

THYROID CANCER TUMOR BOARD

Lymph Node Metastases Can Have a Significant Impact on Recurrence of Thyroid Cancer

Wendy Sacks and Pouyan Famini

CASE PRESENTATION ● ● ● ● ● ● ● ● ● ●

In April 2012, a 28-year-old woman at 5 weeks postpartum presented to her obstetrician because she felt a new lump in the right side of her neck. She was referred to an endocrinologist for further evaluation. Neck ultrasound demonstrated a 4.1-cm nodule in the right thyroid lobe; the nodule had irregular borders and microcalcifications. In addition, multiple enlarged, abnormal, cystic lymph nodes were visualized in the central and lateral neck at levels III, IV, and VI, ranging from 1.5 to 3.5 cm (Figures 1 and 2). Fine-needle aspiration (FNA) of the right thyroid nodule and a right level IV lymph node confirmed papillary thyroid cancer (PTC) with lymph-node metastasis.

In May 2012, the patient underwent subtotal thyroidectomy with central compartment and right modified neck dissection. Surgical pathology demonstrated multifocal classic variant PTC involving the entire right lobe, with the largest nodule in the isthmus measuring 2.4 cm. The tumor extended beyond the

thyroid and into the soft tissue and fibrous connective tissue of the neck. Eighteen of 18 central compartment lymph nodes and 8 of 12 level III/IV lymph nodes were involved, with extranodal extension (pT3, pN1b, pMX). In June, 2012, she received 155 mCi of ¹³¹I following recombinant human TSH (rhTSH) stimulation. The 7-day posttreatment whole-body scan (WBS) demonstrated focal intensive activity in both sides of the thyroid bed, focally increased activity in the superior mediastinum, and low-grade, nonspecific uptake in the high posterior right neck. Further imaging with CT or MRI was recommended. Her thyroglobulin (Tg) was 6 ng/ml on thyroid hormone suppression prior to ¹³¹I treatment.

In September 2012, with TSH <0.01 mU/L, her Tg was 5.4 ng/ml. Six months after RAI treatment, the patient underwent thyroid ultrasonography, which showed two oval, circumscribed, avascular nodules in the left thyroid bed and no irregular lateral neck lymph nodes; however, a neck MRI

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Figure 1. Transverse view of 4.1-cm right-lobe nodule with microcalcifications.



Figure 2. Two cystic level IV nodes. The larger node measures 3.5 by 2.8 by 2.0 cm.

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performed to evaluate right-salivary-gland enlargement showed a 2-cm mass in the right posterior triangle, level II, just posterior and medial to the tail of the parotid gland but deep to the sternocleidomastoid muscle. FNA of this right level II lymph node demonstrated metastatic PTC. A chest CT (without contrast material) demonstrated a 6-mm nodular area on each side of the trachea in the region of the thyroid bed, possibly corresponding to the focal intense uptake seen on the prior WBS. There was no evidence of pulmonary metastases. In April 2013, she underwent resection of this biopsy-proven metastatic lymph node as well as four adjacent benign lymph nodes. Current thyroglobulin remains elevated, at 4.2 ng/ml with TSH <0.01 mU/L, and the thyroid-bed ultrasound shows stability in size of the 0.6- and 0.8-cm left thyroid bed nodules, but now there are cystic changes and microcalcifications in these lesions (Figure 3).



Figure 3. Two left-thyroid-bed nodules with microcalcification and cystic change in the thyroid bed.

ANALYSIS AND COMMENTARY ● ● ● ● ●

Despite the extensive locoregional tumor involvement with extrathyroidal extension, lateral lymph-node metastases, and extranodal extension, most would agree that this patient's overall disease-specific survival is still excellent as prognosticated by various staging systems: Stage I by AJCC/UICC, MACIS score <6 ("low risk"), and low risk by AGES. What is the prognostic impact and the risk for recurrence of overt lymph-node metastases?

There are several prognostic factors for persistent or recurrent PTC with cervical lymph-node metastases. These include a high number of lymph nodes with metastatic disease at presentation (more than 10), number of lymph nodes with extracapsular invasion (more than 3), and elevated Tg at 6 to 12 months after levothyroxine withdrawal. Furthermore, the impact of nodal metastases depends on age, with a negative impact on outcome seen mainly in older patients.

In addition, the number of nodes, their location and size, and the presence of extracapsular extension are important prognostic factors for patients with PTC (1-3). At postoperative follow-up, patients who achieve undetectable serum Tg levels can expect a high rate of disease-free survival with a low risk for recurrent disease up to 10 years after initial treatment. However, patients with elevated serum Tg levels and a higher number of metastatic lymph nodes at presentation are at greater risk for recurrence or persistent disease. This latter group of patients should therefore be more closely monitored (1).

A recent review of prospectively maintained surgical databases at the University of Sydney and University of Wisconsin endocrine surgical units between 2000 and 2010 identified 121 patients with PTC and lateral neck nodal metastases who underwent concurrent total thyroidectomy and central and lateral compartment neck dissections (4). Ninety-eight percent also

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received postoperative RAI ablation. At a median follow-up of 31 months (2.6 years; range, 12 to 140 months), 66% had disease-free survival (N = 76). Approximately one third of the patients had recurrence of lymph-node metastases (4). In 2010, Tuttle et al. (5) published the Memorial Sloan-Kettering risk-adapted approach for estimating the risk of recurrence in patients risk-stratified by ATA criteria (6). Focusing on the intermediate-risk patients, as in our case, persistent structural disease or recurrence was identified in 21%. If the Tg was <1 ng/ml without structural evidence of disease within 2 years after initial treatment, the recurrence risk dropped to 2%. However, with an incomplete response to initial therapy (suppressed Tg >1 ng/ml and structural disease identification within the first 2 years of follow-up), the likelihood of persistent structural disease or recurrence was 41%. Our patient falls in the latter category, with high risk for additional treatments including repeat surgery, radioiodine treatment, or both. Occasionally, external-beam radiation is used, particularly in older patients for locoregional control. Because morbidity is high for these procedures, the

completeness of initial surgical resection is crucial. In hindsight, perhaps our patient's initial surgery should have included a level II dissection. At least one study has demonstrated that patients with lateral neck lymph-node metastases in levels III and IV have occult disease in level II almost 20% of the time (7).

Conclusions

The patient's clinical data were reviewed by our multidisciplinary institutional Thyroid Cancer Tumor Board. Questions posed to the group included whether the patient would benefit from a second dose of ¹³¹I versus continued monitoring with tumor markers and neck ultrasound. Consideration was also given to repeat left central neck dissection if the lesions in the left thyroid bed are confirmed to be cancer; however, the risk of surgical complications is high for a second surgery in this location. While there are no data to suggest that another dose of RAI will improve her overall survival, perhaps it may decrease her risk for further recurrence. The majority of the group recommended a second dose of ¹³¹I for ablation. To date, the patient has refused further treatment.

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