:10.1016/0002-9610(69)90208-6