CASE REPORT

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HETEROTOPIC PARATHYROID INCLUSION IN A CERVICAL LYMPH NODE

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Abstract: Background. During the pathologic examination of neck dissection specimens, unexpected findings within the lymph nodes may be discovered. Such findings may include benign epithelial inclusions, a second primary tumor, or chronic inflammatory diseases.

Methods. We report a case of a 59-year-old man who underwent a laryngectomy and bilateral neck dissection for a right transglottic squamous carcinoma of the larynx. During the procedure, a large lymph node measuring 2.5 × 2.2 × 0.8 cm was found at the right level IV.

Results. Histologic examination of the neck dissection specimen revealed benign parathyroid inclusions in the enlarged lymph node. The heterotopic cells expressed parathyroid hormone. This case represents a unique example of heterotopic parathyroid inclusions in a cervical lymph node.

Conclusion. Parathyroid tissue should be included in the differential diagnosis of cervical intranodal epithelial inclusions.

Keywords: parathyroid; heterotopia; neck; lymph node

Benign epithelial inclusions are sometimes unexpectedly encountered during histologic examination of lymph nodes.1,2 This article reports a unique case of heterotopic parathyroid tissue in a cervical lymph node found during microscopic examination of a neck dissection specimen. To the best of our knowledge, this is the first time that this type of heterotopia has been reported.

CASE REPORT

A 59-year-old man with a history of bronchoalveolar carcinoma of the right middle lobe of the lung was seen with progressive shortness of breath, fatigue, weight loss, and dysphagia over the previous 3 to 4 months. The patient’s medical history was significant. He had had a right middle lobectomy 12 years earlier for the removal of a bronchoalveolar carcinoma, and then had undergone resection of a pulmonary recurrence 5 years later. He had also undergone a total thyroidectomy 12 years ago for the removal of a thyroid mass, which was diagnosed as follicular adenoma.

At our institution, a CT scan of the larynx showed a T4 lesion with cartilage invasion. The patient underwent bronchoscopy with biopsies of the lung, which revealed no pathologic evidence of carcinoma. However, examination of multiple
laryngeal biopsy specimens revealed squamous cell carcinoma of the right vocal cord. The patient also underwent a tracheostomy later followed by a total laryngectomy with bilateral cervical lymph node dissection. Laboratory test results, including calcium and phosphorus levels, were normal.

**Pathologic Findings.** Macroscopic examination of the neck dissection specimen revealed a 3.0-× 2.3-× 1.5-cm³, fungating, poorly circumscribed, tan-gray mass involving the right glottic, and subglottic regions invading the thyroid cartilage. Microscopically, the mass was diagnosed as a moderately differentiated, invasive squamous cell carcinoma. Neither perineural nor lymphovascular invasion was identified.

Of 39 lymph nodes examined, one 2.5-× 2.2-× 0.8-cm grossly unremarkable lymph node was identified at level IV. It was step sectioned and entirely submitted for histologic examination. Microscopic analysis of the lymph node disclosed a 1.5-× 1.5-mm², subcapsular cluster of small, clear, polygonal cells with regular nuclear contours, vesicular chromatin, inconspicuous nucleoli, and a pale-staining, slightly acidophilic cytoplasm. The cells were organized in solid nests composed of tightly packed cords (Figures 1 and 2). There was no evidence of mitotic activity or necrosis. The tissue did not bear any histologic resemblance to the laryngeal, moderately differentiated squamous cell carcinoma for which the cervical lymph node dissection had been performed or to the previously resected bronchoalveolar carcinoma and thyroid follicular adenoma.

Nevertheless, the morphology of the intralymphatic nodule raised the suspicion of a benign inclusion of parathyroid tissue because of the resemblance of the cells to the chief cells of the parathyroid glands. The cells diffusely and strongly stained for parathyroid hormone, which confirmed the initial microscopic impression (Figure 3). The cells did not stain for thyroglobulin and thyroid transcription factor 1. Cells in the bronchoalveolar carcinoma and in the follicular adenoma of the thyroid also did not stain for parathyroid hormone.

![FIGURE 1. Capsular and subcapsular epithelial nests (hematoxylin-eosin stain; original magnification ×25). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]](image1)

![FIGURE 2. Uniform cells with clear cytoplasm. Notice lack of anaplasia, necrosis and mitosis. (hematoxylin-eosin stain; original magnification ×200). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]](image2)

![FIGURE 3. Cells expressing parathyroid hormone (PTH immunostain; original magnification ×200). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]](image3)
DISCUSSION

The parathyroid glands are derived from the pharyngeal pouches, the superior glands from the fourth pouch, and the inferior glands from the third pouch. They are normally located behind the thyroid gland, 1 at each end of the upper and lower poles, usually in the capsule that covers the lobes of the thyroid. Sometimes they are embedded in the thyroid gland, but they can also be found in the mediastinum, lying beside the thymus, which originates from the same pharyngeal pouches.3

In a review of 37 parathyroid heterotopias, Phitayakorn and McHenry4 found 23 (62%) ectopias of the inferior parathyroid glands with the following distribution: intrathyrmic (30%), anterosuperior mediastinal (22%), intrathyroidal (22%), within the thyrothymic ligament (17%), and submandibular (9%). The 14 (38%) cases of ectopias of the superior parathyroid glands were distributed as follows: tracheoesophageal groove (43%), retroesophageal (22%), posterosuperior mediastinal (14%), intrathyroidal (7%), carotid sheath (7%), and paraesophageal (7%).

Despite its infrequent occurrence, ectopia of the parathyroid tissue has been well-recognized in the medical literature as a reason for negative findings from a parathyroid surgical exploration in symptomatic patients with hyperparathyroidism. Imaging may also miss the pathologic gland. Despite its rarity, the possibility of an intrathyroidal parathyroid should therefore be considered, and when meticulous bilateral exploration of the neck fails to identify the hyperfunctioning gland, a hemithyroidectomy should be considered.5

Another problem is that, if left undetected, even the nonhyperfunctioning ectopic parathyroid glands may become clinically significant, as they are subject to neoplastic transformation or may mimic a variety of metastatic neoplasms in these ectopic sites. Regarding the latter situation, our patient shows that if it were not for the distinct histologic discrepancy between the patient’s primary neoplasms (bronchoalveolar carcinoma of the lung and follicular adenoma of the thyroid) and the intranodal inclusion, a metastatic lesion to the lymph node would have been strongly suspected. Of particular concern is the clear cell lesions of the parathyroid; when intrathyroidal in location, the lesions may be considered in the differential diagnosis of a clear cell thyroid tumor and clear cell renal carcinoma metastasis.6,7

We cannot overemphasize the importance of being aware of such ectopias, as well as being able to differentiate them from true metastasis. For example, a pathologist may misconstrue a benign-looking epithelial inclusion with a cytologically bland-looking metastatic neoplasm. Conversely, histopathologic scrutiny of lymph nodes can reveal not only benign epithelial inclusions but unexpected important pathologic processes that might not yet be clinically apparent.1,2

In the cervical lymph nodes, the most common heterotopias are the thyroid inclusions1,2,8 and salivary gland inclusions.9,10 Less common are nesus cell aggregates11,12 and benign intranodal tumors, such as myofibroblastosomas13 and leiomyomas.14 Also, primary intranodal benign and malignant salivary gland tumors have been found secondary to heterotropic salivary gland tissue.15–17 Of these cervical lymph node heterotopias, the most controversial have been the thyroid inclusions. Some authors believe that thyroid nodal heterotopias, no matter how microscopically innocuous, invariably signify metastatic spread.18 Others believe that non-neoplastic thyroid tissue can be ectopically displaced into lateral neck lymph node and, in the absence of cellular atypia, is of no clinical significance.19 Rosai et al20 have suggested several histologic criteria for distinguishing benign thyroid inclusions from metastatic papillary thyroid carcinoma. A diagnostic algorithm that may aid in further work-up and treatment in these unusual cases was proposed by Fliegelman et al21 and Vassilopoulous and Weber.22

In other organs, these benign inclusions often are a potential pitfall for the pathologist. For example, in the abdominal-pelvic region of women, these inclusions, which are most often found in endometrial (müllerian-type) glands, may also present with squamous metaplasia in nodal locations,23 decidual reaction,24 or, rarely, hyperplastic mesothelial cells.25 These intranodal glandular inclusions and mesothelial cells should be distinguished from metastatic tumors; a misinterpretation could result in inaccurate staging in a patient with a known tumor or prompt a futile search for an occult primary tumor.26 Other unusual, abnormal findings in axillary lymph nodes include benign epithelial cells, vascular lesions, and megakaryocytes.27–30

Finally, there is the possibility that some of these nodal inclusions are the result of mechanical transport during diagnostic (e.g., fine-needle aspiration) or therapeutic procedures. More specifically, a previous thyroidectomy or neck dissection may dislodge parathyroid tissue into adjacent soft tissue or lymph nodes. However, we cannot exclude the possibility that some of these heterotopias are congenital abnormalities, and devel-
oped as analogous phenomena as the ones resulting in salivary gland inclusions in intraparotid lymph nodes. Similarly, breast epithelial cells have been found in the dermal angiolymphatic spaces and sentinel lymph nodes and were not obviously the result of true tumor spread. The diagnostic, histogenetic, and prognostic problems raised by these various nodal inclusions in different organs are, of course, distinct. However, they all have commonalities—the ectopic presence of epithelial tissue in a lymph node, its clinical and prognostic significance, and the possibility of an unaware pathologist misinterpreting it as a metastasis.

In summary, this case report emphasizes the significance of recognition of benign epithelial inclusions in lymph nodes, specifically, the identification of parathyroid tissue as a rare occurrence and potential pitfall when metastatic disease needs to be excluded.

REFERENCES