Level IIB Lymph Node Metastasis in Laryngeal and Hypopharyngeal Squamous Cell Carcinoma: Single-Institution Case Series and Review of the Literature

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Objectives/Hypothesis: To determine the incidence of level IIB lymph node metastasis in patients with laryngeal or hypopharyngeal squamous cell carcinoma and to evaluate the need for elective and therapeutic neck dissection of level IIB.

Study Design: Retrospective cohort study and review of the literature.

Methods: Patients with laryngeal or hypopharyngeal squamous cell carcinoma (N = 65) were primarily treated with surgery at Mayo Clinic (Rochester, Minnesota) from 2004 through 2010. Neck dissection specimens were analyzed by a pathologist, and metastases to level IIB were reported. In addition, 18 previously published studies, totaling 1,114 neck dissections, were reviewed.

Results: Level IIB lymph node metastases were present in 4% and 17% of elective and therapeutic neck dissections, respectively. Ipsilateral IIB metastasis was more common than contralateral IIB metastasis in elective and therapeutic neck dissection specimens. Level IIB lymph node metastasis was not significantly associated with level IIA nodal metastasis, level III nodal metastasis, clinical primary tumor stage, clinical nodal stage, or pathologic confirmation of extracapsular spread in either laryngeal or hypopharyngeal squamous cell carcinoma.

Conclusions: The rate of occult IIB metastasis in laryngeal and hypopharyngeal squamous cell carcinoma is exceedingly low. In a clinically node-negative case, the ipsilateral and contralateral level IIB nodal packet should not be dissected. For clinically node-positive cases, ipsilateral level IIB dissection should be performed; contralateral IIB dissection should be performed only when indicated.

Key Words: Hypopharynx, larynx, level IIB, squamous cell carcinoma.

Level of Evidence: 4.

INTRODUCTION

Cervical lymph node (LN) metastasis is an important determinant of survival in patients with head and neck cancer.1–4 The incidence of clinically detectable LN metastasis in supraglottic and transglottic laryngeal squamous cell carcinoma (L-SCC) and hypopharyngeal squamous cell carcinoma (HP-SCC) ranges from 65% to 85%, and the incidence of occult LN metastasis is 17% to 56%.5–11 Unique to supraglottic and transglottic L-SCC and HP-SCC is the propensity for bilateral LN metastasis.5,7,9,12 Glottic L-SCC has a lower rate of metastasis to the neck, but when it does occur, it rarely involves the contralateral neck.13

Surgical treatment of neck metastasis has evolved to provide oncologic efficacy while minimizing treatment-associated morbidity. Greater understanding of the specific lymphatic spread of upper aerodigestive tract squamous cell carcinoma (SCC) has allowed for the selective neck dissection, in which the LNs at greatest risk of metastasis are resected.9,14,15

The evolution of the neck dissection has focused on maintaining oncologic efficacy while reducing morbidities such as postoperative shoulder syndrome (SS). Nahum et al.16 defined SS as shoulder pain exacerbated by arm abduction, decreased active abduction of the arm, and pathoanatomic changes of shoulder drop such as muscle atrophy and winged scapula. The severity of SS is directly proportional to the extent of neck dissection.17–20 However, SS continues to be a problem, even with selective neck dissection.17,19,21 A level IIB dissection, defined as dissection of the LN packet confined to the triangle formed by the posterior belly of digastic muscle superiorly, spinal accessory nerve (SAN) inferiorly and anteriorly, and sternocleidomastoid muscle...
posteriorly and deep to the plane of the SAN, is associated with SAN traction and devascularization. In an attempt to decrease the risk of SS, surgeons have recently considered not dissecting level IIB. When comparing patients with level IIB dissection versus superselective non-IIB dissection, the degree of SS is less in the latter group.22–24

The goal of our study was to analyze the distribution of LN metastasis in patients with L-SCC and HP-SCC, with specific focus on level IIB to determine whether sublevel IIB dissection could be safely omitted. Included in the study were patients with clinically node negative (cN0) and clinically node positive (cN+) necks at a single tertiary care facility.

MATERIALS AND METHODS

After receiving Mayo Clinic Institutional Review Board approval, we performed a retrospective chart review of all patients (from January 1, 2004, through December 31, 2010) with histologically confirmed upper aerodigestive tract SCC treated with a neck dissection at Mayo Clinic (Rochester, Minnesota). Eligible patients had a previously untreated L-SCC or HP-SCC and underwent elective or therapeutic neck dissection. Exclusion criteria were synchronous head and neck cancers, distant metastasis at presentation, a history of radiotherapy or surgery to the head or neck, a history of head and neck cancer, primary treatment with radiotherapy (with or without chemotherapy), or pathology specimens that were not appropriately labeled by location (level).

The primary cancer was staged using the 2010 American Joint Committee on Cancer’s Cancer Staging Manual (seventh edition),25 LN groups were identified based on American Academy of Otolaryngology–Head and Neck Surgery criteria.15,26 Patients were preoperatively clinically staged as cN+ or cN0 on the basis of physical examination findings and available imaging studies. Radiologic criteria for cervical nodal metastasis included LNs >10mm in diameter, irregular enhancement consistent with central necrosis, spherical LN shape, and increased uptake of fluorine-18 fluorodeoxyglucose by positron emission tomographic imaging. Patients with clinically palpable nodal disease or radiologically positive nodal disease (or both) were identified as cN+ in our study.

Patients were treated with bilateral neck dissection if they had a primary tumor that crossed the midline or was located centrally or had clinical evidence of bilateral neck LN metastasis. In the case of bilateral neck dissection, each dissection was counted individually. Standard neck dissections were performed, and the boundaries of level IIB were clearly tagged with an Allis clamp. The specimen was placed on a towel, and the boundary between levels IIA and IIB was drawn on the towel and labeled before sending the specimen to the pathology department. The specimen was analyzed by a pathologist, using both frozen and permanent sections. Histopathologic analysis indicated the number of LNs resected per cervical area and the number of cervical metastatic nodes at each specific level. Follow-up information, including adjuvant treatment, recurrence (local, regional, or distant), and patient outcome at last follow-up visit, was recorded.

Statistical Evaluation

Continuous features were summarized with means, standard deviations, medians, and ranges; categorical features were summarized with frequency counts and percentages. Comparisons between features were evaluated using χ² tests. Statistical analyses were performed using the SAS software package (SAS Institute, Cary, NC). All tests were two-sided, and P values <.05 were considered statistically significant.

Review of the Literature

Our case series was supplemented by a review of the international English-language literature on level IIB LN metastasis in L-SCC and HP-SCC from 1990 through 2012. Studies were selected using the following criteria: 1) the boundary of level IIB was clearly defined, 2) the contents of level IIB were analyzed separately from the remainder of the specimen, and 3) the patients included in the study had L-SCC or HP-SCC that had not been treated previously.

RESULTS

Patient Information

The study group included 51 cases of primary L-SCC and 14 cases of primary HP-SCC. Of the 65 patients, 49 (75%) were men. The average patient age was 63.5 years (median = 64.5, range = 44–83). Ninety-one percent of patients used alcohol or tobacco products (or both).

Clinical and Pathologic Staging

The clinical primary tumor (cT) and nodal stage (cN) are described in Table I. In total, 102 neck dissections were performed (28 unilateral, 37 bilateral). Fifty-four (53%) were elective dissections (cN0 necks), and 48 (47%) were therapeutic dissections (cN+ necks). Nine (17%) cN0 neck dissections were node positive upon pathologic evaluation, as were 33 (69%) cN+ necks. The locations of positive LNs are summarized in Table II. The most common sites of occult LN metastases were in levels IIA and III (44% for each). One metastasis at level V was identified.

Incidence of Level IIB Metastasis

Of the 102 dissections, 10 (10%) were positive for level IIB LN metastasis. These included two (4%) of the 54 cN0 dissections and eight (17%) of the 48 cN+ dissections. Clinical data for the seven patients (10 neck dissections) with level IIB metastasis are presented in Table III. Sixty percent of level IIB metastases were from patients with primary supraglottic L-SCC. No level IIB metastases occurred in primary glottic L-SCC.
Forty percent of IIB metastases were from patients with primary pyriform sinus HP-SCC. Among the 10 dissections with at least one positive LN in level IIB, there was at least one positive LN in level I in three, in level IIa in six, in level III in seven, and in level IV in four. There was one dissection with an isolated positive LN in level IIB only, whereas the remaining nine dissections had at least one positive LN in two (n = 3), three (n = 2), four (n = 2), or five (n = 2) levels.

**Clinicopathologic Predictors of Level IIB Nodal Metastasis**

There were no statistically significant associations between level IIB LN metastasis and level IIA LN metastasis, level III LN metastasis, clinical primary tumor stage, clinical LN stage, or pathologic identification of extracapsular nodal spread in L-SCC or HP-SCC.

**Literature Review**

We identified 17 additional studies from the international literature that evaluated level IIB LN metastasis in L-SCC or HP-SCC (or both; Table IV). Six studies included only patients with L-SCC,37–32 two studies included only patients with HP-SCC,33,34 and the remaining studies included patients with head and neck cancer at multiple sites and various histopathologies.4,35–42

Our literature identified a total of 1,114 neck dissections in patients with L-SCC and HP-SCC. The overall rate of level IIB LN metastasis was 5%. The rate of level IIB LN metastasis was 1.9% and 12% in cN0 and cN+ necks, respectively. In the L-SCC group, the rate of level IIB LN metastasis was 3.9%; specifically, rates were 1.7% and 11.4% in cN0 and cN+ neck dissections, respectively. In the HP-SCC group, the rate of level IIB LN metastasis was 11.6%; specifically, rates were 3.3% and 20% in cN0 and cN+ neck dissections, respectively.

None of these studies showed a statistically significant correlation between IIB metastasis and sex, age, location of primary tumor, cT, cN, or extracapsular spread.

**DISCUSSION**

This study aimed to determine the relative risk of level IIB nodal metastasis in L-SCC and HP-SCC. Understanding this risk will help physicians determine...
which patients undergoing neck dissection should have level IIB LNs removed. The goal of judiciously applying regional nodal dissection only to those patients at higher risk of level IIB metastasis should reduce the incidence of postoperative SS without affecting oncologic outcomes.

The larynx and hypopharynx primarily drain to LNs in levels II, III, and IV,47,42 but the role of level IIB LNs in laryngeal and hypopharyngeal metastasis is less clear. We summarized findings of 18 studies, including the current study, that presented sufficient data on level IIB LN metastasis in L-SCC and HP-SCC (Table IV).4,27–42 The cumulative rate of level IIB metastasis in L-SCC was 3.9% (cN0, 1.7%; cN1, 11.4%).

Several of these studies deserve specific mention. Koybasoglu et al.30 studied 49 patients who underwent 74 neck dissections for L-SCC and found no level IIB metastases. They concluded that level IIB could remain undissected in patients with cN0 necks. Coskun et al.27 found no level IIB metastases in 113 cN0 neck dissections. Other studies found very few cases (ranging from 1% to 6%) of level IIB metastases in cN0 L-SCC.27–29,31,32 The consensus from these studies was that preservation of level IIB was acceptable for patients with cN0 L-SCC.

The overall rate of level IIB LN metastasis from the review of literature for HP-SCC was 11.6% (cN0, 3.3%; cN1, 20%). Two studies exclusively reviewed IIB metastasis in HP-SCC. Kim et al.33 examined 50 patients with HP-SCC undergoing a total of 93 neck dissections (59 were elective, 34 were therapeutic). The overall rate of level IIB metastasis was 14% (13 of 93; cN0, 3%; cN1, 32%). Wiegand et al.34 studied 50 patients with HP-SCC who underwent a total of 72 neck dissections. The overall rate of IIB metastasis was 4.2%, with 3.5% that were IIB-positive in the elective dissection group and 4.7% in the therapeutic dissection group. The conclusion from both studies was that level IIB could remain undissected in a patient with cN0 HP-SCC.

Our single-institution series of 51 L-SCC and 15 HP-SCC, in which 10% of necks showed positive level IIB metastasis, was consistent with the literature. The rates of positive level-IIB metastases in the cN0 and cN+ groups were 4% and 17%, respectively. Our data support the opinion that level IIB should not be dissected in a patient with cN0 L-SCC or HP-SCC. For all patients with L-SCC and HP-SCC undergoing therapeutic neck dissections, level IIB LNs should be removed.

Also, rarely does a metastasis to level IIB occur in isolation.2,38,40 We could find no statistically significant correlation between level IIB metastasis and the variables listed previously in L-SCC or HP-SCC subgroups.

Larger, long-term, controlled studies evaluating objective and subjective SAN function and risk of postoperative SS, as well as oncologic outcome, are needed to confirm that leaving level IIB undissected truly makes a functional difference and is oncologically safe.

**CONCLUSION**

L-SCC and HP-SCC rarely metastasize to level IIB in a cN0 neck; thus, level IIB should remain undissected
in such a patient. In a patient with a eN+ neck, ipsilateral and (when indicated) contralateral level IIb should be dissected for optimal treatment and staging. At this time, the effect of not dissecting level IIb on shoulder function awaits further study.

BIBLIOGRAPHY


