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# The oncocytic variant of papillary thyroid carcinoma with multifocal involvement: a case report

## Multifokal tutulumlu papiller tiroid karsinomunun onkositik varyantı: Olgu sunumu

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The oncocytic variant of papillary thyroid carcinoma is an uncommon form of neoplasm, the clinicopathological features and biological behavior of which have not been precisely defined. The pattern of multifocal growth is an uncommon feature. The case was a 64-year-old female patient with multinodular goiter who had undergone total thyroidectomy. Microscopic examination of cross-sections of the multiple nodules revealed a tumoral lesion characterized by a predominant follicular growth pattern, and sparse, small, abortive papillary structures. Most of the tumor cells also displayed the classical nuclear features of papillary carcinoma, like optically clear nuclei, overlapping of the nuclei, irregular nuclear membranes, and sparse nucleoli. Prominent nuclear grooves and intranuclear pseudoinclusions were seen in many of the neoplastic cells. Due to the presence of the characteristic nuclear features, the diagnosis was papillary carcinoma. The oncocytic variant of papillary carcinoma, although rare, appears to represent a morphologically distinctive variant of papillary cancer.

**Key words:** Multifocal pattern; oncocytic variant; papillary thyroid carcinoma.

Papiller tiroid karsinomunun onkositik varyantı, klinikopatolojik özellikleri ve biyolojik davranışı tam olarak tanımlanmamış nadir bir neoplazmdır. Multifokal büyüme paternide yaygın olmayan bir özelliktir. Bu olgu total tiroidektomi uygulanan multinoduler guatrlı 64 yaşında kadın hastadır. Multipl nodüllerinden hazırlanan kesitlerinin mikroskopik incelenmesinde, belirgin foliküler büyüme paterni ve abortif, küçük ve seyrek papiller yapılar ile karakterize tümöral lezyon izlendi. Tümör hücrelerinin çoğu, berrak nukleus, *overlapping* nukleus, düzensiz nükleer membran ve seyrek nükleol gibi papiller karsinomun klasik nükleer özelliklerini göstermekte idi. Belirgin nükleer *groove* ve intranükleer psödoinklüzyonlar neoplastik hücrelerin çoğunda görülmektedir. Karakteristik nükleer özelliklerin varlığı nedeniyle papiller karsinom tanısı verildi. Papiller tiroid karsinomun onkositik varyantı, nadir görülmesine rağmen, papiller kanserin morfolojik olarak farklı bir varyantını temsil ettiği düşünülmektedir.

**Anahtar sözcükler:** Multifokal patern; onkositik varyant; papiller tiroid karsinomu.

Papillary carcinoma (PC) is the most common primary malignant neoplasm of the thyroid gland. PC is a tumor, displaying evidence of follicular cell differentiation and characterized by distinctive nuclear features. Several morphological variants of PC have been recognized based on the architecture, growth pattern, cellular, and stromal features.[1-4] The recognition of these variants depends on clinical course, because some of them are associated with a more aggressive behavior, such as diffuse sclerosing, tall cell, and columnar cell variants.[2-4] The oncocytic variant of PC of the thyroid represents a relatively unusual neoplasm in which clinicopathological features and biological behavior have not yet been thoroughly characterized.[1-4]

Oncocytic change is defined as cellular enlargement characterized by an abundant eosinophilic granular cytoplasm due to accumulation of mitochondria.[1-6] Various designations including oncocytes, Hurthle cells, Askanazy cells, oxyphilic or large cells, have been used for these elements.

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[1,3,4,6,7] Oncocytes are generally regarded as functional variants of follicular epithelial cells due to evidence of thyroglobulin immunoreactivity.[6-8] Oncocytic change in thyroid follicular cells is a morphologically distinctive phenomenon that can take place in a variety of pathological conditions, including inflammatory/autoimmune processes (Hashimoto's thyroiditis), and benign and malignant neoplasms (Askanazy/Hurthle cell adenoma and carcinoma, medullary carcinoma).[2-6,9,10]

We believe that it is important to distinguish this variant of PC from other oncocytic thyroid neoplasms because of its different biological and prognostic implications, and we described a rare variant of oncocytic PC of the thyroid, designated with pattern of multifocal growth.

## CASE REPORT

A 64-year-old female patient with multinodular goitre, administrating medical treatment for hyperthyroidism for four years, with very high thyroglobulin levels underwent total thyroidectomy. During gross examination, nodular structures were observed in both of the lobes and isthmuse. The cut surfaces of nodules of right lobe were white to tan-yellow, finely granular, and focally hemorrhagic. Nodules of left lobe and isthmuse were bright and rich in colloid. Microscopic examination of cross sections of the multiple nodules of the right lobe revealed a tumoral lesion characterized by a predominant follicular growth pattern containing dens colloid within the follicles (Fig. 1), and sparse, small, abortive papillae were identified on extensive search (Fig. 2). Both the papillary and follicular structures were composed of large polygonal cells with abundant pink and granular cytoplasm which are characteristic properties of oncocytes (Fig. 3). Most of the tumor cells also displayed the classical nuclear features of papillary carcinoma, like optically clear nuclei, overlapping of the nuclei, irregular nuclear membranes, and seldom nucleoli. Prominent nuclear grooves and intranuclear pseudoinclusions were seen in many of the neoplastic cells (Fig. 4). Very low number of mitosis was encountered in the tumor. No psammoma bodies were seen in the tumor. Areas of calcifications were detected in the tumor. No blood vessel invasion was observed. The surrounding thyroid parenchyma denoted the features of hyperplastic thyroid and focal peritumoral lymphocytic thyroiditis. The tumor was observed in surgical borders. The immunohistochemical reactions, pankeratin and cytokeratin-19 (Fig. 5) and thyroglobulin (Fig. 6) were positive for this tumor. Due to the presence of the characteristic nuclear features, the diagnosis was oncocytic variant of PC of the thyroid with the pattern of multifocal growth.

## CONCLUSION

Oncocytic or Hurthle cell tumors are rare thyroid neoplasms of follicular cell origin.[6-11] Oncocytic cell tumors of the thyroid include adenomas and carcinomas which are characterized by a predominant (usually more than 75% of the tumor area) population of eosinophilic mitochondrion-rich cells. They may be separated into oncocytic cell adenomas and oncocytic cell carcinomas. Recently, oncocytic variant of PC has also been described.[6-12]

In the most recent World Health Organization International Histological Classification of Thyroid Tumors, Hedinger and colleagues have defined papillary thyroid carcinoma as "a malignant epithelial tumor showing evidence of follicular cell differentiation, with typical papillary and follicular structures as well as characteristic nuclear changes".[2,3,12] This variant accounts for 1-11% of all cases of thyroid PC; the differences among reported series are probably result of application of different classification criteria.[1,12] Furthermore, histopathological criteria for diagnosis and biological behavior of the oncocytic variant of PC have remained poorly defined.[1,7]

The diagnosis of oncocytic variant of PC remains controversial. Oncocytic PCs may have papillary or follicular architecture. The papillary type is characterised by complex branching papillae in which oncocytic cells cover thin fibrovascular stromal cores. Oncocytic PC with follicular architecture may be macrofollicular or microfollicular with variable colloid storage. The oncocytic cells are usually polygonal but may be columnar; they have abundant granular, pale, eosinophilic cytoplasm. The diagnosis of papillary differentiation is based on the nuclear features of these lesions. Berho and Suster proposed that the diagnosis of oncocytic PC

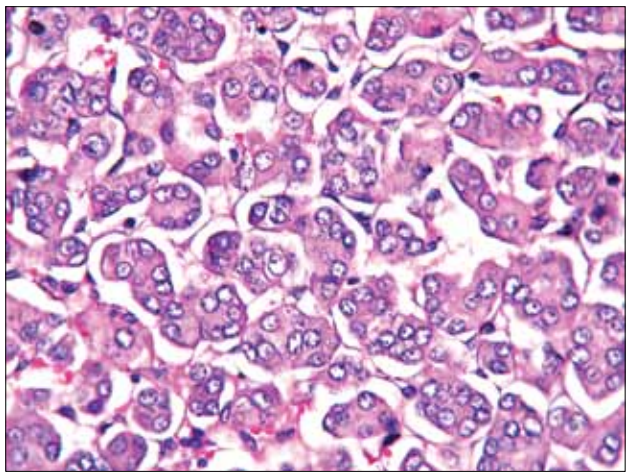

**Fig. 1.** Follicular growth pattern in oncocytic variant of papillary thyroid carcinoma (H-E x 200).

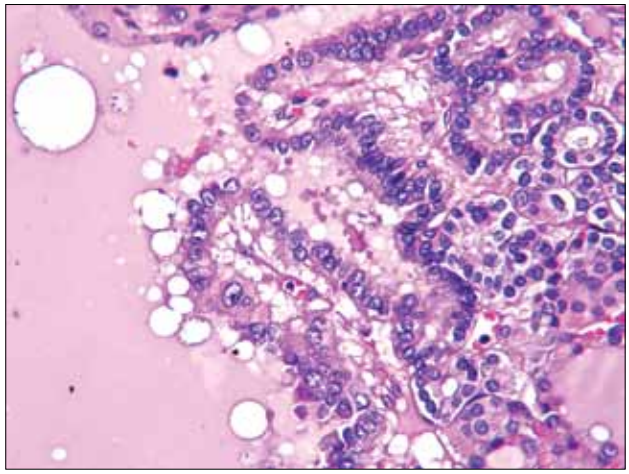

**Fig. 2.** Complex branching papillae in oncocytic variant of papillary carcinoma (H-E x 400).

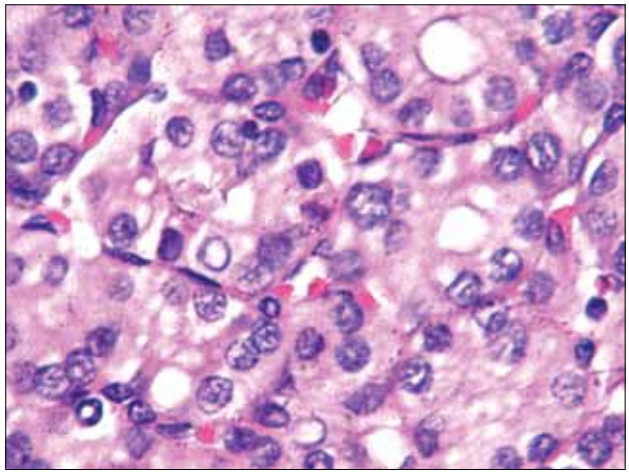

**Fig. 3.** Papillary carcinoma with oncocytes characterized with abundant pink and granular cytoplasm (H-E x 400).

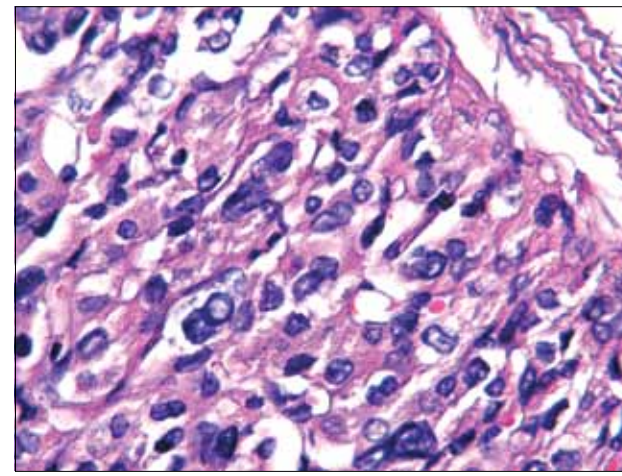

**Fig. 4.** Nuclear features of papillary carcinoma: clear nuclei and nuclear grooves (H-E x 400).

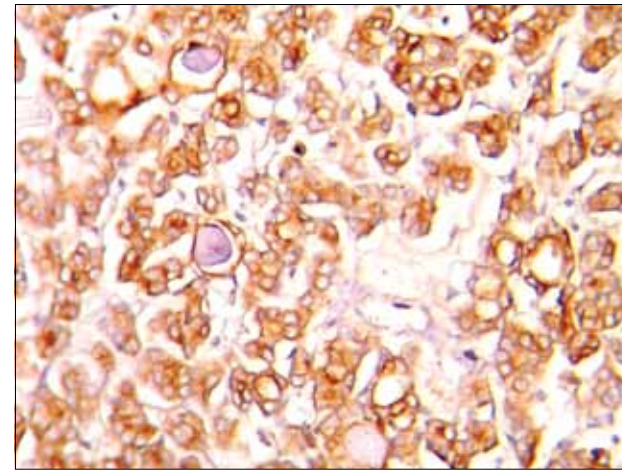

**Fig. 5.** The expression of cytokeratin-19 in papillary carcinoma (B-SA, DAB, x 400).

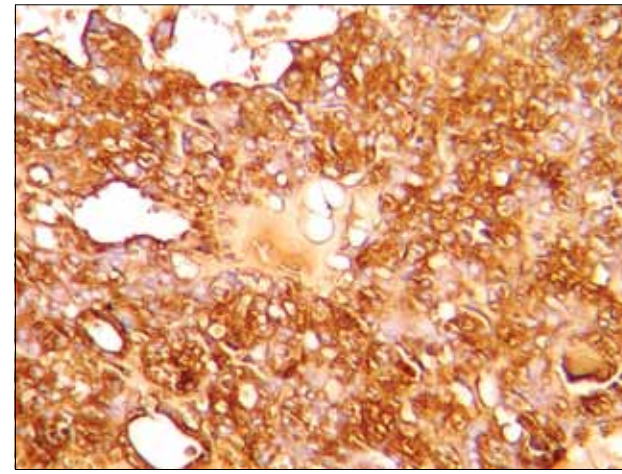

**Fig. 6.** Thyroglobulin immunoreactivity in oncocytic variant of papillary carcinoma (B-SA, DAB, x 400).

should be based primarily on nuclear features like the typical optically clear nuclei with the characteristic intranuclear cytoplasmic inclusions and the presence of nuclear grooves. These features are currently attributed to be more important than the presence of papillae as diagnostic criteria for PC.[2-8,12] The nuclear features determined in our case supported the diagnosis of oncocytic PC. It is important to identify these features in well delineated lesions with follicular architecture.[2,5,8,12]

Recently, an unusual oncocytic PC partly cystic type with abundant lymphoid stroma, that is bearing a resemblance to "Warthin's tumor of salivary gland" has been described.[1,5] The "Warthin-like" tumor has abundant chronic inflammatory cells and is freguently associated with Hashimoto's thyroiditis.[1-3] The extensive lymphocytic infiltration in oncocytic PC and their association with chronic lymphocytic thyroiditis, may suggest the role of immunological mechanisms in the pathogenesis of thyroid tumors,[1,2,7] rather than the expression of the inherent biological characteristics of the tumor cells.[2] There was focal peritumoral lymphocytic thyroiditis in our case. In addition to these findings, we designeted the pattern of multifocal growth which is actually rarely encountered.[4]

The reported clinical behavior of oncocytic tumors is variable. In the 1950s, the American Cancer Society recommended to classify all thyroid tumors with oncocytic features as malignant. Since then, most studies have indicated that oncocytic neoplasm can be classified into adenomas and carcinomas by using the morphological criteria that is valid for follicular non-oncocytic tumors.[1,5,12] The overall mortality rate of oncocytic carcinoma (both follicular and papillary) was said to be considerably higher than that of non-oncocytic tumors.[1,6,9,12] Herrera et al. defined that oncocytic variant of PC should be more widely recognized as a tumor variant with a truly more aggressive biologic behavior as confirmed in previous studies.[12] On the contrary, Berho and Suster believed that these lesions appeared to have a low-grade clinical behavior akin to conventional PC.[2] The study of Cheung et al, which depends on molecular basis of Hurthle cell PC, indicated that this tumor may behave in a fashion analogous to typical PC.[7]

The oncocytic variant of papillary thyroid carcinoma, although rare, appears to represent a morphologically distinctive variant of papillary cancer. Application of strict histological criteria is therefore necessary to distinguish these lesions from other primary thyroid neoplasms that is characterized by similar oncocytic cytoplasmic features.[2,7,12] Further research is needed for the management of oncocytic variant of papillary carcinoma of the thyroid.

## REFERENCES


1. Ludvíková M, Ryska A, Korabecná M, Rydlová M, Michal M. Oncocytic papillary carcinoma with lymphoid stroma (Warthin-like tumour) of the thyroid: a distinct entity with favourable prognosis. Histopathology 2001;39(1):17-24.
2. Berho M, Suster S. The oncocytic variant of papillary carcinoma of the thyroid: a clinicopathologic study of 15 cases. Hum Pathol 1997;28(1):47-53.
3. LiVolsi VA, Albores-Saavedra J, Asa SL, Baloch ZW, Sobrinho-Simões M, Wenig B, et al. Papillary carcinoma. In: DeLellis RA, Lloyd RV, Heitz PU, Eng C, editors. World Health Organization Classification of Tumours. Pathology and genetics of tumours of endocrine organs. Lyon: IARC Press; 2004. p. 57-66.
4. Rosai J. Thyroid gland. In: Rosai J, editor. Rosai and Ackerman's Surgical Pathology. 9th ed. China: Mosby; 2004. p. 515-94.
5. Asa SL. My approach to oncocytic tumours of the thyroid. J Clin Pathol 2004;57(3):225-32.
6. Flint A, Lloyd RV. Hürthle-cell neoplasms of the thyroid gland. Pathol Annu 1990;25:37-52.
7. Cheung CC, Ezzat S, Ramyar L, Freeman JL, Asa SL. Molecular basis off hurthle cell papillary thyroid carcinoma. J Clin Endocrinol Metab 2000;85(2):878-82.
8. Stojadinovic A, Ghossein RA, Hoos A, Urist MJ, Spiro RH, Shah JP, et al. Hürthle cell carcinoma: a critical histopathologic appraisal. J Clin Oncol 2001;19(10):2616-25.
9. Volante M, Bozzalla-Cassione F, DePompa R, Saggiorato E, Bartolazzi A, Orlandi F, et al. Galectin-3 and HBME-1 expression in oncocytic cell tumors of the thyroid. Virchows Arch 2004;445(2):183-8.
10. Yutan E, Clark OH. Hürthle cell carcinoma. Curr Treat Options Oncol 2001;2(4):331-5.
11. Hanief MR, Igali L, Grama D. Hürthle cell carcinoma: diagnostic and therapeutic implications. World J Surg Oncol 2004;2:27.
12. Herrera MF, Hay ID, Wu PS, Goellner JR, Ryan JJ, Ebersold JR, et al. Hürthle cell (oxyphilic) papillary thyroid carcinoma: a variant with more aggressive biologic behavior. World J Surg 1992;16(4):669-75.