Case of the Month

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A 40 year-old Hispanic female with a right thyroid nodule

Contributed by Howard H. Wu, M.D.

Associate Professor of Clinical Pathology and Laboratory Medicine, Indiana University

Pathologist, Indiana University Health

Diplomate of the American Board of Pathology in Anatomic/Clinical Pathology and Cytopathology

Special Interest: Surgical Pathology and Cytopathology

Clinical history:

Patient is a 40 year-old Hispanic woman who was noted to have a 0.8 cm right thyroid nodule and an enlarged 1.0 cm right paratracheal lymph node by ultrasound. Fine needle aspirations were performed on both thyroid nodule and cervical lymph node followed by a total thyroidectomy with right cervical lymph node resection three weeks later.

Fine Needle Aspiration:

See Figure 1 (Diff-Quik-stained x 400) and Figure 2 (Papanicolaou stained x 400)

Gross examination:

Sectioning the right thyroid lobe revealed an ill-defined white-tan mass measuring 0.8 x 0.6 x 0.5 cm in the mid-portion. The nodule abutted the inked thyroid capsule. The left lobe and pyramidal lobe were unremarkable.

Microscopic examination:

Figure 1:
Figure 2:
Figure 3: Microscopic section from the thyroid nodule (H&E x 400)
Final diagnosis:

**Tall cell variant of papillary thyroid carcinoma**

Discussion:

The tall cell variant of papillary thyroid carcinoma (PTC) is an uncommon tumor, accounting for 1.3–12% of all PTCs. It is associated with an aggressive clinical behavior with high mortality rates. Compared with classical PTC, tall cell variant of PTC occurs more commonly at an older age, has a higher rate of extrathyroidal disease and poorer 5-year disease-specific survival. Most patients with tall cell variant of PTC have lymph node metastasis at the time of presentation. These tumors tend to be larger than the classical PTCs.
The tall cell variant was first described by Hawk and Hazard in 1976. The tall cell is twice as tall as it is wide and its cytoplasm is often eosinophilic, therefore these tumors maybe referred as “pink cell” variant of papillary thyroid carcinoma. Tall cells should comprise of at least 30% of the tumor cells to make the diagnosis of tall cell variant. However even a minor component of tall cells component (5-10%) in an otherwise classic type of PTC should be mentioned in the pathology report.

The tall cell variant of PTC usually shows complex papillary architecture comprising of elongated papillae; sometimes may simulate a trabecular and/or solid growth pattern on low power microscopic examination. The cells are large, round to oval in shape with well-defined cellular border and the cytoplasm is often eosinophilic without cytoplasmic granularity; a feature which distinguishes them from true oncocyctic follicular/Hürthle cells. The nuclei are elongated with irregular nuclear membrane, have prominent intranuclear grooves, clearing and intranuclear inclusions.

In fine-needle aspiration (FNA) specimens, special attention should be paid to these characteristic cytological features, described by some pathologists as 'tail-like cells' or 'tadpole cells'. Tall cell variant of PTC demonstrated distinctive cytologic features, which can distinguish them from classic PTC. These included elongated/tall cells, dense cytoplasm and distinct cell border which were also found to be statistically significant (P<0.0001). Multiple inclusions within the same nucleus imparting a “soap bubble appearance” to the nucleus are frequent features of tall cell variant of PTC and are rarely seen in classical PTC.

There is a general consensus that as a group, tall cell variant of PTC has a higher recurrence and death rate than classical PTC. Initially, this was attributed to the fact that tall cell variant of PTC presented as large tumors with extrathyroidal extension in older patients. However, recent data support that tall-cell histology alone remains a significant prognostic factor independent of age, gender, and tumour size and extrathyroidal extension. A meta-analysis of 131 cases of that tall cell variant of PTC showed 4.5 times recurrence rate and 14 times greater disease-related mortality as compared with classical PTC. The aggressive behavior of the tall cell variant of PTCs could be related to certain factors elaborated by the tumour. The high expression of Muc1 and type IV collagenase (matrix metalloproteinase-2) in these tall cell variant of PTCs may allow for degradation of stroma.
and greater invasive properties. The aggressive behavior of that tall cell variant of PTC may also be related to the higher prevalence of BRAF mutations; as these mutations in PTC have been associated with higher frequency of extraglandular extension and nodal metastases. The importance of tall cell variant of PTC is accentuated by the fact that it is overrepresented in those fluorodeoxyglucose positron-emission tomogram (FDG-PET)-positive thyroid carcinomas that are refractory to radioactive iodine therapy constituting 20% of these incurable tumors.

Tall-cell variant of papillary microcarcinoma (<1 cm) is also found more aggressive and the management should be differentiated from other papillary microcarcinomas. Berstein et al. compared 27 patients with tall-cell papillary with 26 patients with classic papillary microcarcinomas. All the patients underwent total thyroidectomy. The average size of the cancer was about 7 mm and the average age of the patients was 53-56 years for tall cell variant of papillary microcarcinoma, neither of which was different between both groups. Spread of the cancer outside of the thyroid was seen in 33% of tall-cell cancers but in none of the classic microcarcinomas (p = 0.002). 36% of patient with tall cell variant of papillary microcarcinoma presented at an advanced stage (stage III/IVA) compared to 7.7% for classic papillary microcarcinoma (p= 0.02). The BRAF mutation was found in 93% of the tall-cell microcarcinomas and in 77% of the classic papillary microcarcinomas. Total thyroidectomy is warranted for tall cell variant of papillary microcarcinoma.

In summary, tall cell variant of PTC is a biologically and clinically aggressive thyroid carcinoma independent of age, gender, and tumor size. Therefore, it is prudent that presence of any foci of tall cells should be mentioned in a pathology report regardless of the percentage of tall cell cytology found. This should prompt the clinician to fully treat and carefully monitor the patient for recurrence and distant metastasis.

References:

1. Baloch Z, LiVolsi VA, Tondon R. Aggressive variants of follicular cell derived thyroid carcinoma; the so called “real thyroid carcinoma” J Clin Pathol 2013, 66:733-743
