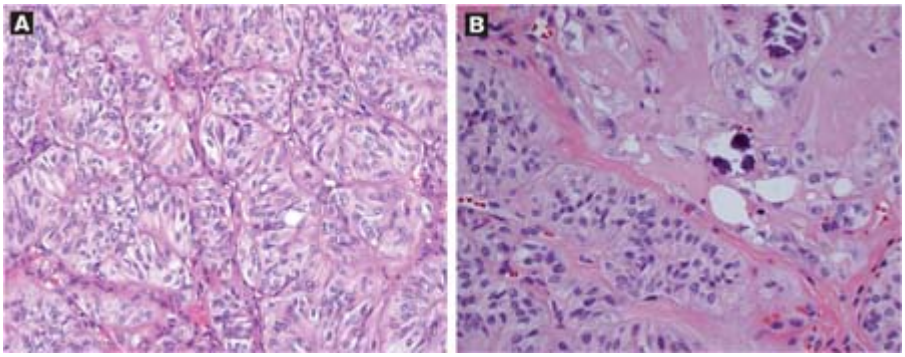
Hyalinizing trabecular adenoma of the thyroid gland.

by Lester D. R. Thompson, MD

Hyalinizing trabecular ade-noma (HTA) is a very rare tumor (<1% of all primary thyroid gland tumors) of thyroid follicular cell origin with a trabecular pattern of growth and marked intratrabecular hyalinization (figure 1). For all intents and purposes, this is a benign tumor, although there is a case report of pulmonary metastasis with invasion, suggesting the term tumor be used instead of adenoma. A few cases have occurred following radiation exposure, and there may be a relationship to thyroid papillary carcinoma, as there have been reports of *RET/PTC* rearrangements.

Figure 1. A: Hematoxylin and eosin stain shows a trabecular architecture composed of cells arranged perpendicular to the axis of the trabeculae. The cells are spindled to fusiform. There is pink hyalinization within and between the epithelial groups. B: Higher magnification demonstrates remarkable inter and intratrabecular hyalinization. Note the calcifications (blue concretions) within the tumor. The nuclei have open to vesicular nuclear chromatin distribution.



Most patients with HTA are middle-aged (mean, 50 years), and this tumor has a female predominance (female-to-male, 6:1). Patients are usually asymptomatic, with a mass found incidentally during a routine physical exam.

Conservative but complete excision (lobectomy) yields a cure in nearly all cases. Ultrasonography typically shows a solid nodule with hypoechoic or heterogeneous echogenicity.

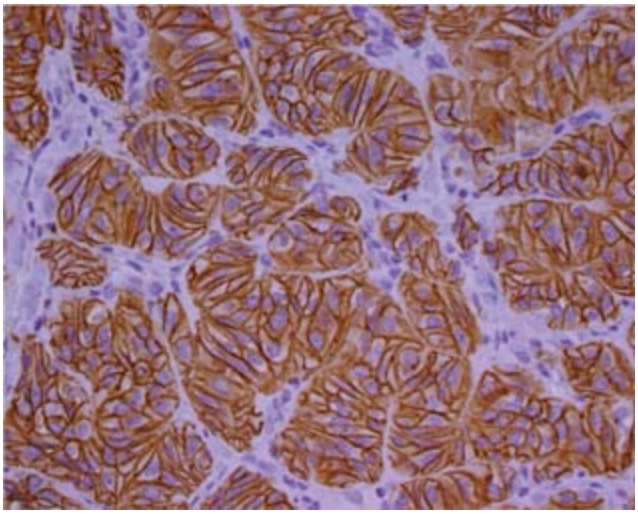
The tumors are usually small (mean, 2.5 cm), solitary, solid, encapsulated masses, with a lobulated, yellow-tan cut surface showing patulous vessels and rare calcifications. The circumscribed tumors are surrounded by a thin, irregular, and uneven fibrous connective-tissue capsule. The cellular tumors are arranged in trabecular, alveolar, or insular growth patterns. The trabeculae are straight to curvilinear groups of cells, 2 to 4 cells thick. There is scant to absent colloid.

The medium to large, polygonal to fusiform cells contain oval to elongated nuclei arranged perpendicular to the long axis of the trabeculae and fibrovascular stroma. The nuclei show prominent grooves, contour irregularities, and intranuclear cytoplasmic inclusions. Perinucleolar halos are also seen. The cytoplasm is homogeneous, glassy to granular, occasionally containing distinctive round, refractile, paranuclear yellow bodies or vacuoles.

The tumor cells are surrounded by dense, intratrabecular, heavily hyalinized, eosinophilic fibrovascular stroma, which spills out into the intertrabecular zones. The hyalinization shows zonation, with greater deposition at the periphery of the trabeculae. Calcospherites (psammoma or calcific bodies) may be seen. Mitoses are rare.

The neoplastic cells show strong and well-developed positive reactions with thyroglobulin, TTF-1, keratin, and CK7. A unique membranous and cytoplasmic reaction with Ki-67 (Dako MIB1 antibody) is different from the usual nuclear reaction with this antibody (figure 2). No *BRAF* or *RAS* mutations are identified in this tumor.

Figure 2. Ki-67 immunohistochemistry stain shows a very strong and characteristic membrane and peripheral cytoplasmic reactivity. The membranous staining is only identified with the Dako MIB1 antibody and not with those of other manufacturers.



The differential diagnosis includes *thyroid papillary carcinoma* (there is usually invasive growth; very rare to have extensive intratrabecular stromal hyalinization; yellow bodies are not present; MIB1 membranous reaction is absent), *follicular adenoma* or *carcinoma* (there can be intertrabecular hyalinization, but usually no intratrabecular hyalinization; yellow bodies are absent; perpendicular nuclear arrangement is usually absent; MIB1 membranous reaction is absent), *medullary thyroid carcinoma* (an invasive tumor that lacks colloid; amyloid is unique; shows calcitonin and chromogranin immunoreactivity) and, rarely, *paraganglioma* (may have a similar growth pattern, but the strong chromogranin and/or synaptophysin reaction with S-100 protein sustentacular reaction will help with classification).

Suggested reading

1. Carney JA, Hirokawa M, Lloyd RV, et al. Hyalinizing trabecular tumors of the thyroid gland are almost all benign. Am J Surg Pathol 2008; 32 (12): 1877-89.
2. Carney JA, Ryan J, Goeliner JR. Hyalinizing trabecular adenoma of the thyroid gland. Am J Surg Pathol 1987; 11 (8): 583-91.
3. LiVolsi VA. Hyalinizing trabecular tumor of the thyroid: Adenoma, carcinoma, or neoplasm of uncertain malignant potential? Am J Surg Pathol 2000; 24 (12): 1683-4.
4. Nosé V, Volante M, Papotti M. Hyalinizing trabecular tumor of the thyroid: An update. Endocr Pathol 2008; 19 (1): 1-8.

Ear Nose Throat J. 2011 September;90(9):416-417.