

CASE REPORT

Cervical lymphatic malformation demonstrating thyroglobulin on fine needle aspirate washout

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Abstract

A case report highlighting the importance of cautious interpretation of thyroglobulin washouts in fine needle aspirates when deciding on management of differentiated thyroid cancer, so as to avoid unnecessary surgery.

KEYWORDS

lymphangioma, lymphatic malformation, papillary thyroid cancer, thyroglobulin, thyroid

1 | INTRODUCTION

A case of an elderly gentleman presenting with a level IV neck lump, high thyroglobulin in fine needle aspirate washout (FNA-Tg) and TIRADS TR5 thyroid nodule on ultrasound. Postoperative histology revealed this as a lympho-vascular malformation, highlighting the careful interpretation of FNA-Tg when managing differentiated thyroid cancer.

The gold standard diagnostic test for differentiated thyroid cancer is obtaining a tissue specimen for cytopathology. In the preoperative period, it is now common practice to obtain a fine needle aspirate of any clinically or radiologically suspicious lesions; whether they are identified as nodules within the thyroid or regional lymph nodes. Preoperative diagnosis of metastatic neck disease is important when planning the surgical approach. The current American Thyroid Association (ATA) guidelines recommend use of FNA-Tg in select patients where cytological analysis is inadequate or divergent from sonographic evaluation, and also advise careful interpretation in patients with intact thyroid glands where high levels may originate from lymphatic drainage of

malignant thyroid cells as opposed to true metastatic synthesis.¹ While some have suggested effective cutoff values of 1 ng/mL for FNAB-Tg levels,² others would recommend utilizing a cutoff value \geq to serum thyroglobulin, proposing better accuracy in cases with detectable serum thyroglobulin.^{2,3} Performing FNAB-Tg has been reported to have an increased sensitivity (81.4%) when compared to cytology (78.0%) alone.⁴

This case report describes a 70-year-old gentleman whose preoperative FNAB was highly suggestive of papillary thyroid cancer (PTC) within a FNAB-Tg-positive regional metastasis; however, final pathology revealed insignificant papillary microcarcinomas and a level IV benign lymphatic malformation.

2 | CASE REPORT

A 70-year-old male patient was referred for specialist opinion with a history of a right level IV neck mass. It was incidentally identified on a CT chest the patient had undergone for investigation of a chronic cough. He had no symptoms

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related to the mass; there was no pain and no upper aerodigestive tract symptoms such as hoarseness, dysphagia, or bleeding. There was no past medical history of malignancy. He had had a basal cell carcinoma removed from the forehead in the past. His mother had a benign goiter surgically removed.

Examination found a mass in his right lower lateral neck that did not elevate with swallowing. On palpation, there was a firm, mobile mass measuring approximately 4 cm in size. Flexible nasal endoscopy demonstrated a normal upper aerodigestive tract. Office-based ultrasound demonstrated a 4.7×3.7 cm thin-walled cystic mass lateral to the carotid sheath in the level IV region of the neck. Within the lower portion of the right thyroid lobe was a hypochoic, taller than wide, irregular nodule that had areas of calcification within, deeming it a TIRADS score of TR5. This appeared to be wholly intrathyroidal.

He was biochemically euthyroid but had a raised serum thyroglobulin of $458 \mu\text{g/L}$ (normal 3-40 in patients with intact thyroid glands) and antithyroglobulin antibodies of 79 IU/mL (normal < 115). A CT scan revealed a right-sided well-defined, nonenhancing cystic lesion within level IV, situated lateral to the common carotid artery and posterior to the internal jugular vein (Figures 1 and 2). It measured 43 mm in width, 18 mm in depth and extended over a vertical length of 55 mm. Furthermore, the CT scan identified a small hypodense nodule within the right thyroid lobe measuring 9 mm in diameter.

An ultrasound-guided FNAB of the right thyroid lesion revealed moderate numbers of thyroid follicular cells with a background of abundant hemosiderin-laden histiocytes and scant amount of colloid. The cytospin slide shows moderate

numbers of atypical cells with nuclear features suspicious for PTC (Bethesda V). The right level IV neck mass aspirate yielded lymphoglandular bodies and a mixed population of mature lymphocytes and occasional histiocytes without evidence of malignancy. A thyroglobulin washout was performed, giving a measurement of $1075 \mu\text{g/L}$.

The case was discussed at a regional Head and Neck multidisciplinary meeting (MDM). Consensus was reached that the likely working diagnosis was primary thyroid carcinoma with cervical metastases, clinically staged as cT1N1bM0. The MDM recommended a total thyroidectomy, central neck, and right selective neck dissection (levels II-IV).

Histology of the main thyroid specimen demonstrated two foci of papillary microcarcinoma (0.4 and 0.5 mm) in the medial aspect of right lobe, adjacent to the isthmus, and mid-right lobe without vascular invasion or extension into the capsule. Otherwise, the examined thyroid gland contained multiple benign nodules. In the background, there was diffuse nodular hyperplasia, and frequent foci of Hürthle cell change consistent with lymphocytic/Hashimoto's thyroiditis.

All 33 submitted nodes from the neck dissection were benign. The level IV cystic structure demonstrated a thin fibrous wall and lymphocytes within. The lining consisted of bland cells that were immunohistochemically negative for TTF1, thyroglobulin, parathyroid hormone, and AE1/AE3. Immunohistochemical staining with D-240, which is positive in the lining of lymphatics, was also performed and found to be positive. The structure was absent of colloid or malignant

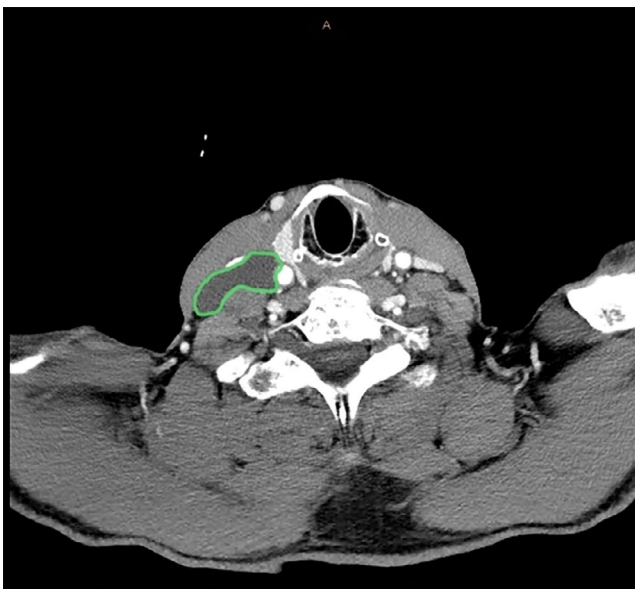


FIGURE 1 The level IV neck mass as seen on transverse computed tomography

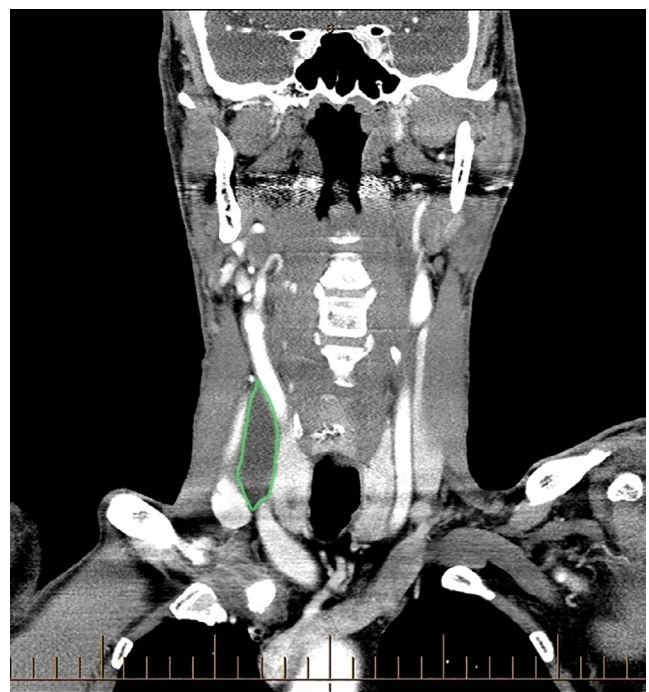


FIGURE 2 The level IV neck mass as seen on coronal computed tomography

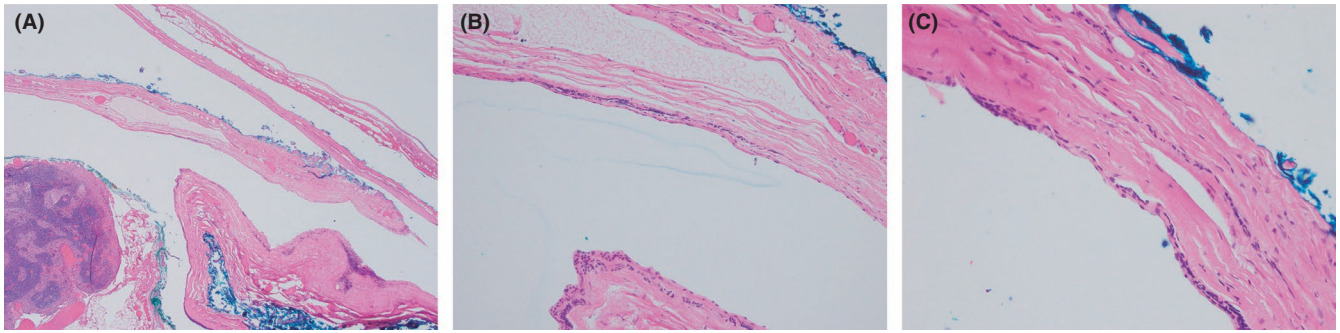


FIGURE 3 H&E stain showing lymph node with adjacent cystic lymphangioma adjacent to it (A), the higher power images showing the cells lining the cystic space (B) and (C)

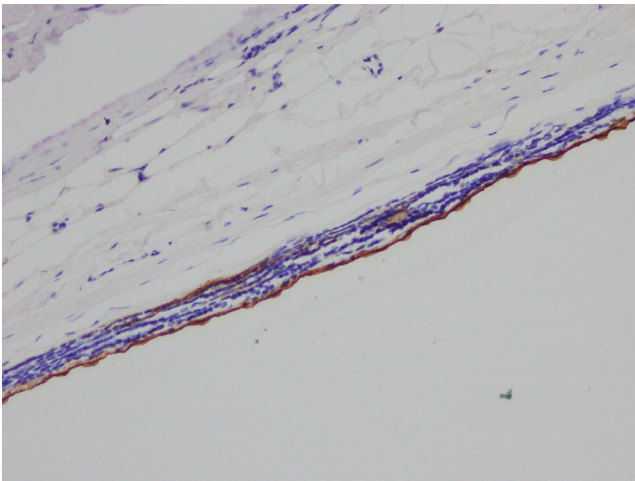


FIGURE 4 High power slide with D-240-positive immunostaining, brown line

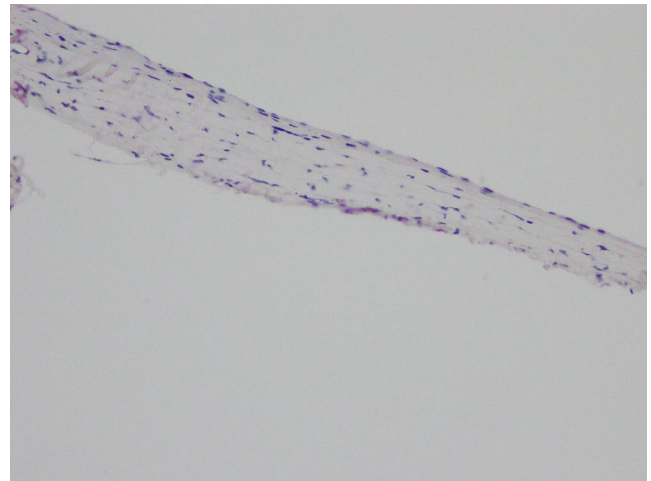


FIGURE 5 High power slide with TTF1-negative immunostaining

features. The overall pathological impression was that this structure was consistent with a lymphatic malformation (Figures 3-5).

3 | DISCUSSION

There have been numerous animal studies that demonstrate that the natural flow of thyroglobulin is from the thyroid gland, into lymphatics and then into the bloodstream. One study in monkeys and baboons⁵ examined lymph collected by cannulating lymphatics both near the thyroid gland and the cervical trunk, compared with fluid obtained from the thoracic trunk and lymphatics from the groin as controls. Both local thyroid and cervical lymph demonstrated positivity for thyroglobulin when compared to control data, as well as serum obtained from peripheral and thyroid veins. The concentration of cervical lymph thyroglobulin was also noted to increase with interval administration of thyroid-stimulating hormone. Concomitant gentle massage of the thyroid gland reached even higher concentration levels to a maximum of

5000 ng/mL, hours before falling down to 10 ng/mL. This suggests that thyroglobulin reaches the blood stream via the lymphatics.

FNAB-Tg measurement of suspicious lymph node specimens is encouraged in the context of differentiated thyroid cancer with a sensitivity of 95.7%, specificity of 50%, and positive predictive value of 95.7%.⁶ However, in another study, lymph nodes from humans with known thyroid malignancies were studied using monoclonal antithyroglobulin antibody staining, compared with normal cervical lymph node specimens obtained from patients with no history of thyroid disease.⁷ Thyroglobulin positivity was found both within lymphoid histiocytes and lymphatic channels in patients with primary thyroid cancer without histological evidence of regional metastasis. All control lymph nodes within this study were negative for TG staining. Such individual studies suggest caution against interpretation of thyroglobulin positivity in FNAB-Tg as definite evidence of metastatic thyroid cancer. A recent systematic review also shows that there is potential for raised false positives as current standardized cutoffs are yet to be established.¹

The presentation of this patient demonstrates that while finding thyroglobulin in washout specimens from lymph nodes plays a role in the surgical management, this does not necessarily confirm malignancy.

4 | CONCLUSION

Although the presence of thyroglobulin within regional lymph nodes in the neck suggests ectopic production from metastatic cells, thyroglobulin has been shown to drain via cervical lymphatics physiologically, and this phenomenon can be exaggerated in pro-inflammatory states. Assuming that FNAB-TG washout positivity in such specimens reliably predicts cancer, may lead to unnecessary surgery.

ACKNOWLEDGMENTS

We acknowledge Dr Lisa Peart from the Auckland Anatomical Pathology Service for her comprehensive analysis and providing histology slides.

CONFLICT OF INTEREST

Written informed consent for publication of clinical details and images was obtained from the patient and is available on demand. There are no conflicts of Interest, and this case has not previously been presented. The write up of this report was self-funded by the authors involved.

AUTHOR CONTRIBUTIONS

JC and WB: investigated and managed the patient. GB: reviewed the current literature and guidelines. AA and NL: wrote the manuscript with support from JC, WB, and GB.

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How to cite this article: Agnihotri A, Lilic N, Chaplin J, Braadvedt G, Bagg W. Cervical lymphatic malformation demonstrating thyroglobulin on fine needle aspirate washout. *Clin Case Rep*. 2020;8: 2834–2837. <https://doi.org/10.1002/ccr3.3234>