Impact of Retropharyngeal Lymph Node Metastasis in Head and Neck Squamous Cell Carcinoma

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Background: The impact of metastasis to the retropharyngeal lymph node (RPLN) group is poorly understood because of the difficult access of the retropharyngeal space. Previous studies concluding to the negative impact of RPLN metastasis rely heavily on radiographic assessment, which introduces the possibility of diagnostic error.

Objective: To better define the prognostic significance of metastatic retropharyngeal adenopathy in patients with non-nasopharyngeal squamous cell carcinoma of the head and neck.

Study Design: A retrospective cohort study of patients with non-nasopharyngeal squamous cell carcinoma of the head and neck who underwent resection of the RPLN group and were followed up for an average of 24 months.

Setting: Tertiary care academic medical center.

Patients: The 51 patients included in the study had been treated for advanced-stage squamous cell carcinoma of the oral cavity, oropharynx, hypopharynx, and/or supraglottic larynx via a surgical approach to the primary tumor that afforded access to the RPLN group. All patients underwent dissection and pathologic interpretation of the RPLNs, most patients received postoperative radiotherapy, and 43 patients met survival analysis criteria.

Main Outcome Measures: Local and regional recurrence rates, the development of distant metastasis, and disease-free and overall survival.

Results: Metastasis to the RPLN group was confirmed pathologically in 14 (27.5%) patients. There was no statistically significant difference between patients with and without RPLN metastasis in rates of local recurrence (24.8% vs 28.4%), regional recurrence (17.5% vs 19.6%), distant metastasis (17.0% vs 11.2%), disease-free survival (40.5% vs 30.5%), and overall survival (40.6% vs 38.5%).

Conclusion: Metastasis to the RPLN group does not impact disease control or survival in patients with advanced non-nasopharyngeal squamous cell carcinoma of the head and neck treated with multimodality therapy.


Very little is known about the significance of retropharyngeal adenopathy for patients with non-nasopharyngeal carcinomas of the head and neck. The basis for this clinical obscurity is the relative remoteness of the retropharyngeal lymph node (RPLN) group. The retropharyngeal space is not typically evaluated in the standard head and neck examination, nor is it routinely dissected during extirpative procedures. Not surprisingly, then, our understanding of retropharyngeal adenopathy in patients with head and neck cancer relies heavily on radiographic assessment.

The RPLNs are divided into 2 anatomically distinct subgroups, medial and lateral.2 The medial retropharyngeal lymph nodes, located near the midline and anterior to the prevertebral musculature, are normally small and not visualized with standard imaging techniques such as computed tomography (CT) and magnetic resonance imaging. Thus, if medial retropharyngeal adenopathy is seen, it is considered pathologic.2 In contrast, metastatic and benign adenopathy can both be visualized in the lateral retropharyngeal space between the internal carotid artery and the longus colli muscle. In fact, the lateral RPLNs (or nodes of Rouvière) are seen on CT in two thirds of healthy patients, ranging in size from 3 to 7 mm.2 Therefore, there can be considerable similitude in the appearance of metastatic and benign adenopathy in the lateral RPLN group, especially when size is

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the only criterion evaluated. The sensitivity of CT for determining the presence or absence of metastatic retropharyngeal adenopathy has been shown to be no better than 50%. Even more concerning, metastatic RPLNs have been harvested from patients with clinical and radiographic NO neck, suggesting that these nodes may provide a first-echelon drainage pathway for some oropharyngeal and hypopharyngeal tumors. The purpose of this study was to better delineate the impact of metastasis to the RPLN group in patients with non-nasopharyngeal squamous cell carcinoma of the head and neck (SCCHN), using histopathologic rather than radiographic data.

PATIENT POPULATION

From 1996 to 2001, all patients scheduled for primary surgical excision of a SCCHN at Oregon Health & Science University were considered for concomitant resection of the RPLNs. From this cohort, 56 patients were treated with procedures that afforded exposure to the RPLN group, including pharyngectomy, laryngopharyngectomy, composite resection with partial mandibulectomy, or midline mandibulectomy. Five of the 56 patients who underwent dissection of the retropharyngeal space were excluded because their final histopathologic reports did not document the presence of metastatic lymph nodes. Thus, a total of 51 patients confirmed to have had the RPLN group dissected and examined histologically were included in this study.

SURGICAL TECHNIQUE

The approach to the RPLN group has previously been outlined in detail. Retropharyngeal lymph node excision is generally undertaken at the completion of the primary resection and neck dissection. For jaw-splitting procedures, including midline mandibulectomy and segmental mandibulectomy, the retropharyngeal plane is entered above the levels of the posterior belly of the digastric muscle, the hypoglossal nerve, and the lingual artery. Division of this muscle and inferior displacement of the nerve and artery, while not mandatory, can facilitate dissection when there is limited exposure. The pharyngeal wall is then progressively opened in a superior direction toward the skull base by division of the middle layer of the deep cervical fascia. Usually, several pharyngeal veins that traverse this space require cautery and division. The pharyngeal wall is retracted medially and the position of the internal carotid artery, the lateral limit of dissection, is identified by palpation. Lympho-fatty tissue containing the RPLNs and situated between the internal carotid arteries is then excised inferiorly to superiorly. The superior sympathetic ganglion lies just medial to the internal carotid artery, and care should be taken to avoid including this structure in the specimen.

With this approach the small nerves of the pharyngeal plexus are divided in the process of separating the pharyngeal wall and the structures of the carotid sheath. This may result in increased severity of postoperative dysphagia. In the present study virtually all patients had undergone simultaneous resection of the structures of the oropharynx or hypopharynx that preserves the pharyngeal plexus. At the conclusion of the neck dissection the structures of the carotid sheath are approached from the posterior aspect and mobilized. They are then retracted anteriorly and medially to allow access to the retropharyngeal plane. Once the retropharyngeal plane is entered the superior sympathetic ganglion is identified above the level of the hyoid bone. The RPLN group lies in the fibrofatty tissue medial to the superior sympathetic ganglion between the superior constrictor muscle anteriorly and the longus colli and longus capitus muscles posteriorly. Its potential for less postoperative dysphagia makes this approach superior to the anterior approach when simultaneous resection of the structures of the oropharynx and hypopharynx is not planned.

ADJUVANT TREATMENT

Postoperative radiation was administered to patients based on final histopathologic results. Full-course radiotherapy (5500-6500 rad [55-65 Gy]) was initiated within 6 weeks of surgery in all indicated cases. The indications for postoperative radiation were lymph nodes with extracapsular spread, multiple positive cervical lymph nodes, bulky preoperative cervical adenopathy (>3 cm), positive surgical margins, and perivascular or perineural spread of tumor. Retropharyngeal lymph node metastasis was not, by itself, an indication for adjuvant radiotherapy.

Cervical radiation treatments were administered to patients by any of several radiation oncologists according to geographic location and patient preference. The heterogeneity of individual radiation protocols precluded any modification of the radiation ports to specifically accommodate the retropharyngeal space.

RESULTS

Of the 51 patients who underwent dissection and pathologic interpretation of the RPLNs, 31 (76.5%) were male and their mean age was 59.1 years (range, 31-84 years). Most of the patients had advanced disease, and the tumors of more than half of the patients were classified as T4 lesions (Table 1). Likewise, most patients showed neck nodal stage N2 or higher (Table 2). Postoperative radiotherapy was administered to 49 patients (87.5%).

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Patients were followed up for an average of 24 months (range, 1-53 months).

Primary tumor sites included the oral cavity, oropharynx, hypopharynx, and supraglottic larynx, but 90% of the patients were treated for tumors of the oral cavity or oropharynx. Four patients (8%) with pyriform sinus tumors and 1 patient (2%) with squamous cell carcinoma of the supraglottic larynx also underwent RPLN dissection in conjunction with surgical excision of the primary lesion.

For the entire treatment group, metastasis to the RPLNs was confirmed histopathologically in 14 patients (27.5%) (Table 3). Metastatic retropharyngeal adenopathy was least likely to be found in patients with tumors arising from the oral cavity (12.5%). Tumors of the oropharynx (26.3%) were much more likely to result in retropharyngeal metastasis. Retropharyngeal lymph node dissection yielded an average of 1.6 metastatic lymph nodes (range, 1-5). Metastatic retropharyngeal adenopathy was noted in 1 patient with N0 neck. The remainder of the patients with RPLN metastasis (13/14) were confirmed to have additional cervical disease with N0 to N3 neck stage.

Eight disease-free patients were excluded from long-term analysis because their follow-up was less than 2 years, which left a total of 43 patients for survival analysis. Local recurrence rates were similar for patients with (24.8%) and without (28.4%) metastatic retropharyngeal adenopathy (Figure 1). Likewise, regional recurrence rates were not significantly different between treatment subgroups (17.5% vs 19.6%; P=.68) (Figure 2). In fact, there was no statistically significant difference between patients with and without RPLN metastasis with respect to any of the additional outcome measures analyzed, in-
including development of distant metastasis \((P = .37)\), disease-free survival \((P = .94)\), and overall survival \((P = .40)\) (Figures 3, 4, and 5).

**COMMENT**

In 1964, Ballantyne\(^7\) observed that “the lymphatic structures which lie between the carotid arteries have received comparatively little attention as sites of metastasis.” His landmark article recorded a 44% incidence of histopathologically confirmed metastatic retropharyngeal adenopathy in 34 patients treated surgically for SCCHN. None of the patients received adjuvant radiation treatment. He noted poorer survival among the patients with metastatic RPLNs and consequently hypothesized that “removal of positive retropharyngeal nodes may increase chances for survival in cancers of selected sites.”

Unfortunately, during the last 4 decades since Ballantyne’s study only a handful of articles have evaluated the significance of RPLNs in cancer of the head and neck. Because the retropharyngeal contents are relatively inaccessible, most of these subsequent studies have focused on radiographic assessment. In 1981, Mancuso et al\(^8\) prospectively analyzed neck CT scans in 41 patients with SCCHN. They identified 6 patients with non-nasopharyngeal squamous cell carcinoma metastatic to the RPLN group, most of whom had recurrent disease. As only 2 (33%) of the 6 patients survived, they concluded that metastatic retropharyngeal adenopathy portends a poor prognosis. Several authors have since supported the criteria of Mancuso et al\(^8\) for radiographically abnormal retropharyngeal adenopathy, ie, nodal necrosis or node size greater than 10 mm.\(^9,10\)

McLaughlin et al\(^11\) conducted the largest radiographic study evaluating retropharyngeal adenopathy. They retrospectively reviewed pretreatment CT and magnetic resonance imaging scans of 619 patients with SCCHN. Of the 605 patients with non-nasopharyngeal SCCHN, they identified 42 patients (6.9%) who met radiographic criteria for RPLN metastasis. Most patients were treated nonsurgically (82%) and nearly every one received radiotherapy (92%). With 2 years of follow-up, the authors noted a statistically significant difference between patients who showed radiographic evidence of RPLN metastasis and those who did not with respect to neck recurrence, distant metastasis, and disease-free and overall survival.

There are 2 studies of note evaluating the significance of retropharyngeal metastasis via pathologic—rather than radiographic—examination. In 1994, Hasegawa and Matsuura\(^4\) retrospectively reviewed their results treating 24 patients with squamous cell carcinoma of the oropharynx and hypopharynx. They found retropharyngeal metastasis in 12 patients (50%) but were unable to identify any difference in survival between patients with and without RPLN metastasis. More recently, Amatsu et al\(^5\) retrospectively compared results for 82 patients treated surgically for squamous cell carcinoma of the hypopharynx and cervical esophagus who underwent RPLN dissection with results for 69 patients with similar tumors who did not. They, too, found no difference in survival between the treatment groups. Even so, both studies advocated for treatment of the RPLN group in patients with radiographic evidence of retropharyngeal metastasis or advanced neck nodal stage.
In the present study, we identified metastatic retropharyngeal adenopathy in more than a quarter of the patients. This incidence is well within the broad range of pathologically confirmed metastatic rates reported in the literature, eg, 16% to 50%. Most of our patients with metastasis to the RPLN group had tumors involving the oropharynx or hypopharynx. Tumors of the oral cavity appeared to be the least likely to spread to the RPLNs (12.5%). Although the number of patients with tumors of the pyriform sinus and supraglottic larynx is limited in our study, the data show that these sites are also capable of metastasizing to the RPLN group.

Most of our patients with metastatic retropharyngeal adenopathy (93%) also demonstrated neck disease. However, we observed metastatic retropharyngeal lymph nodes in 1 patient with N0 neck. This isolated tumor metastasis implicates the RPLN group as a potential first-echelon drainage pathway for squamous carcinomas of the oropharynx and hypopharynx. Other authors have similarly reported solo retropharyngeal metastasis to the RPLN group, underscoring the importance of the retropharyngeal lymphatic drainage basin.

We found no difference between patients with and without pathologically confirmed retropharyngeal metastasis in the ultimate development of local recurrence, regional recurrence, or distant metastasis. Further, we identified no survival advantage for patients without metastasis to the RPLN group compared with patients who had metastasis. Our findings match those noted in previous histopathologically based studies of the RPLN group. These results seem to defy clinical logic and early dogma, as one would expect patients with retropharyngeal metastasis to fare worse than those without. The most plausible explanation is that our cohort consisted primarily of patients with advanced disease, since most of them had received adjuvant radiotherapy. And since most of our patients were given multimodality therapy to the RPLN group, a potentially beneficial effect of surgical excision in the metastatic subgroup may have been masked.

Ultimately, the discrepancy in results between pathologically based and radiographically based retrospective studies of RPLN metastasis may hinge on the different treatment approaches used at the various reporting institutions. Histopathologically based studies, by design, include surgical resection of all suspected retropharyngeal metastasis. Since this patient population typically presents with advanced disease, it is often treated with adjuvant therapy such as radiation and/or chemotherapy. In contrast, most of the patients included in radiographically based studies have been treated solely with radiation therapy. Thus, the bulk of the data to date on RPLN metastasis suggest that more aggressive, multimodality treatment may mitigate the potentially negative prognostic effect of tumor spread to the RPLNs.

Squamous cell carcinoma metastatic to the RPLN group can be clinically and radiographically silent. Conventional methods of assessing this region have proven to be inadequate, particularly for early-stage lesions. This study set out to better define the importance of metastasis to the RPLN group in patients with SCCHN. Although we found no difference in tumor control or survival rates between patients with and without RPLN metastasis, our data support the elective treatment of the retropharyngeal adenopathy for tumors in selected sites. We found a high incidence of RPLN metastasis in patients with squamous cell carcinoma arising in the oropharynx, and consequently believe that these patients are best served with some form of comprehensive treatment to the retropharyngeal space, either surgically or with radiotherapy. Patients with tumors involving the hypopharynx or supraglottic larynx likewise appear to be at a high risk for RPLN metastasis. However, the small number of such patients in our study precludes any definitive treatment recommendations for this subgroup.

There is a high incidence of RPLN metastasis in patients with tumors of the oropharynx, hypopharynx, and supraglottic larynx. However, metastasis to the RPLN group does not impact disease control or survival in patients with advanced non-nasopharyngeal SCCHN treated with multimodality therapy.

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REFERENCES


