TÜBİTAK

CASE REPORT

Turk J Med Sci
2006; 36 (6): 387-392
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The Oncocytic Variant of Papillary Thyroid Carcinoma*

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Abstract: Papillary thyroid carcinoma (PTC) has many subtypes. A rare subtype consisting of papillary projections covered by cells oncocytic in character has been defined in recent years. Oncocytes with characteristic nuclear features of PTC are seen in the thyroid aspiration cytology of this subtype. In the cytological diagnosis, this variant could be confused with other oncocytic lesions of the thyroid.

We discuss here the cytological and histopathological features of the oncocytic variant of PTC diagnosed in the aspiration biopsy and thyroid resection material in a 42-year-old female patient.

Key Words: Papillary thyroid carcinoma, oncocytic variant, aspiration cytology, histopathology

Papiller Tiroid Karsinomu Onkositik Varyantı Bir Olgu Sunumu

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Özet: Papiller tiroid karsinomunun bir çok alttipi vardır. Son yıllarda onkositik karakterde hücreler ile döşeli papiller yapılardan ibaret olan nadir bir alt tip tanımlanmıştır. Tiroid aspirasyon sitolojisinde papiller tiroid karsinomunun karakteristik nükleer özelliklerine sahip onkositler görülmektedir. Sitolojik incelemede bu alt tip, tiroidin diğer onkositik lezyonları ile karışabilir.

Burada, 42 yaşındaki kadın hastada tanısı konan onkositik varyant papiller tiroid karsinomunun aspirasyon yaymalarındaki sitolojik özellikleri ve rezeksiyon materyalindeki histopatolojik özelliklerini tartışıyoruz.

Anahtar Sözcükler: Tiroid papiller karsinoma, onkositik varyant, aspirasyon sitolojisi, histopatoloji.

Introduction

The oncocytic variant of papillary thyroid carcinoma (oncocytic variant of PTC) is a very rare subtype of PTC. This variant has also been termed as Hürthle cell variant or oxyphilic variant. Although this variant has been known for about 35 years, it has not been sufficiently reported in the literature. Its biological behavior has been poorly defined because histological and cytological criteria have not been clearly determined for the diagnosis (1).

We report our case diagnosed as oncocytic variant of PTC on both cytological and histopathological bases, and we analyze the cytological and histopathological features of our case, with an accompanying review of the related literature.

Received: June 12, 2006
Accepted: December 07, 2006

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Case Report

A 42-year-old female patient was admitted with complaints of palpitation, sweating and swelling of the neck for two years. There was nothing remarkable in her family's medical history. In physical examination, asymmetry in the thyroid was noted. In addition, a mobile nodule with firm consistency involving both thyroid lobes was determined. The neck computerized tomography revealed the cystic lesion, 3x2x1.5 cm in size, as a centrally placed solid nodule in the isthmus. In addition, multiple bilateral cervical lymphadenopathies were determined. Fine needle aspiration biopsy performed on the cystic lesion revealed cellular, three-dimensional groups (Figure 1A). Some of these groups were papillary in character and others showed follicular organization. The

* This manuscript was presented as a poster at the 1st National Congress of Cytopathology, 2-5 March 2006, Antalya - TURKEY

cells had large, pleomorphic nuclei with rough chromatin. Also, bi-nuclei forms were rarely present in the smears. Intranuclear inclusions were extensive and some nuclei had prominent nucleoli (Figure 1B). These cells also had cytoplasm with oncocytic appearance. Foamy macrophages and mature lymphocytes were sparsely seen in the background. According to these cytological findings, the present case was evaluated as malignant thyroid tumor with prominent oncocytic cell changes.

The patient underwent bilateral total thyroidectomy and neck dissection. Thyroidectomy specimen was totally 14x9x4 cm in size. The right and left lobes could not be differentiated in the specimen due to distortion of the thyroid. Extensive nodulation in the thyroidectomy was present. In macroscopical examination, a nodule with firm consistency, 2.5x2x1.5 cm in size, was noted in the isthmus. The sections of this lesion also showed a cystic component, 1 cm in the longest diameter.,Punctuating calcified micropapillary structures were determined in the cystic component. Solid areas were brown, gray-whitish in appearance. The tumor was not well demarcated (Figure 2). The tumoral nodule was close to the peripheral surgical border. Eight lymph nodes were dissected from the paratracheal region during surgery. No lymph nodes were determined in the level III neck dissection specimen. In the microscopical examination, the tumor had extensively infiltrated to adjacent skeletal muscle, and adipose and fibrous tissues. Vascular-perineural invasions were extensively observed in the tumor. Papillary projections were noted in some areas,

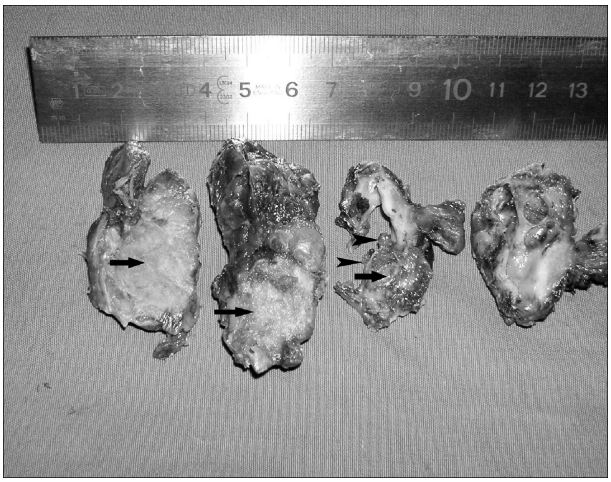

Figure 2. Gross appearance of the tumor consisting of solid brownish areas with indistinct borders (arrows) and cystic component with intracystic papillary structures (arrowheads).

especially as intracystic (Figure 3A). Papillary stalks were covered with oncocytic cells with characteristic nuclear features of PTCs. Nuclear features frequently observed were optically clear nuclei, nuclear grooves, chromatin clumping and nuclear crowding (Figure 3B). Intranuclear inclusions in the tumor were noted to a lesser degree. Papillary stalks were mostly present in the cystic component. The tumor had mostly follicular and microfollicular organization. Microfollicular areas were usually infiltrative pattern. All neoplastic follicles also lined by cells showed characteristic nuclear features of PTC and the cytoplasms of these cells were also oncocytic

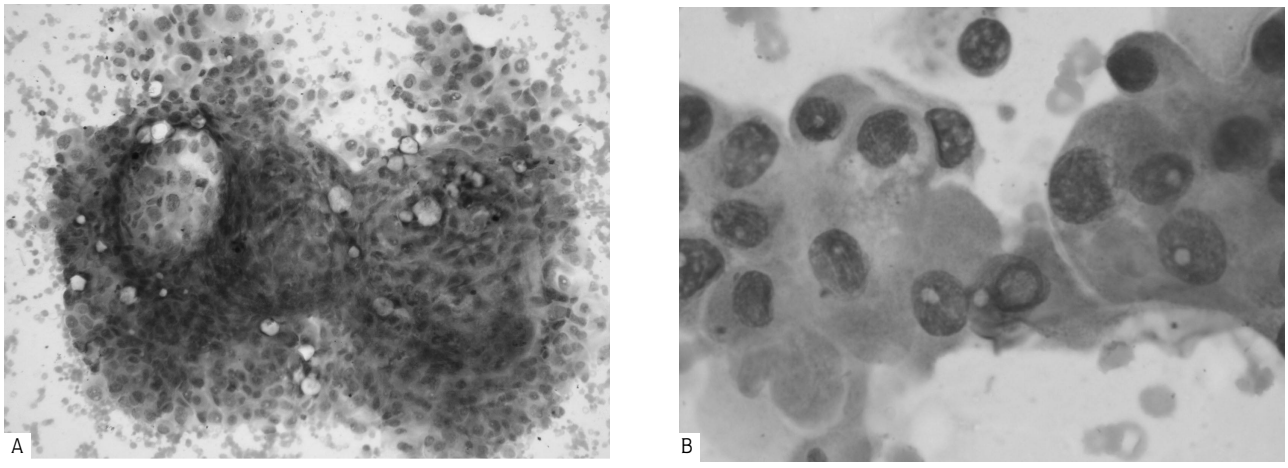

Figure 1. A) The three-dimensional cell cluster in thyroid aspiration smears (MGG, X40).
B) The atypical thyrocytes with large cytoplasm in oncocytic character and pleomorphic, large nucleus with coarse chromatin pattern in aspiration smears. Note the intranuclear inclusion (MGG, X100).

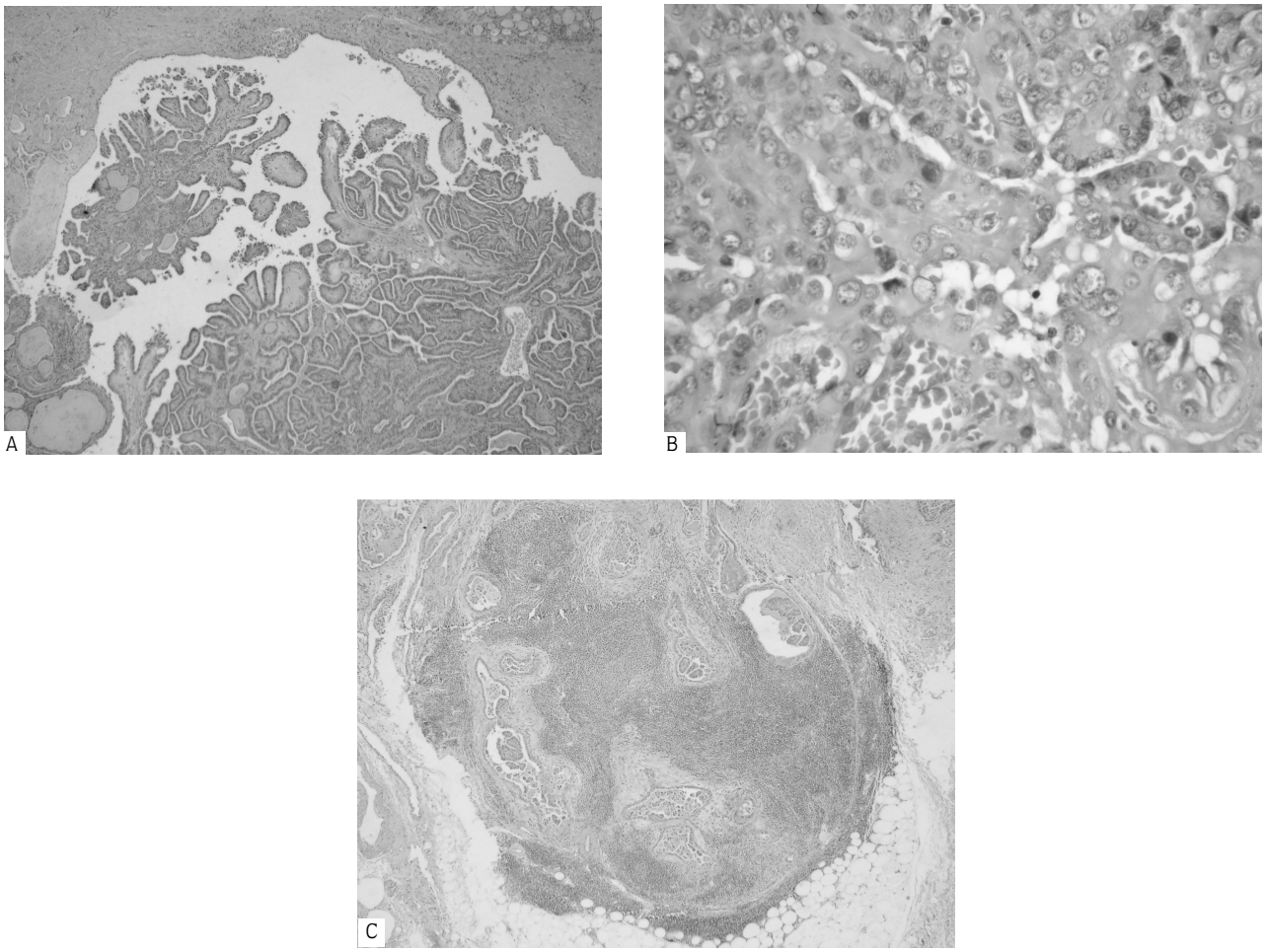

Figure 3. A) Intracystic papillary growth pattern in the tumor (HE, X5)
B) The oncocytic tumor cells showed nuclei characterized by nuclear crowding, optically clear chromatin and nuclear grooves (HE, X40).
C) The pericapsular lymph node showed tumor metastasis (HE, X5).

in character. Non-tumoral thyroid tissues showed lymphoplasmacytic cell infiltration consisting of lymphoid follicles with germinal center formation. Oncocytic cell changes were rarely observed in the non-tumoral thyroid tissue. Non-tumoral thyroid tissues were concordant with autoimmune thyroiditis. Two metastatic lymph nodes were determined in the pericapsular region of the thyroid (Figure 3C). In addition, five of the eight lymph nodes dissected from the paratracheal region showed tumor metastasis.

Discussion

Papillary carcinoma of the thyroid (PTC) may exhibit a broad spectrum of morphological appearances. These variants have different prognoses and some are associated with a more aggressive behavior, such as the diffuse sclerosing variant, tall cell and columnar cell variants (2-6). The oncocytic variant of PTC is a rather unusual form of thyroid cancer. The World Health Organization's (WHO) classification of thyroid neoplasms recognizes this variant, but the oncocytic variant of PTC has not been reported sufficiently in the literature (1). The oncocytic variant of PTC accounts for 1%-11% of all PTCs (1,7,8).

The cytological features of PTC on aspiration biopsy include a characteristic arrangement of cells in papillary clusters with fibrovascular cores and nuclear changes, such as enlargement, clear chromatin, grooves and inclusions. The oncocytic variant of PTC is characterized by oncocytes with abundant, coarsely granular cytoplasm

and the classic nuclear features of papillary adenocarcinoma. The features of oncocytic PTC on aspiration cytology have also not been well described (9).

Oncocytic lesions of the thyroid gland encompass benign and reactive processes, such as Hashimoto's thyroiditis and hyperplastic nodules, through malignant processes, such as oncocytic follicular and papillary thyroid carcinomas. There is no single criterion to differentiate these entities. The criteria described for PTC, i.e. nuclear enlargement, optically clear nuclei and the presence of nuclear grooves and inclusions, has also been described in a variety of lesions of the thyroid gland. Also, oncocytic cells with coarsely granular cytoplasm are observed in benign, reactive and malignant thyroid lesions. Therefore, these criteria are not sensitive or specific for the diagnosis of oncocytic variant of PTC (9,10).

The clinicopathologic features and biologic behavior of this variant have not been fully characterized, since most of the reports are based on single cases or small series. For the same reason, there is also conflicting information in the medical literature about the incidence (1).

The most important issue is determining that a cell showing oncocytic cytoplasmic features is actually a true Hürthle cell. A prominent nucleolus is an important feature for this discrimination. Moreira et al. (9) reported that prominent nucleoli were present in 57% of follicular neoplasms and absent from all PTCs. In cytological slides, the absence of nucleoli in the oncocytes associated with a background containing colloid, multinucleated giant cells and macrophages was suggested to be the most reliable criterion in establishing the diagnosis of PTC. Nuclear grooves and inclusions are not helpful in distinguishing the type of oncocytic neoplasm. Although nuclear inclusions are seen more frequently in PTCs, they can also be seen in a small percentage in oncocytic follicular neoplasms (1). Hashimoto's thyroiditis is another entity in the differential diagnosis of the oncocytic variant of PTC with metastasis to a lymph node. Cytological material aspirated from such a lymph node or non-tumoral thyroid tissue areas containing an autoimmune thyroiditis will show oncocytic cells in a background of lymphoid hyperplasia. In most cases of Hashimoto's thyroiditis, the smears will show flat sheets of oncocytic cells with small, round nuclei with single nucleolus. However, nuclear atypia with prominent nuclear grooves and pleomorphism have also been described in Hashimoto's thyroiditis (9). Both conditions (lymph node metastasis and an autoimmune thyroiditis in non-tumoral thyroid tissue) were also present in our case, but the aspirates did not show intensive lymphoid cell hyperplasia.

In aspiration slides of our case, we determined macrophages and papillae-like clusters formed of oncocytic cells in a background containing colloid. Some oncocytic cells had intranuclear inclusions and nuclear grooves. However, prominent nucleoli were noted in most oncocytic cells. High cellularity of aspirates, the presence of three-dimensional clusters and prominent pleomorphism of oncocytic cells supported a malignant thyroid tumor.

In our case, extensive tumoral infiltration of peri-thyroidal tissues was determined in the thyroidectomy. Two pericapsular lymph nodes and five lymph nodes dissected from neck dissection material showed tumor metastasis. Both papillary and follicular structures were formed by large polygonal cells with abundant pink, granular cytoplasm. When oncocytic tumor cells were evaluated on high magnification, it was noted that almost all nuclei showed grooves and optically clear chromatin pattern. In addition, extensive nuclear overlapping was noted. Intranuclear inclusions were also present in a lot of nuclei, but were less seldom seen than the former two classic nuclear changes. No psammoma bodies were seen in the tumor. Focal limited calcification foci were present. The presence of extensive intracystic true papillary stalks, nuclear grooves and optically clear chromatin pattern in most nuclei and nuclear overlapping in both papillary organization and follicular arrangement areas of the tumor supported PTC. Extensive oncocytic cell changes indicated the oncocytic variant of PTC. Histological and cytological features observed in the tumor of our case fulfilled the diagnostic histological criteria suggested for the oncocytic variant of PTC in the study of Berho et al. (1). The tumoral lesion of the present case was concordant with PTC with respect to many histological features. But at the time of diagnosis, extensive pericapsular tumoral spread was not an expected finding for PTC. This finding is particularly expected in follicular thyroid carcinomas. The biological behavior of the oncocytic variant of PTC seems quite variable, based on the different series reported in the literature. It is believed that these discrepancies might reflect the lack of more precise histological criteria to define these

neoplasms, leading to inclusion of a broad range of oncocytic tumors within such studies. As a result of the lack of more precise criteria, the line that divides "true" oncocytic PTC from other oncocytic thyroid tumors (particularly papillary Hürthle cell tumors) has been very indistinct (1). The studies in which papillary configuration rather than characteristic nuclear features was used as the overriding criterion for diagnosis of PTC are noted in the literature (11-13). It thus appears that the studies previously reported concerning the oncocytic variant of PTC might contain a heterogeneous mixture of tumors of varying biological potential sharing in common only their oncocytic cytoplasmic features and papillary architecture. Distinguishing the oncocytic variant of PTC from other oncocytic thyroid neoplasms with different biological behavior is important. The most important entity among these neoplasms is papillary Hürthle cell carcinoma (14,15), which has different nuclear features from PTC, consisting mainly of round-shape, vesicular chromatin pattern and prominent centrally placed nucleolus. Focal hyperchromasia, binucleation and marked nuclear atypia are frequent accompanying nuclear features of these cells (16). Infiltration of the soft tissues surrounding the thyroid is not an uncommon event in these neoplasms. Distant metastasis, especially to lung and bones, occurs more frequently in Hürthle cell carcinomas. The overall five-year survival for Hürthle cell carcinoma ranges from 50% to 60% in most series. However, the prognosis of PTC is excellent (1). In our case, peri-thyroidal soft tissue infiltration was noted on the histopathological examination. This feature is more likely in Hürthle cell carcinoma. In addition, prominent nucleoli and vesicular chromatin pattern also suggested Hürthle cell carcinoma. Our case also frequently showed prominent nucleoli in the histologic sections. However, we evaluated our case as PTC because extensive nuclear groove formation and intranuclear inclusions, extensive papillary structures and a cystic component were present in the tumor. Regarding histopathological and cytological features and the clinical situation, the present case could be evaluated as a hybrid neoplasm sharing the features of both PTC and Hürthle cell carcinoma.

Other diagnostic considerations in the histological differential diagnosis of these tumors include the tall cell variant of PTC and the oncocytic variant of medullary carcinoma of the thyroid. Neoplastic cells of tall cell variant of PTC are twice as tall as wide, with elongated dark nuclei. The oncocytic variant of medullary carcinoma is characterized by a solid or follicular growth pattern with prominent oncocytic cell changes, absence of the characteristic nuclear features of PTC, and the presence of more conventional areas of medullary carcinoma within the tumor (4,5,17,18).

In conclusion, the oncocytic variant of PTC is a morphologically distinct and rare variant of papillary thyroid cancer. Additional studies with longer follow-up periods are necessary to further define the spectrum of biological activity and metastatic potential of these neoplasms. In addition, strict histological criteria should be established to separate these lesions from other thyroid neoplasms characterized by oncocytic cell changes.

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