The Diffuse Sclerosing Variant of Papillary Thyroid Cancer Presenting as Innumerable Diffuse Microcalcifications in Underlying Adolescent Hashimoto’s Thyroiditis

A Case Report

Sun Hye Jeong, MD, Hyun Sook Hong, MD, PhD, Eun Hye Lee, MD, PhD, and Jeong Ja Kwak, MD, PhD

Abstract: Hashimoto’s thyroiditis is the most common diffuse thyroid disease and is characterized by diffuse lymphocytic infiltration. However, the ultrasonographic findings of papillary thyroid carcinomas that arise from Hashimoto’s thyroiditis in the pediatric and adolescent population are not well known.

We report a rare ultrasonographic finding in a 22-year-old woman diagnosed with the diffuse sclerosing variant of papillary thyroid carcinoma that arose from underlying Hashimoto’s thyroiditis: innumerable diffuse microcalcifications instead of a typical malignant-appearing nodule.

(Introduction) The Diffuse Sclerosing Variant of Papillary Thyroid Cancer

Hashimoto’s thyroiditis is the most common diffuse thyroid disease and is characterized by diffuse lymphocytic infiltration. It affects 1.3% of children and adolescents and has a female predominance.1–3 Hashimoto’s thyroiditis is the most important cause of hypothyroidism in children and adolescents. Although still controversial, evidence suggests an increased risk of papillary thyroid carcinoma in patients with Hashimoto’s thyroiditis.4–6 Given its rarity, however, the ultrasonographic findings of papillary thyroid carcinomas that arise from Hashimoto’s thyroiditis in the pediatric and adolescent population are not well known. Here, we report the ultrasonographic findings of papillary thyroid cancer with underlying adolescent Hashimoto’s thyroiditis.

CASE
Institutional Review Board approval was obtained for this retrospective study, and the requirement for informed consent was waived.

A 22-year-old woman was followed and diagnosed with Hashimoto’s thyroiditis at the age of 13 years old. She had no family history of thyroid cancer. At the age of 13, ultrasonography of the neck revealed diffusely enlarged thyroid lobes bilaterally, with diffusely increased vascularity but no focal masses or calcifications (Figure 1A and B). We diagnosed this as compatible with thyroiditis. Three years later, follow-up ultrasonography (Figure 1C) showed diffuse low parenchymal echogenicity compared with the previous examination.

Six years after the last ultrasonography, she visited our institution complaining of a palpable lesion in her anterior neck. Serum thyroglobulin (TG) autoantibodies (Ab) (70.12 U/mL; normal, 0–0.3 U/mL) and microsomal Ab titer (>100 U/mL; normal, 0–0.3 U/mL) were high. The free T4 level was 1.39 ng/dL (normal, 0.89–1.7 ng/dL) and the thyroid-stimulating hormone level was 0.01 (normal, 0.25–4 ng/dL). Diagnostic neck ultrasonography showed innumerable microcalcifications with an ill-defined hypoechoic lesion replacing almost the entire left lobe of the thyroid gland (Figure 1D and E). Metastatic lymph nodes were seen at level VI on the left neck. We suspected that the thyroid lesion was a malignancy and performed ultrasonography-guided fine needle aspiration. The cytological result was a follicular lesion of undetermined significance, not otherwise categorized. Subsequently, we performed an ultrasonography-guided core needle biopsy.

PATHOLOGY
Microscopically, the thyroid core biopsy showed extensive lymphocytic infiltration with lymphoid follicles, diffuse tumor growth with tumor aggregates, and abundant psammoma bodies. There were many tumor foci within lymphatic channels. These findings were compatible with the diffuse sclerosing variant of papillary thyroid carcinoma (Figure 1F and G). No B-type Raf kinase mutation was detected.

She didn’t have operation in our institution.

DISCUSSION
Hashimoto’s thyroiditis is diagnosed based on TG-Ab or microsomal Ab seropositivity, accompanied by at least one of the following: abnormal thyroid function, enlarged thyroid gland, and morphological changes such as a heterogeneous
echotexture, diffuse hypoechogenicity, and hypoechogenic micronodules with a surrounding echogenic rim on thyroid ultrasonography.

The ultrasonographic appearance of thyroid cancer in patients with Hashimoto’s thyroiditis is not well reported. Durfee et al.\textsuperscript{7} reported that the sonographic characteristics of cancerous nodules were similar in patients with and without Hashimoto’s thyroiditis. However, they focused on nodules and diffuse lesions such as diffuse microcalcifications, and non-mass-like hypoechogenic lesions were not included. Another study reported the ultrasonographic findings of 3 pediatric papillary thyroid carcinomas associated with Hashimoto’s thyroiditis. In all 3 cases, irregularly shaped hypoechogenic nodules with microcalcifications were noted on ultrasonography of the thyroid gland.\textsuperscript{8} In this study, however, the variant type of the papillary thyroid carcinoma was not mentioned.

There have been case reports of 15- and 18-year-old girls with the diffuse sclerosing variant of papillary thyroid carcinoma presenting as Hashimoto’s thyroiditis.\textsuperscript{9,10} In these cases, the ultrasonographic findings of the thyroid glands included a diffusely altered thyroid parenchyma, with a snow-storm appearance, and generally enlarged thyroid lobes with diffusely prominent microcalcifications. However, the researchers overlooked possibility of causal relationship and did not make clear the order of the incident between Hashimoto’s thyroiditis and papillary thyroid carcinoma.

To our knowledge, the relationship between Hashimoto’s thyroiditis and the diffuse sclerosing variant of papillary thyroid carcinoma is not well established. Our patient was an extremely rare case of the diffuse sclerosing variant of papillary thyroid carcinoma arising from adolescent Hashimoto’s thyroiditis. We performed ultrasonography twice before making the diagnosis of papillary carcinoma, and there were no suspicious features on these examinations. Therefore, it took <6 years for thyroiditis to develop into overt extensive papillary carcinoma in Hashimoto’s thyroiditis.

Pediatric and adolescent thyroid carcinoma has a relatively favorable prognosis in terms of mortality, but a high risk of
Younger patients tend to present with more advanced disease, including node metastasis. The American Thyroid Association Guidelines include management guidelines for children. For patients with autoimmune thyroiditis, evaluation by an experienced thyroid ultrasonographer should be performed in any patient with a suspicious thyroid examination (suspected nodule or significant gland asymmetry), especially if associated with palpable cervical lymphadenopathy. However, they did not mention diffuse microcalcifications in autoimmune thyroiditis as a suspicious feature. Here, we report sclerosing variant of papillary thyroid cancer arising from adolescent Hashimoto’s thyroiditis which ultrasonographic findings were innumerable diffuse microcalcifications replaced almost the entire left lobe. We wish our case would be helpful when deciding the management of thyroid lesions presenting with these features.

REFERENCES
1. Babcock DS. Thyroid disease in the pediatric patient: emphasizing imaging with sonography. Pediatr Radiol. 2006;36:299–308quiz 372-293.
2. Pearce EN, Farwell AP, Braverman LE. Thyroiditis. N Engl J Med. 2003;348:2646–2655.
3. Yeh HC, Futterweit W, Gilbert P. Micronodulation: ultrasonographic sign of Hashimoto thyroiditis. J Ultrasound Med. 1996;15:813–819.
4. Ko MS, Jeong KS, Shong YK, et al. Collapsing benign cystic nodules of the thyroid gland: sonographic differentiation from papillary thyroid carcinoma. AJNR Am J Neuroradiol. 2012;33:124–127.
5. Arabi M, Dvorak R, Smith LB, et al. Fluorodeoxyglucose positron emission tomography in primary thyroid lymphoma with coexisting lymphocytic thyroiditis. Thyroid. 2011;21:1153–1156.
6. Karnak I, Ardicli B, Ekins C, et al. Papillary thyroid carcinoma does not have standard course in children. Pediatr Surg Int. 2011;27:931–936.
7. Durfee SM, Benson CB, Arthaud DM, et al. Sonographic appearance of thyroid cancer in patients with Hashimoto thyroiditis. J Ultrasound Med. 2015;34:697–704.
8. Koibuchi H, Omoto K, Fukushima N, et al. Coexistence of papillary thyroid cancer and Hashimoto thyroiditis in children: report of 3 cases. J Ultrasound Med. 2014;33:1299–1303.
9. Vukasović A, Kuna SK, Ostović KT, et al. Diffuse sclerosing variant of thyroid carcinoma presenting as Hashimoto thyroiditis: a case report. Coll Antropol. 2012;36(Suppl 2):219–221.
10. Chen CC, Chen WC, Peng SL, et al. Diffuse sclerosing variant of thyroid papillary carcinoma: diagnostic challenges occur with Hashimoto’s thyroiditis. J Formos Med Assoc. 2013;112:358–362.
11. Francis G, Waguespack SG, Bauer AJ, et al. Management Guidelines for Children with Thyroid Nodules and Differentiated Thyroid Cancer The American Thyroid Association Guidelines Task Force on Pediatric Thyroid Cancer. Thyroid. 2015;25:716–759.