CASE REPORT

doi: 10.5455/medarh.2018.72.367-370
MED ARCH. 2018 OCT; 72(5): 367-370
RECEIVED: AUG 14, 2018 | ACCEPTED: SEP 19, 2018

Rare Occurrence of Incidental Finding of Noninvasive Follicular Thyroid Neoplasm With Papillary–Like Nuclear Features in Hürthle Cell Adenoma

Biserka Pigac[1], Silvija Masic[2], Zdenka Hutinec[3], Valentina Masic[4]

[1]Pathology, Cytology and Forensic Medicine Unit, Varazdin General Hospital, Varazdin, Croatia

[2]Clinical Department of Pathology and Cytology "Ljudevit Jurak", University Hospital Centre Sestre Milosrdnice, Zagreb, Croatia

[3]Department of Pathology, University Hospital Centre Zagreb, Zagreb, Croatia

[4]Faculty of Education and Rehabilitation Sciences, University of Zagreb, Zagreb, Croatia

Corresponding author: Silvija Masic, MD, PhD. Clinical Department of Pathology and Cytology "Ljudevit Jurak", University Hospital Centre Sestre Milosrdnice, Vinogradska cesta 29, 10000 Zagreb, Croatia. Phone: +385 01 37 87 907, Fax: +385 1 37 87 244, ORCID ID: 0000-0003-2261-3329. E- mail: silvijamasic57@gmail.com

ABSTRACT

Introduction: Hürthle cell adenoma is a rare benign lesion of the thyroid gland, however, controversies about its potential malignant behavior still remain. Among thyroid neoplasms, papillary carcinoma is the most common variant with great variety of histological subtypes demonstrating different biological behavior. **Aim:** To raise the awareness of possible coexistence of these two lesions and discussion about possible therapeutic approaches. **Case report:** A 42 year old female patient was examined because of the pain in the thyroid area. Cytological examination suggested Hürthle cell adenoma. Subsequently, right thyroid lobectomy was performed. Intraoperative frozen sections confirmed the diagnosis, yet final histological analysis revealed encapsulated follicular variant of papillary thyroid carcinoma (EFVPTC), now reclassified as noninvasive follicular thyroid neoplasm with papillary- like nuclear features (NIFTP) within the adenoma, which was not noticed through scintigraphy, ultrasound, cytological and frozen section analysis. **Conclusions:** Problems concerning both diagnostic and therapeutic approach to these lesions are being discussed, since opinions reported in the literature are divided, posing great challenge for the clinician in determining adequate therapeutic procedures.

Keywords: Hürthle cell adenoma, thyroid, papillary cell carcinoma, NIFTP.

1. INTRODUCTION

Hürthle cell adenoma is defined as a rare, benign thyroid neoplasm composed of oncocytic cells (Hürthle cells) that comprise more than 75% of adenoma cell population. Despite characterization of this lesion as a benign one, controversy considering its behavior exists, since literature reports cases exhibiting behavior common for malignant lesions (1). Papillary carcinoma is the most frequently encountered thyroid gland malignancy including different histologic variants (2) with different patterns of biological behavior (2). Hürthle cell adenoma with papillary carcinoma arising within, represents rare, but clinically important finding (3, 4), due to different opinions considering therapeutical approach to these two lesions. We describe a case of a female patient with noninvasive follicular thyroid neoplasm with papillary- like nuclear features (NIFTP), formerly named encapsulated follicular subtype of papillary thyroid carcinoma (EFVPTC) in Hürthle cell adenoma and emphasize problems in both diagnostic and treatment process. To the best of our knowledge, no cases of this carcinoma subtype arising in Hürthle cell adenoma have been reported in the literature. Also, the paper aims to raise the awareness of possible coexistence of these two lesions and provides discussion about possible therapeutic approaches.

2. CASE REPORT

Due to constant pain in the thyroid gland area, a 42 year- old female patient was referred to otolaryngologist. She has so far had no medical problems. Physical neck examination revealed slightly enlarged and painful thyroid gland. Ultrasound demonstrated both thyroid lobes to be enlarged, with dimensions of the left lobe: 1,5 x 1,8 x 5,5 cm, yet the right lobe appeared to be more enlarged measuring 2,2 x 1,8 x 5,7 cm. Also, in the upper half of the left lobe, an oval hypoechoic structure, 0.8 cm in its largest diameter was observed,

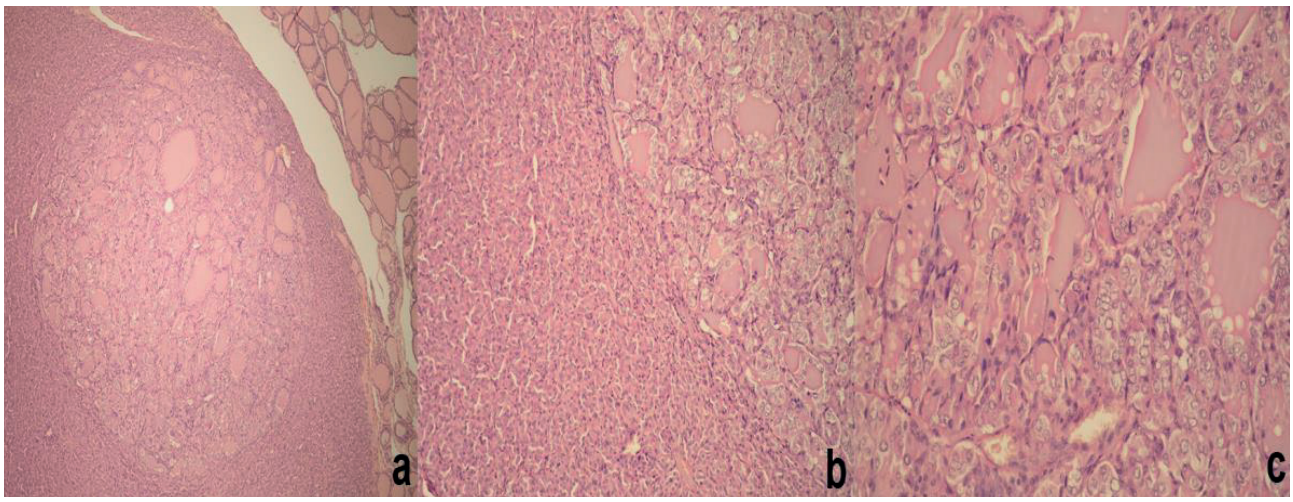

Figure 1. a) Noninvasive follicular thyroid neoplasm with papillary- like nuclear features in Hürthle cell adenoma (H&E, objective x 4), b) and c) Oncocytic cells of Hürthle cell adenoma and well- demarcated, noninvasive follicular thyroid neoplasm with papillary–like nuclear features composed of multiple variably sized follicle cells lined with enlarged nuclei demonstrating cytologic features of papillary carcinoma (H&E, objective x 10, 20)

while in the lower half of the right thyroid lobe, partially hypoechoic oval structure, also being warm nodule on scintigraphy, 0.8 cm in diameter was found. After her initial visit to the specialist, the patient decided not to do more tests. Since the pain continued, she returned 4 years later for further examination. Subsequent results of laboratory analysis demonstrated normal values of: thyroid stimulating hormone (0.53 mIU/L), free T4 (14.46 pmol/L) and free T3 (4.73 pmol/L). Right lobe nodule was now measuring 1 cm, while the left lobe had a cyst 1,3 cm in size. Cytological examination of the right lobe lesion revealed Hürthle cells without signs of atypia, so the patient was prepared for right thyroid lobectomy. Intraoperatively, a segment of thyroid gland tissue, 6 cm in diameter was sent for frozen section consultation. On the cut surface, a nodule measuring 1 cm was observed and microscopically determined as Hürthle cell adenoma. From the remaining tissue, routine hematoxylin and eosin sections were done and revealed the tumor composed of large follicular cells with abundant granular and eosinophilic cytoplasm, round nuclei and prominent nucleoli, in concordance with the intraoperative diagnosis, yet inside the adenoma, a tumor 2 mm in diameter, comprised of different sized multiple thyroid follicles filled with hypereosinophilic colloid and lined by cells with optically clear, overlapping nuclei was found. Also, the tumor was sharply demarcated from the surrounding adenoma by thick fibrous capsule, suggesting diagnosis of NIFTP in Hürthle cell adenoma (Figure 1a, b and c). Thyroid capsule was intact, without any signs of invasion by Hürthle cells or papillary carcinoma cells. Also, no vascular invasion was seen. Postoperative course was uneventful. According to the fact that both Hürthle cell adenoma and papillary carcinoma were found, total thyroidectomy was done, without no signs of malignancy in the additionally removed thyroid tissue. Scintigraphy demonstrated no signs of metastasis. Also, the patient will be regularly monitored.

3. DISCUSSION

Hürthle cells are oncocytic cells characteristic for their abundant granular cytoplasm due to large amount of intracytoplasmic mitochondrias and are considered to be the type of epithelial follicular cells (1). Cytoplasmic mitochondrial accumulation occurs because of changes in mitochondrial DNA that encodes for enzymes, which results in stimulation of transcription factors (5). Hürthle cells can be seen in benign conditions, such as adenomas and Hashimoto's thyroiditis, but also in malignant thyroid lesions, which poses difficulties in determining the proper diagnosis (1, 6). Further more, fine- needle aspiration analysis is often unreliable in distinguishing Hürthle cell lesions, especially from papillary carcinoma, particularly follicular or cystic variants, since they demonstrate abundant granular cytoplasm and nuclear crowding lack (7). Pathohistological examination is more reliable in distinguishing adenoma from Hürthle cell hyperplasia (75% or more Hürthle cells in the lesion are in favor of adenoma). Also, the difference between Hürthle cell adenoma and Hürthle cell carcinoma can be determined by the pathologist, since capsular, vascular or peri-thyroid invasion suggest malignancy together with lymph node and distant metastasis (1, 5). Although being considered benign, some reports in the literature suggest that Hürthle cell tumors have malignant potential, that criteria for differentiating adenoma from carcinoma are uncertain and therefore, any Hürthle cell lesion should be treated by performing total thyroidectomy (1, 8). However, there are opinions on treating Hürthle cell adenoma only by performing lobectomy with later continuous patient follow- up. These consider complete thyroid removal necessary only in cases of carcinoma (6, 8). Malignancy found in our patient can be considered as incidental thyroid carcinoma, which represents tumor that is accidentally found during thyroid surgery and confirmed by final pathohistological examination. However, only tumors with diameter smaller than 1 cm can be considered as incidental carcinomas (9). Their treatment is still controversial. Maturo et al consider to-

tal thyroidectomy necessary, since those tumors are usually related to multifocal and bilateral appearance and occult lymph node metastasis and therefore should be treated as common thyroid cancer. On the other hand, some authors consider conservative surgical approach to be sufficient (9). Papillary thyroid carcinoma is the most common thyroid malignancy (10) and is found in various histological patterns without firm criteria for subtypes definition (2). Most common subtypes include classic and follicular variant, while others include tall cell, papillary microcarcinoma, oncocytic, columnar cell, diffuse sclerosing, clear cell, cribriform-morular, macrofollicular, solid, papillary thyroid carcinoma with prominent hobnail, with dedifferentiation to anaplastic carcinoma features variant (2). Tall cell and columnar cell variant exhibit more aggressive behavior (2). Follicular subtype of papillary carcinoma is second most often seen type of this carcinoma after classic one (10) and can be recognized by the presence of follicles, which are lined by cells with nuclear features of papillary carcinoma (nuclear clearing, pseudoinclusions, overlapping, grooves) (11). Incidence of this variant is 9 to 22.5% of cases with papillary thyroid carcinoma (10). In our case, the patient had encapsulated, noninvasive follicular variant of papillary carcinoma, now classified as noninvasive follicular thyroid neoplasm with papillary- like nuclear features (NIFTP). Criteria for the diagnosis of this type include: encapsulation or clear demarcation from the surrounding tissue, follicular tumor growth, nuclear features characteristic for papillary thyroid carcinoma, complete capsular visualization, no vascular or capsular invasion (11, 12). Controversies in treating this type exist, with some authors considering only lobectomy necessary (13). It is currently believed that this variant is biologically indolent, so the reclassification was performed in order to reduce overtreatment of patients since in most cases this type is treated as classic variant of papillary carcinoma (14). However, opinions that this subtype should be more seriously treated exist, for example Baloch et al. reports a case of EFVPTC with distant metastasis (13, 15). In most cases, follicular variant behaves as classic variant of papillary thyroid carcinoma and demonstrates similar prognostic outcome (16). NIFTP is now considered a low- risk thyroid neoplasm which still can exhibit malignant behavior and requires patient follow- up (17). Papillary carcinoma usually has very good prognosis, so the patients with disease limited to the thyroid gland have five year survival around 99.7%, cases with metastasis to regional lymph nodes 96.9% and those with distant metastasis 57.8% (18). Survival rates become smaller with larger tumor size and extrathyroid spread (18). Lethal outcome usually occurs due to distant metastasis, death occurs in around 10% of patients, 20–90 % experience carcinoma lymph nodes metastasis and up to 30 % of patients end up with disease relapse (19). Indicators of poor prognosis are lateral compartment lymph node metastasis, extrathyroidal disease and distant metastasis (20), but also male gender, larger size of the tumor and advanced age at the time of the diagnosis establishment (21). The most important therapeutical method for papillary carcinoma is surgery, whose extent is determined by performing preoperative ultrasound, fine–needle aspiration biopsy and intraoperative frozen sections (18).

4. CONCLUSION

To sum up, problems regarding diagnostic and therapeutic approach to Hürthle cell adenoma, certain variants of thyroid carcinoma, reliability of diagnostic procedures and treatment certainly exist and we are facing great responsibility in the process of deciding which option is the best for our patients. Also, when deciding on possible therapeutic measurements, benefits and possible negative outcomes should be considered. Clinician should decide on treatment based on disease staging and also consider that more aggressive variants are associated with more expressed risk factors (22). We consider cooperation between pathologist and clinician essential for optimal patient treatment.

- **Authors contribution:** BP–conception, design, acquisition of data, analysis, interpretation of data, revising, final approval of the version; SM–design, acquisition of data, interpretation of data, drafting the article, revising, final approval of the version; ZH–acquisition of data, analysis, interpretation of data, revising, final approval of the version; VM–acquisition of data, analysis, interpretation of data, revising, final approval of the version.
- **Conflict of interest:** none declared.

REFERENCES

1. Barnabei A, Ferretti E, Baldelli R, Procaccini A, Spriano G, Appetecchia M. Hürthle cell tumours of the thyroid. Personal experience and review of the literature. Acta Otorhinolaryngol Ital. 2009; 29(6): 305-311.
2. Lloyd RV, Buehler D, Khanafshar E. Papillary thyroid carcinoma variants. Head Neck Pathol. 2011; 5(1): 51-56. doi: 10.1007/s12105-010-0236-9.
3. Kim YJ, Hong HS, Jeong SH, Lee EH, Kwak JJ. Papillary thyroid carcinoma arising within a follicular adenoma: a case report, ultrasound features, and considerations. Ultrasound Q. 2017; 33(1): 62-65. doi: 10.1097/RUQ.0000000000000235.
4. Ono JC, Wilbur DC, Lee H, Yang J, Krane JF, Bongiovanni M, et al. Cytologic features of focal papillary thyroid carcinoma arising within follicular adenoma: a masked cytomorphologic analysis of 17 cases. Acta Cytol. 2011; 55(6): 531-538. doi: 10.1159/000333240.
5. Cannon J. The significance of Hürthle cells in thyroid disease. Oncologist 2011; 16(10): 1380-1387. doi: 10.1634/theoncologist. 2010-0253.
6. Stanciu M, Bera LG, Popescu M, Grosu F, Popa FL. Hashimoto's thyroiditis associated with thyroid adenoma with Hürthle cells–case report. Rom J Morphol Embryol. 2017; 58(1): 241-248.
7. Renshaw AA. Fine-needle aspirations of papillary carcinoma with oncocytic features: an expanded cytologic and histologic profile. Cancer Cytopathol. 2011; 119(4): 247-253. doi: 10.1002/cncy.20148.
8. Wasvary H, Czako P, Poulik J, Lucas R. Unilateral lobectomy for Hürthle cell adenoma. Am Surg. 1998; 64(8): 729-732.
9. Maturo A, Tromba I, De Anna L, Carbotta G, Livadoti G, Donello C, et al. Incidental thyroid carcinomas. A retrospective

study. G Chir. 2017; 38(2): 94-101.
10. Gupta S, Ajise O, Dultz L, Wang B, Nonaka D, Ogilvie J, et al. Follicular variant of papillary thyroid cancer. Encapsulated, nonencapsulated, and diffuse: distinct biologic and clinical entities. Arch Otolaryngol Head Neck Surg. 2012; 138(3): 227-233. doi: 10.1001/archoto.2011.1466.
11. Mainthia R, Wachtel H, Chen Y, Mort E, Parangi S, Sadow PM, et al. Evaluating the projected surgical impact of reclassifying noninvasive encapsulated follicular variant of papillary thyroid cancer as noninvasive follicular thyroid neoplasm with papillary-like nuclear features. Surgery. 2018; 163(1) :60–65. doi: 10.1016/j.surg.2017.04.037.
12. Hirokawa M, Higuchi M, Suzuki A, Hayashi T, Kuma S, Miyauchi A. Noninvasive follicular thyroid neoplasm with papillary-like nuclear features: a single-institutional experience in Japan. Endocr J. 2017; 64(12): 1149-1155. doi: 10.1507/endocrj.EJ17-0214.
13. Ghossein R. Problems and controversies in the histopathology of thyroid carcinomas of follicular cell origin. Arch Pathol Lab Med. 2009; 133(5): 683-691. doi: 10.1043/1543-2165-133.5.683.
14. Range DE, Jiang XS. An update on noninvasive follicular thyroid neoplasm with papillary-like nuclear features. Curr Opin Oncol. 2018; 30(1): 1-7. doi: 10.1097/CCO.0000000000000416.
15. Baloch ZW, LiVolsi VA. Encapsulated follicular variant of papillary thyroid carcinoma with bone metastases. Mod Pathol. 2000; 13(8): 861–865.
16. Yoon JH, Kwon HJ, Kim EK, Moon HJ, Kwak JY. The follicular variant of papillary thyroid carcinoma: characteristics of preoperative ultrasonography and cytology. Ultrasonography. 2016; 35(1): 47-54. doi: 10.14366/usg.15037.
17. Parente DN, Kluijfhout WP, Bongers PJ, Verzijl R, Devon KM, Rotstein LE, et al. Clinical Safety of Renaming Encapsulated Follicular Variant of Papillary Thyroid Carcinoma: Is NIFTP Truly Benign? World J Surg. 2018; 42(2): 321-326. doi: 10.1007/s00268-017-4182-5.
18. Sojak J, Sičák M, Kališ A, Slašťan M. Papillary thyroid carcinoma: analysis of the central compartment's lymph nodes metastases. Acta Medica (Hradec Králové). 2017; 60(1): 44-50. doi: 10.14712/18059694.2017.49.
19. Serag Eldien MM, Gaber Abdou A, Rageh T, Abdelrazek E, Elkholy E. Immunohistochemical expression of ER-α and PR in papillary thyroid carcinoma. Ecancermedicalscience. 2017; 11: 748-758. doi: 10.3332/ecancer.2017.748.
20. Girardi FM, Barra MB, Zettler CG. Variants of papillary thyroid carcinoma: association with histopathological prognostic factors. Braz J Otorhinolaryngol. 2013; 79(6): 738-744. doi: 10.5935/1808-8694.20130135.
21. LiVolsi VA. Papillary thyroid carcinoma: an update. Mod Pathol. 2011; 24(2): 1-9. doi: 10.1038/modpathol.2010.129.
22. Silver CE, Owen RP, Rodrigo JP, Rinaldo A, Devaney KO, Ferlito A. Aggressive variants of papillary thyroid carcinoma. Head Neck. 2011; 33(7): 1052-1059. doi: 10.1002/hed.21494.