Hyalinizing trabecular adenoma (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.

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 inter trabecular 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.

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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).

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