Hyalinizing trabecular tumor, a rare histologically unique tumor of the thyroid, coexisting with papillary thyroid carcinoma

Chiu-Hsuan Cheng*
Department of Anatomical Pathology, Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation and Tzu Chi University, Hualien, Taiwan

A 60-year-old woman with a history of well-controlled hypertension, type II diabetes mellitus, and hyperlipidemia presented to our hospital due to neck enlargement for 5 months. Her neck ultrasonography disclosed three well-defined tumors, a 3.43 cm × 2.03 cm hypoechoic nodule at the right lower thyroid, a 0.68 cm × 0.8 cm heterogeneous nodule with calcification at the right upper thyroid, and a 0.51 cm × 0.36 cm hypoechoic nodule at the left thyroid. Fine-needle aspiration (FNA) cytology smears from the first and second nodules were reported as the Bethesda system for reporting thyroid cytology category-II (TBS-II). The patient was in the euthyroid state. The serum antithyroglobulin antibody level was high (53.1 IU/mL). Intraoperative frozen section of the left nodule proved to be papillary thyroid carcinoma (PTC). Bilateral total thyroidectomy was performed. The patient recovered well without any complication and was arranged regular follow-ups.

Grossly, the first tumor was a well-defined pale gray soft nodule [Figure 1]. The second and third tumors were white firm nodules.

Microscopically, the first tumor was an encapsulated one [Figure 2] composed of polygonal cells in trabecular pattern and abundant intratrabecular hyaline material [Figure 3]. The cells had wrinkle nuclear membrane, nuclear grooving, and nuclear pseudoinclusions [Figure 3]. The hyaline material was diastase resistant and periodic acid–Schiff (PAS) positive but Congo red negative. The cells expressed thyroid transcription factor-1 (TTF-1) and thyroglobulin but not human bone marrow endothelial marker -1 (HBME-1), chromogranin A, and synaptophysin. Hyalinizing trabecular tumor (HTT) was diagnosed. The second and third tumors were PTCs [Figure 4]. The background thyroid revealed lymphocytic thyroiditis [Figure 1].
HTTs are uncommon neoplasms with unique histological and immunohistochemical characteristics. They are thyroid follicular cell-derived neoplasms of mostly benign nature, with only once reported as malignant case [1].

Grossly, almost all HTTs are circumscribed or encapsulated soft to firm, round to oval, white to yellow tumors of sizes ranging from 0.5 to 7.5 cm. Microscopically, polygonal cells are arranged in trabecular pattern with variable amounts of intratrabecular and intertrabecular diastase-resistant PAS-reactive hyaline material. The trabecular arrangement and presence of hyaline material confuse them for medullary thyroid carcinomas or paragangliomas. The cellular morphology is characterized by finely granular eosinophilic cytoplasm, vesicular nuclei with small nucleoli, nuclear grooves, and intranuclear pseudo-inclusions [1]. These nuclear features share with PTCs which make FNA cytology and frozen section challenging.

HTTs express thyroid follicular cell markers such as thyroglobulin and TTF-1 but not calcitonin, neuroendocrine markers such as chromogranin-A and synaptophysin, and malignancy-related markers such as HBME1 and cytokeratin-19. The Ki67 using MIB1 clone at room temperature can be diagnostically conclusive due to the unique cell membrane reactivity of HTTs [1].

Another interesting fact about HTTs is that they frequently coexist with lymphocytic thyroiditis and/or PTCs [2,3]. Moreover, they share the same molecular genetics of PTCs. Papotti et al. [2] reported that 28.6% of HTTs exhibit RET proto-oncogene alteration. Cheung et al. [3] reported that six of the eight HTTs have RET/PTC gene rearrangement. Neither RAS nor BRAF gene mutation is noted in HTTs studied by Liu et al. [4] although individual reports had been claimed to detect BRAF mutation [5].

Declaration of patient consent
The authors certify that the patient has obtained appropriate patient consent form. In the form, the patient has given the consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initial will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES
1. Lloyd RV, Osamura RY, Kloppel G, Rosai J. WHO classification of tumors of endocrine organs. 4th ed. Lyon: the International Agency for Research on Cancers (IARC); 2017, p. 73-4.
2. Papotti M, Volante M, Giuliano A, Fassina A, Fusco A, Bussolati G, et al. RET/PTC activation in hyalinizing trabecular tumors of the thyroid. Am J Surg Pathol 2000;24:1615-21.
3. Cheung CC, Boerner SL, Macmillan CM, Ramyar L, Asa SL. Hyalinizing trabecular tumor of the thyroid: A variant of papillary carcinoma proved by molecular genetics. Am J Surg Pathol 2000;24:1622-6.
4. Liu Y, Huang X, Hu Y, Wang F, Du T, He W, et al. Hyalinizing trabecular tumor of the thyroid: A clinicopathological analysis of four cases and review of the literature. Int J Clin Exp Pathol 2017;10:7616-26.
5. Jang SM, Oh YH, Jeon YK, Park YW, Park MH. Cytological features and BRAF mutation of hyalinizing trabecular adenoma of the thyroid-A case report with review of the literature. Korean J Pathol 2011;45:428-33.

Figure 3: Polygonal tumor cells having wrinkle nuclear membranes, nuclear grooves (black arrows), and nuclear pseudo-inclusions (white arrows) arranged in trabecular pattern (H and E, ×400) (Insert: The cells had wrinkle nuclear membrane, nuclear grooving, and nuclear pseudo-inclusions in thyroid aspiration cytology, Papanicolaou stain, ×400)

Figure 4: Coexisting conventional papillary carcinoma of the left lobe of thyroid (H and E, ×200)