CASE REPORT

Paraganglioma like Adenoma of Thyroid: Rare Neoplasm of Thyroid: Case Report and Review of Literature

Surabhi Garg, Loreno Enny, Tarun Patel

Department of Surgery, Sarojini Naidu Medical College, Agra, Uttar Pradesh, India

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ABSTRACT

Paraganglioma like adenoma of thyroid (PLAT) also known as Hyalinizing trabecular adenoma is a rare neoplasm of the thyroid, arising mostly in middle-aged women. The histological resemblance to paraganglioma, papillary and medullary carcinoma of thyroid may often lead to confusion. Immunohistochemical markers often help establish a diagnosis. The biology and clinical course of such tumors is often considered benign. However, further studies are needed to establish the same. We herein present a case of a 30 year old lady who presented with a long-standing goitre, and was diagnosed to be a case of PLAT on final histopathology.

Keywords: Paraganglioma-like adenoma of Thyroid (PLAT), Hyalinizing trabecular tumour of thyroid (HTT), Thyroidectomy

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INTRODUCTION

Paraganglioma like adenoma of thyroid (PLAT) also known as hyalinizing trabecular adenoma is a rare thyroid neoplasm that is typically benign but can be easily mistaken for papillary thyroid carcinoma and primary paraganglioma thyroid as they share some similar microscopic features.[1,2] PLAT can be associated with several thyroid conditions but has been found to be more commonly associated with chronic lymphocytic thyroiditis.[3] It is usually seen in middle aged patients with a female predilection. Grossly, it resembles typical adenoma and are usually well-circumscribed, yellow-tan, solid, and encapsulated with thin fibrous capsule. Microscopically, it is a follicular-derived neoplasm composed of medium to large cells with a prominent trabecular and nesting growth pattern. A colloid is usually scant and psammomas bodies may be seen. The cytoplasm is pale and eosinophilic and nuclei are round to oval. They usually stain positive for thyroglobulin and TTF-1 on immunohistochemistry and also may be positive for S-100 and neuron specific enolase.[4] Molecular studies have shown RET/PTC rearrangement in this type of tumor which is also the most common rearrangement associated with PTC.[5] Surgery, usually lobectomy, is the treatment of choice.

CASE

A 30-year-old female presented with gradually enlarging mass over the neck for 15 years, which was painless. There was no history suggesting thyroid dysfunction or other compressive symptoms. On examination, a large irregular swelling with bosselated surface was present over the neck extending from angle of mandible to below suprasternal notch (overhanging suprasternal notch), which moved with deglutition. No lymph nodes were palpable and bilateral carotids were pushed posterolaterally (Figure 1). USG revealed a bulky bilateral thyroid lobe with multiple echogenic lesions containing solid and cystic components with smooth margins and mild internal vascularity. CECT revealed heterogeneous, massively enlarged both lobes of thyroid with irregular cystic changes (Figure 2a and 2b). FNAC was suggestive of Bethesda-2 (Benign etiology).

Total thyroidectomy was performed and the post-operative course of which was uneventful. The histopathological examination revealed multiple follicles with hyperplastic epithelium, some dilated follicles showing papillary projections, with areas of ruptured follicles and secondary changes like calcification. Cells are arranged in organoid (Zellballen) pattern and are surrounded by richly vascular septa (Figure 3a and 3b). Cells are rounded in shape with eosinophilic cytoplasm with uniform dispersed chromatin. Described features were suggestive of benign colloid goiter with secondary changes along with PLAT. Immunohistochemistry was positive for thyroglobulin and TTF-1 but was negative for S-100, Synaptophysin, and chromogranin.

DISCUSSION

PLAT, more commonly known as hyalinizing trabecular tumor (HTT) is a rare thyroid gland neoplasm that was first

**Author for Correspondence: dehd.girl@gmail.com*

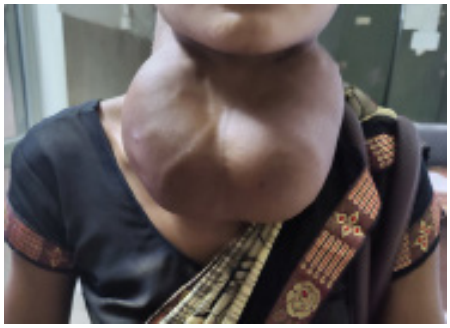

Figure 1: 30-year-old lady with gradually enlarging neck mass

described in 1987 by Carney et al.[3] It is a thyroid tumour of a follicular origin and is characterized by trabecular pattern and intratrabecular hyalinization.[6] HTT entered World Health Organization's (WHO) Thyroid Tumour Classification in 2004.[7]

According to WHO classification of Endocrine Organ Tumours, HTT is described as "an uncommon tumour of follicular origin characterized by trabecular pattern of growth and marked intra-trabecular hyalinization.[7] HTT is a well-circumscribed, encapsulated lesion and usually asymptomatic; it can be seen in forms of single or numerous nodules or incidentally after thyroidectomy. It mostly occurs in middle aged women, with female to male ratio of 6:1. Mostly it is common in middle-aged women; female:male ratio is 6:1.[8] More recently, occurrence of HTT have been found to be increasingly in relation to chronic lymphocytic thyroiditis or Hashimoto's thyroiditis.[8]

Fine needle aspiration cytology is often inconclusive in HTT. The pathologist may often report it as atypia/follicular neoplasm of unknown significance or suspicious of malignancy. The basic histological structure of HTT is characterized with a hyalinizing trabecular pattern, cytoplasmic inclusions at cell cytoplasm and matrix, and nucleus with grooves. Their special features are perivascular hyalinization, dominant stroma, and trabecular arrangement.[9] Macroscopically, these tumors are well-circumscribed and encapsulated like other adenomas. Due to the organoid structures accompanying this trabecular pattern, they are called "paraganglioma-like adenoma". By immunohistochemistry, HTT is positive for thyroglobulin and TTF1 with unique membraneous expression of Ki-67, and also may be positive for S-100 and neuron specific enolase.[4] However, they are negative for other markers for neuroendocrine tumors like chromogranin A and synaptophysin, which help to differentiate them from primary thyroid paraganglioma. Primary thyroid paraganglioma is an uncommon neuroendocrine tumor supposed to originate from the inferior laryngeal paraganglia. They are composed of two types of cells: polygonal chief cells and elongated sustentacular cells. Tumor cells formed distinctive nesting or organoid growth pattern (Zellballen), recapitulating the structure of normal paraganglion.[10] The lack of chromogranin A or synaptophysin reactivity in the tumor cells, the failure to find neurosecretory granules by electron microscopy, may help in differentiating primary paragangliomas from HTT.

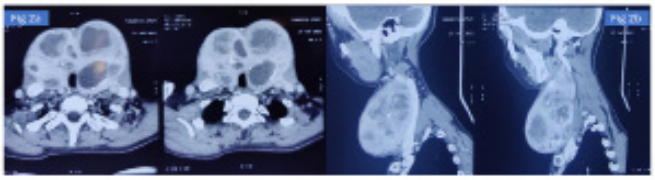

Figure 2a and 2b: CECT revealed heterogenous, massively enlarged both lobes of thyroid with irregular cystic changes

Some authors also suggest the group of tumors designated as PLAT may need further clarification. Bronner *et al*.[1] first used the term PLAT in describing nine encapsulated thyroid tumours with the lobulated, Zellballen arrangement of spindle to oval cells in a vascular back- ground typical of paraganglioma. Because of their thyroglobulin-positive and neuro-filament-negative immunostaining, it was concluded that these tumours were of follicular epithelial rather than neuroepithelial origin, and the authors compared them to a group of tumors having similar cytologic and architectural characteristics as well as thyroglobulin-positive immunostaining, previously described as HTT. Despite the similarities between these groups of tumors, there were significant differences, including the hyalinized, amyloid-negative stroma and nuclear grooves and inclusions that were seen in HTT, but not observed, or at least not described in PLAT. Only very few cases show purely or predominantly alveolar or Zellballen pattern that might be mistaken for paraganglioma as seen in the present case.

Another controversial point on HTT is the benign or malignant status of the tumor. In 1987, when Carney *et al*.[3] first described the tumor, they said that HTT is a benign lesion and does not cause to vascular invasion or metastasis. After that, HTT was claimed to be a benign lesion in many cases; however, the literature shows malignant forms that cause capsule and vessel invasion or lung and lymph node metastasis.[9,11]

HTT can often be confused with papillary or medullary carcinoma of the thyroid Histologically, the detection of intranuclear groove, pseudo inclusions, and psammoma bodies cause confusion with papillary carcinoma of thyroid (PTC). In cytologic specimens, intranuclear cytoplasmic inclusions are detected in almost 100% of HTTs and 75% of PTCs, and the incidences of nuclear grooves are 100% of the

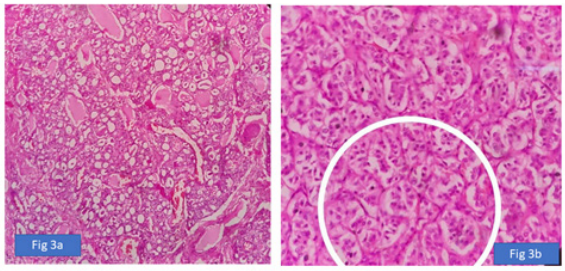

Figure 3: a) The histopathological examination revealed multiple follicles with hyperplastic epithelium, some dilated follicles showing papillary projections. B) Cells are arranged in organoid (Zellballen)(within white circle) pattern and are surrounded by richly vascular septa. Cells are rounded in shape with eosinophilic cytoplasm with uniform dispersed chromatin.

PTCs and 81.8% of the HTTs, which makes the differential diagnosis of these diseases difficult. The presence of spindle cells and intratrabecular hyalinization that looks like stromal amyloid may lead to confusion with medullary carcinoma thyroid. However, HTT are negative for calcitonin and stain negatively with Congo red stain, which help in differentiating them from medullary carcinoma.[11] HTT may also be present in the background of benign colloid goitre, as was seen in the present case. FNA maybe inconclusive in such cases. In 1995, Hirokawa *et al.* reported that the staining of MIB-1 (a monoclonal antibody of Ki-67, which normally reacts in cell nuclei in the late G1, S, G2, and M phases) was detected in the cell membrane of HTT cells, and this finding can be helpful to diagnose HTT.[12] Molecular studies have shown RET/PTC rearrangement in this type of tumor which is also the most common rearrangement associated with PTC. Further, the fact that HTT is accompanied by papillary carcinoma and that they have the same immunophenotypic properties cause interpretations that both tumors are similar.[5] Further studies are required to establish the relationship between HTT and PTC.

Ultrasonographic features of HTT have been demonstrated, including round shape, hypoechogenicity, absence of calcifications, and the presence of peri- or intranodular vascularity. Lee *et al.* showed that the appearance of HTT is often similar to that of follicular neoplasm.[13]

Immediate surgery or active surveillance is often recommended for tumors that were cytologically diagnosed as or highly suspected of being HTT with no possibility of being PTC, based on the discretion of attending physicians. Surgery must be performed for tumors that are suspected of being HTT but also present the possibility of being PTC based on cytology.[14]

More recently, genetic studies indicated that the GLIS rearrangements, especially PAX8-GLIS3 gene fusion, are useful to diagnose HTT. Nikiforova *et al.* reported that PAX8-GLIS3 gene fusion was identified in 13 (93%) of 14 HTTs, and the remaining HTTs (7%) showed PAX8-GLIS1 gene fusion. Nikiforova *et al.* also noted that 220 PTCs revealed no PAX8-GLIS3 and one PTC showed PAX8-GLIS1 fusion.[15]

CONCLUSION

Because of its biological and clinical behavior, HTT or PLAT is often approached as a benign neoplasm. However, a meticulous look at aspiration cytology and histopathology need to be done to rule out papillary carcinoma. Other differential diagnoses like primary paraganglioma, medullary carcinoma and follicular adenoma should also be considered. Immunohistochemical markers help in cinching the diagnosis. Treatment is mostly surgery. Further studies are required to establish the clinical course and follow-up protocol for such cases.

REFERENCE

1. Bronner MP, LiVolsi VA, Jennings TA. PLAT: paragangliomalike adenomas of the thyroid. Surg Pathol 1988; 1: 383-9. 2.
2. Smith NR, Bullock MJ, Hart RD, *et al.* Hyalinizing trabecular tumour: review and new insights into the molecular biology. Otolaryngol Head Neck Surg. 2012;41(1):30-34.
3. Carney JA, Ryan J, Goellner JR. Hyalinizing trabecular adenoma of the thyroid gland. Am J Surg Pathol 1987; 11: 583-91.
4. Casey MB, Sebo TJ, Carney JA. Hyalinizing trabecular adenoma of the thyroid gland: cytologic features in 29 cases. Am J Surg Pathol. 2004;28:859-867.
5. Cheung CC, Boerner SL, MacMillan CM, *et al.* Hyalinizing trabecular tumor of the thyroid: a variant of papillary carcinoma proved by molecular genetics. Am J Surg Pathol. 2000;24:1622-1626.
6. Ertan Y, Makay Ö, Veral A, Tamsel S, İçöz G, Tunçyürek M. Hyalinizing trabecular tumor of the thyroid. *Turk Patoloji Derg.* 2009;25:44–46. doi: 10.5146/tjpath.2009.00971.
7. DeLellis RA, Lloyd RV, Heitz PU, Eng C, editors. *Pathology and Genetics of Tumours of Endocrine Organs.* Lyon: IARC Pres; 2004. World Health Organization Classification of Tumours.
8. Lester DR, Thompson MD. Hyalinizing trabecular adenoma of the thyroid gland. *Ear Nose Throat J.* 2011;90:416–417
9. Gowrishankar S, Pai SA, Carney JA. Hyalinizing trabecular carcinoma of the thyroid gland. *Histopathology.* 2008;52:529–531. doi: 10.1111/j.1365-2559.2008.02945.x.
10. Yu BH, Sheng WQ, Wang J. Primary paraganglioma of thyroid gland: a clinicopathologic and immunohistochemical analysis of three cases with a review of the literature. Head Neck Pathol. 2013 Dec;7(4):373-80. doi: 10.1007/s12105-013-0467-7
11. Ergün S, Akıncı O, Öztürk T, Karataş A. Hyalinizing trabecular tumor of the thyroid gland. Turk J Surg. 2018 Jan 3;34(2):149-151. doi: 10.5152/UCD.2017.3221
12. Hirokawa M, Shimizu M, Manabe T, Kuroda M, Mizoguchi Y (1995) Hyalinizing trabecular adenoma of the thyroid: its unusual cytoplasmic immunopositivity for MIB1. *Pathol Int* 45: 399–401.
13. Lee S, Han BK, Ko EY, Oh YL, Choe JH, *et al.* (2011) The ultrasonography features of hyalinizing trabecular tumor of the thyroid are more consistent with its benign behavior than cytology or frozen section readings. *Thyroid* 21: 253–259.
14. Ito Y, Hirokawa M, Kousaka K, Ito M, Kihara M, Miya A, Miyauchi A. Diagnosis and management of hyalinizing trabecular tumor of the thyroid: a single-institution experience. Endocr J. 2021 Dec 28;68(12):1403-1409. doi: 10.1507/endocrj.EJ21-0143. Epub 2021 Jul 6. PMID: 34234050.
15. Nikiforova MN, Nikitski AV, Panebianco F, Kaya C, Yip L, *et al.* (2019) GLIS rearrangement is a genomic hall- mark of hyalinizing trabecular tumor of the thyroid gland. *Thyroid* 29: 161–173.