

CASE REPORT

Thyroid tissue in cervical lymph nodes, not always malignant

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Abstract

Thyroid tissue in cervical lymph nodes is an interesting and rare phenomenon that cannot be directly explained by embryology. Distinguishing malignant from benign thyroid tissue in cervical lymph nodes can be challenging but is essential for treatment and might have legal implications. Patients with incidentally found thyroid tissue in cervical lymph nodes during thyroid surgery were retrospectively identified. Clinical data and findings on pathology were retrospectively collected. Two patients with thyroid tissue in cervical lymph nodes were identified. Conventional pathology complemented with immunohistochemistry and molecular diagnostics showed the thyroid tissue in cervical lymph nodes to be benign. We show that benign thyroid tissue in cervical lymph nodes can be found in the absence or presence of a primary thyroid malignancy. A conservative approach is recommended if pathology shows benign thyroid tissue in cervical lymph nodes.

KEYWORDS

thyroid surgery, thyroid tissue in cervical lymph nodes

1 | INTRODUCTION

Migration of thyroid tissue during embryologic development can leave ectopic depositions at various locations in the body. Ectopic thyroid tissue has been found in lung, heart, mediastinum, ovaries, adrenal glands, duodenum, pancreas, intestine, and different locations in the neck and throat.¹ Thyroid tissue in cervical lymph nodes is often considered to be a metastasis of a primary thyroid malignancy. Since the sixties, several cases of benign ectopic thyroid cervical lymph node tissue have been reported.² Distinguishing between ectopic thyroid tissue, a metastasis or primary thyroid cancer in a cervical lymph node can be challenging.²

In 2016, a Dutch surgeon was issued with a “warning” by the Dutch medical disciplinary judge because he performed a total thyroidectomy and neck dissection in a woman after finding ectopic thyroid tissue in a cervical lymph node. This was considered and treated as a metastasis of thyroid cancer.³ This case shows that failing to make the distinction between malignant or benign thyroid tissue in a cervical lymph node can result in over-treatment and possible litigation.⁴ The low incidence of thyroid tissue in cervical lymph nodes and consequently limited experience makes an univocal approach difficult.

In this paper, we report two cases concerning ectopic thyroid tissue in cervical lymph nodes and our chosen approach.

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2 | CASE REPORT

At the department of endocrine and neck surgery of the Medisch Spectrum Twente in Enschede, the Netherlands, about 120 operations on the thyroid and parathyroid glands are performed annually. In the period from 2010 to 2020, all pathology reports of patients undergoing neck surgery were retrospectively reviewed and cervical lymph nodes containing thyroid tissue were found in two patients. All patients with thyroid tissue in cervical lymph nodes were included and none were excluded.

Clinical data and findings on pathology were retrospectively collected.

Pathology was primarily performed by conventional staining and microscopy, complemented with immunohistochemistry and molecular pathology if necessary. The study was reviewed and approved by our institutional review board.

Case one concerns a 55-year-old female patient with autoimmune hypothyroidism treated with levothyroxine. She developed a multinodular goiter with complaints of airway obstruction and underwent a total thyroidectomy. During surgery two enlarged lymph nodes, measuring 1.6 and 0.4 cm, were found in the right paratracheal groove, and thus, removed. The entire thyroid and lymph nodes were sampled in 46 slides. Pathology showed thyroglobulin positive follicles in both lymph nodes, without any signs of malignancy. Pathologic examinations of the thyroid showed no malignancy but a generalized lymphocytic inflammation consistent with Hashimoto thyroiditis. Additionally, the thyroid and lymph node tissue were revised in a tertiary referral center. No malignancy was found, and therefore, confirmed that the nodal thyroid tissue was benign.

Case two concerns a 49-year-old female patient diagnosed with a papillary carcinoma of the right thyroid lobe by fine needle aspiration. Preoperative ultrasound of the neck showed no enlarged lymph nodes. A right hemithyroidectomy and central neck dissection were performed. All resected thyroid tissue was sampled for pathology. Histology showed a pT1b papillary carcinoma.⁵ Two out of seven resected lymph nodes, measuring 0.4 cm, showed thyroid tissue with a papillary growth pattern and no extra nodal extension was observed (Figures 1,2). At microscopy, the lymph node tissue showed no similarity to the cancerous tissue of the thyroid. Immunohistochemistry was CD56 positive in the non-cancerous thyroid tissue and nodal thyroid inclusions but negative in the papillary carcinoma (Figure 3). Eventually, DNA was extracted from the representative paraffin blocks and a mutation analysis for BRAF, NRAS, and KRAS was done. This showed a BRAF

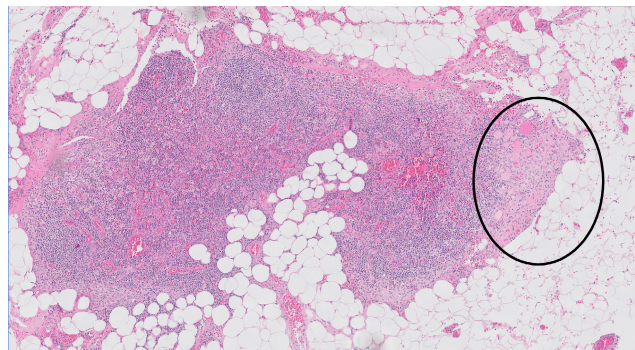


FIGURE 1 Hematoxylin and eosin stain: Lymph node tissue with Thyroid inclusions

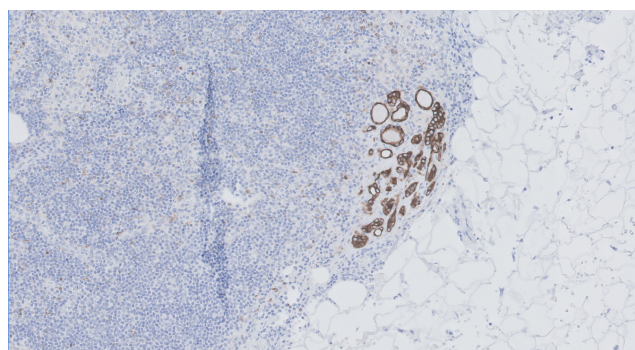


FIGURE 2 Keratine stain: Lymph node tissue with Thyroid inclusions

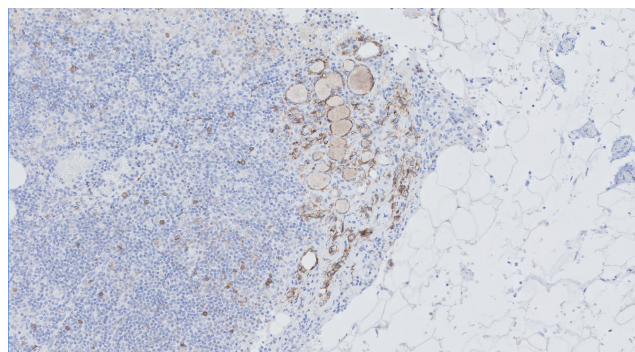


FIGURE 3 Lymph node tissue with CD 56 positive Thyroid inclusions

V600E mutation in the cancerous tissue, but none in the nodal thyroid inclusions. There were no NRAS or KRAS mutations in either tissue.

The histological and immunohistochemical findings and the presence of the BRAF mutation in the malignant thyroid tissue confirms the diagnosis of a papillary thyroid carcinoma. The histological image, presence of CD56 and the absence a BRAF mutation excludes papillary thyroid metastasis and confirms the benign nature in the nodal thyroid tissue.

3 | DISCUSSION

Benign thyroid tissue in cervical lymph nodes is a rare entity with only 17 cases reported in the past 20 years.^{2,6,7} Although there is an obvious risk of publication bias that benign unimpactful findings are underreported.

Glandular salivary, nevoid and thyroid tissue have been found in cervical nodes.² However, how to deal with ectopic thyroid tissue found in cervical lymph nodes is the most controversial. This is because authors consider all thyroid tissue in lymph nodes malignant.^{8–10} This idea was challenged by the finding of benign nodal thyroid tissue in lymph nodes after neck dissection for non-thyroid malignancies in other studies.^{9,11}

A conservative approach in incidentally found thyroid tissue in cervical lymph nodes was suggested.⁹

This was supported in five patients in whom benign thyroid tissue in cervical lymph nodes found in 106 post-mortem neck dissection specimens. Here, no primary thyroid malignancy was found, except for one patient that had a contralateral thyroid malignancy.¹²

More recently, two reports have been published where ectopic nodal thyroid inclusions were treated conservatively.^{6,13} Léon et al. found six cases of nodal thyroid inclusions after neck dissection for non-thyroid head and neck malignancies. After imaging of the thyroid and during the follow-up period, no malignancy was found.¹³

Ansari-Lari et al. reported nine patients with thyroid inclusions in cervical lymph nodes found in neck dissections for head and neck squamous cell carcinoma, melanoma, and hyperparathyroidism.⁶ Tissue sampling of the ipsilateral thyroid in four patients showed no signs of thyroid malignancy. One patient had a papillary carcinoma on the contralateral side. During follow-up in seven out of nine patients, no thyroid malignancy was found.⁵ In both reports, the neck dissection was done for a non-thyroid malignancy. The findings in both reports are similar to our first case.

In our second patient, distinguishing between benign thyroid tissue and a metastasis would have had a direct influence on staging and treatment.⁴ Histologic criteria to distinguish malignant from benign thyroid tissue in lymph nodes have been proposed.^{2,6}

This includes the extent of thyroid follicles compared with the size of the lymph node, silhouette and localization, morphology of thyroid follicles, absence of psammoma bodies, absence of desmoplastic stroma, immunohistochemistry and molecular profiling. Molecular pathology can show BRAF point mutations that are highly diagnostic for papillary thyroid carcinoma.^{14,15} The benefit of molecular pathology in addition to conventional histology in discriminating benign from malignant thyroid tissue in cervical lymph nodes is shown in our second

case. In addition, molecular pathology has shown to be instrumental in diagnosing synchronous nodal metastasis from a follicular and papillary thyroid cancer.¹⁶

Ectopic thyroid tissue in cervical lymph nodes is an interesting phenomenon that has solely been reported in women.² The pathogenesis and natural history are largely unknown. During embryologic development, the thyroid descends medially through the foramen coecum to its final position in the neck.^{1,2} Most ectopic thyroid tissue in lymph nodes is found laterally in the neck and not medially as one might expect on the basis of embryology.² Migration through the lymphatic system, extrusion of thyroid tissue from the gland and abnormalities at embryologic development have been suggested.²

We show that the presence of thyroid tissue in cervical lymph node tissue does not automatically imply lymph node metastasis of thyroid malignancy. Comprehensive pathology is essential in making this distinction and can consequently prevent possible overtreatment.

4 | CONCLUSION

The origin and pathogenesis of ectopic thyroid tissue in cervical lymph nodes is still unclear and cannot be explained by current embryological theories. To date, this phenomenon has only been reported in women.

We show that benign thyroid tissue in cervical lymph nodes can occur in the absence or presence of a primary thyroid malignancy. Immunohistochemistry and molecular diagnostics in addition to conventional pathology can aid in making the distinction between benign and malignant thyroid tissue in cervical lymph nodes. We recommend a conservative approach if pathology shows benign thyroid tissue in cervical lymph nodes.

AUTHOR CONTRIBUTIONS

All authors have contributed equally to this manuscript.

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CONFLICT OF INTEREST

All authors have no conflicts to disclosure, no competing interest to disclosure and no funding information to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author, AFG, upon reasonable request.

ETHICAL APPROVAL

Confirms that this manuscript meets the ethics guidelines and the legal requirements in The Netherlands.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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