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WARTHIN TUMOR-LIKE PAPILLARY THYROID CARCINOMA – CASE REPORT

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Summary

We report a rare case of Warthin tumor-like papillary thyroid carcinoma confirmed by histology. It is an uncommon variant of papillary thyroid carcinoma with about 80 cases reported in the literature and it is often associated with lymphocytic thyroiditis. Morphologically, it resembles Warthin tumors of the salivary glands, with T and B lymphocytes infiltrating the stalks of the papillae lined with large cells with abundant eosinophilic cytoplasm (oncocytic cells). The epidemiologic features of this variant of papillary thyroid carcinoma are similar to the classic papillary carcinoma.

A 58-year-old female patient came to the ultrasound examination of cervical region and the examination detected two nodules; an isoechoic nodule 11 mm in greatest diameter with perilesional vascularisation in the left thyroid lobe and a solid-cystic nodule approximately 15 mm in greatest diameter in the right lobe of the thyroid gland. Ultrasound guided fine needle aspiration (FNA) was performed and cytological analysis indicated papillary carcinoma in the right thyroid lobe. Surgical treatment was performed. Histopathological analysis confirmed the cytological diagnosis and the final histopathological diagnosis were Warthin tumor-like papillary thyroid carcinoma with lymphocytic thyroiditis and intraglandular tumor spread. Lymph node metastases were excluded as well as vascular invasion and nine months after surgery the patient is fine and disease-free.

This tumor can be easily mistaken for Hurthle cell carcinoma and tall cell variant of papillary carcinoma both by FNA and histology but the lymphocytic infiltrate within the stalks of the tumor papillae in the histology specimens is a distinctive factor for its diagnosis. The lymphocytic infiltration in this variant of papillary carcinoma and association with lymphocytic thyroiditis may suggest the role of immunological mechanisms for its pathogenesis and prognosis. In the future, more studies are required for better understanding of its biological behaviour.

KEY WORDS: *papillary carcinoma, Warthin tumor, FNA cytology, histology, prognosis*

PAPILARNI KARCINOM ŠTITNJAČE POPUT WARTHINOVOG TUMORA – PRIKAZ SLUČAJA

Sažetak

Prikazujemo slučaj rijetke varijante papilarnog karcinoma štitnjače poput Warthinovog tumora. To je rijetka varijanta papilarnog karcinoma do sada opisana u literaturi u 80 slučaja i često je povezana s limfocitnim tireoiditisom. Morfološki, tumor oponaša Warthinov tumor žlijezda slinovnica, sa T i B limfocitima koji infiltriraju stapke papila koje su obložene većim stanicama s obilnom eozinofilnom citoplazmom (onkocitne stanice). Epidemiološke značajke ove varijante papilarnog karcinoma štitnjače istovjetne su klasičnom papilarnom karcinomu.

58-godišnja žena došla je na ultrazvučni pregled vrata i pregled je detektirao dva čvora; jedan izoehogeni, pojačano vaskulariziran veličine 11 mm u lijevom režnju štitnjače, i solidno-cistični čvor oko 15 mm u najvećem promjeru u desnom

režnju štitnjače. Učinjena je citološka punkcija pod kontrolom ultrazvuka i citološka analiza je upućivala na papilarni karcinom čvora desnog režnja štitnjače. Učinjen je operativni zahvat. Histopatološka analiza potvrdila je citološku dijagnozu, i završne histološke dijagnoze bile su Warthin-varijanta papilarnog karcinoma štitnjače s limfocitnim tireoiditisom uz intraglandularno širenje tumora. Isključene su metastaze u limfne čvorove kao i vaskularna invazija i devet mjeseci nakon operacije pacijentica je dobro i bez znakova bolesti.

Tumor je lako zamijeniti s Hurthle staničnim karcinomom, varijantom visokih stanica papilarnog karcinoma i to i citološki i histološki, ali limfocitni infiltrat unutar stapki papila tumora u histološkim preparatima jasan je faktor njegove dijagnoze. Limfocitna infiltracija u ovoj varijanti papilarnog karcinoma i povezanost s limfocitnim tireoiditisom sugerira ulogu imunoloških mehanizama u njegovoj patogenezi i prognozi. U budućnosti, biti će potrebno još studija za bolje razumijevanje njegovog biološkog ponašanja.

KLJUČNE RIJEČI: *papilarni karcinom, Warthinov tumor, aspiracijska citologija, histologija, prognoza*

INTRODUCTION

Warthin tumor-like papillary thyroid carcinoma was first described in 1995 by Apel et al (1). It is an uncommon variant of papillary thyroid carcinoma with about 80 cases reported in the literature and is often associated with lymphocytic thyroiditis (2,3). Clinically, it usually presents as a cystic or solid-cystic thyroid nodule. Morphologically, it resembles Warthin tumors of the salivary glands, with T and B lymphocytes infiltrating the stalks of the papillae lined with large cells with abundant eosinophilic cytoplasm (oncocytic cells) (2,3). This variant of papillary carcinoma can pose diagnostic difficulties in distinguishing it from chronic thyroiditis, Hurthle cell nodules in chronic lymphocytic thyroiditis, Hurthle cell tumors, tall cell and oncocytic variants of papillary carcinoma (2). The role of immunohistochemistry in differential diagnosis with Hurthle cell and tall cell carcinomas is limited. Intense staining for the following markers has been reported in the literature: galectin-3, HBME-1, CK19, TTF-1, thyroglobulin, EMA, AE1/AE3, S-100, cyclin D1, and UCHL1, CD3+, CD20+ and CD79+ (for the lymphocytic population) (3). The main diagnostic criteria for the diagnosis of this variant of papillary carcinoma are the detection of the typical nuclear features seen in conventional type papillary carcinoma like clear nuclei, nuclear grooves, and intranuclear pseudoinclusions and also lymphocytic infiltrate within the stalks of a papillae (4). Molecular biology studies have shown that Warthin tumor-like papillary carcinoma and conventional papillary carcinoma share the same BRAF and RET mutations, which support the thesis that Warthin-like papillary carcinoma is a morphological variant of the papillary carcinoma (2,5). Surgical and postoperative management is identical to that of classic papillary carcinoma, while prognosis seems to be favourable (3). Some authors presented this variant of papillary carcinoma with less than 5% of the tumor being occupied by anaplastic tissue and also another case with anaplastic component was reported (2,6). In these cases clinical data and prognosis were worse like in anaplastic changes seen in conventional papillary carcinoma. Because of that recognition of any dedifferentiated component in a Warthin tumor-like papillary thyroid carcinoma should be reported, including its percentage, because it may reflect a more aggressive clinical course (2).

CASE REPORT

A 58-year-old female patient came to the ultrasound examination of the cervical region indicated by an endocrinologist. The examination showed two nodules, one in a left and one in a right lobe of the thyroid gland. Ultrasound guided fine needle aspiration (FNA) of both nodules was performed and materials were stained with May-Grünwald-Giemsa (MGG). The cytological diagnosis were: the elements of thyroid tissue in the left lobe and papillary carcinoma in the right lobe of the thyroid gland. Surgical treatment was indicated, right lobectomy was performed first and intraoperative histology confirmed diagnosis of papillary thyroid carcinoma (Warthin-like). After that, total thyroidectomy with central neck lymphadenectomy was performed and paraffin-embedded tumor samples were sliced into 5 μm sections and haematoxylin stained.

Ultrasound findings

The examination showed a gland with heterogeneous parenchymal echostructure and slightly raised intraglandular vascularisation. There were two nodules detected, the one in the inferior pole of the left lobe was isoechoic nodule, 11 mm in the greatest diameter with perilesional vascularisation, and the second in the inferior pole of the right lobe was solid-cystic nodule approximately 15 mm in the greatest diameter.

Cytological findings

1. The aspirates from the left nodule showed normal thyroid epithelium, colloid, and single cells and the diagnosis of thyroid tissue was reached.
2. The cellular yield from right nodule was quite rich. The aspirates showed groups of cells in syncytial and papillary pattern or singly dispersed cells (Figure 1). The tumor cells had voluminous excentric placed nuclei often with intranuclear pseudoinclusions and the cytoplasms were medium sized (Figure 2 and 3), sharply bordered but mostly with cystic-degenerative changes. There were also some multinucleated giant cells, histiocytes, colloid, some foamy macrophages, and small number of lymphoid cells in the background of the smears. The diagnosis of papillary carcinoma was reached.

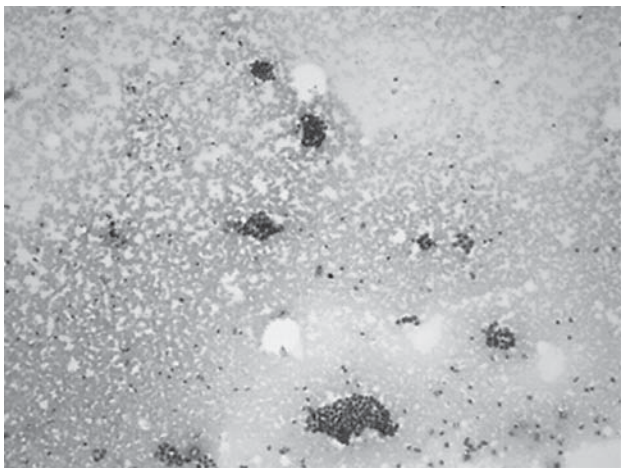

Figure 1. Warthin tumor-like papillary thyroid carcinoma (MGGx20)

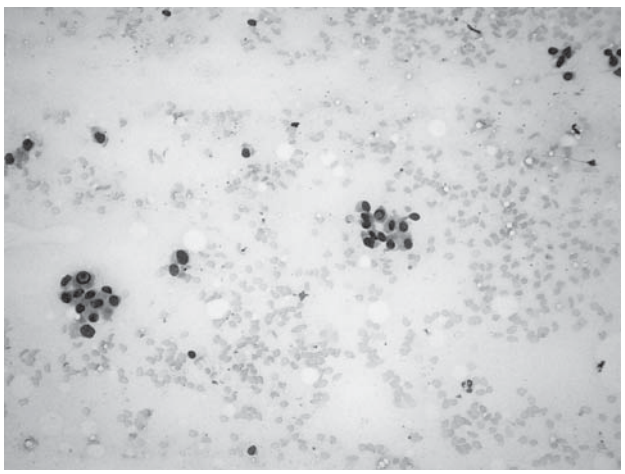

Figure 2. Warthin tumor-like papillary thyroid carcinoma (MGGx20)

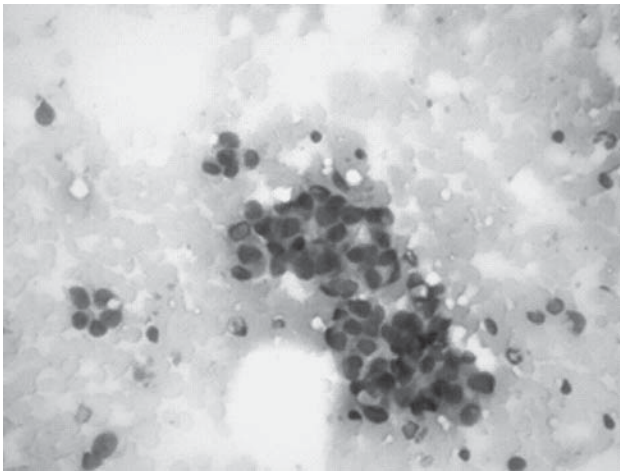

Figure 3. Warthin tumor-like papillary carcinoma (MGGx40)

Histopathological findings

1. Grossly, the right thyroid lobe was red-brown coloured and measured 5.5 cm in the greatest diameter. There was one nodule detected, it was yellowish in colour and sized 13 mm in diameter. Histologically, tumor was composed of papillary stalks filled with inflammatory infiltrate, predominantly lymphocytes and plasma cells (Figure 4). Papillae were lined by tumor cells with oncocytic cytoplasm and round to oval nuclei with nuclear features of papillary carcinoma (Figure 5). The diagnosis of papillary thyroid carcinoma (Warthin-like) was made. Capsular, lymph

node or vascular invasion of the tumor was absent and resection borders were negative. The surrounding thyroid exhibited lymphocytic (Hashimoto) thyroiditis.

2. The material of paratracheal dissection included five lymph nodes from 0.3 to 1.1cm in diameter and histopathological findings excluded lymph node metastases.

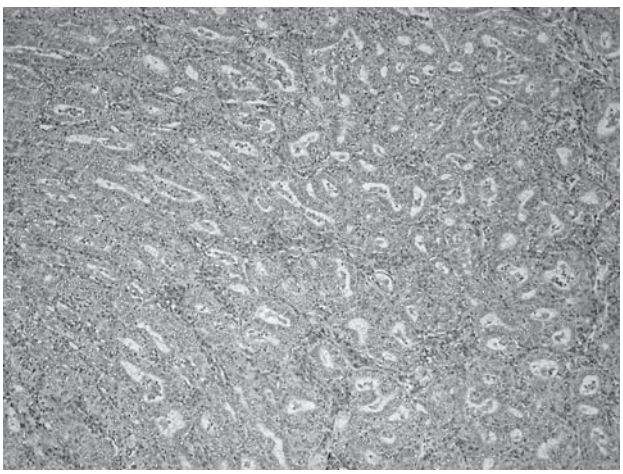

Figure 4. Warthin tumor-like papillary thyroid carcinoma (HβEx10)

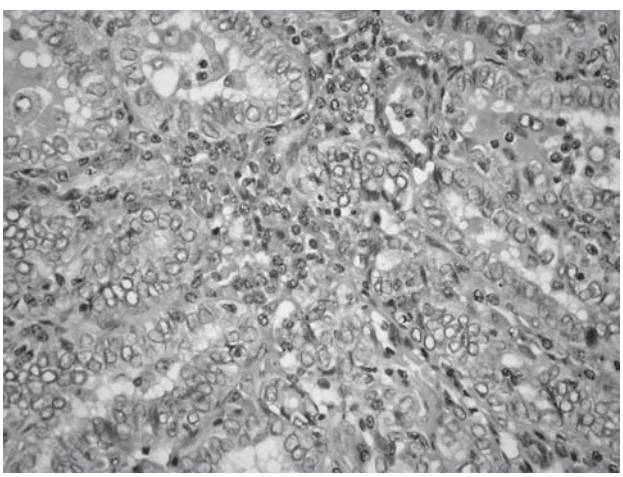

Figure 5. Warthin tumor-like papillary thyroid carcinoma (HβEx40)

3. The left thyroid lobe measured 5.5 cm with one nodule 9 mm in diameter. Histologically, the nodule was composed of tumor papillae lined by oncocytic cells showing nuclear features of papillary carcinoma.

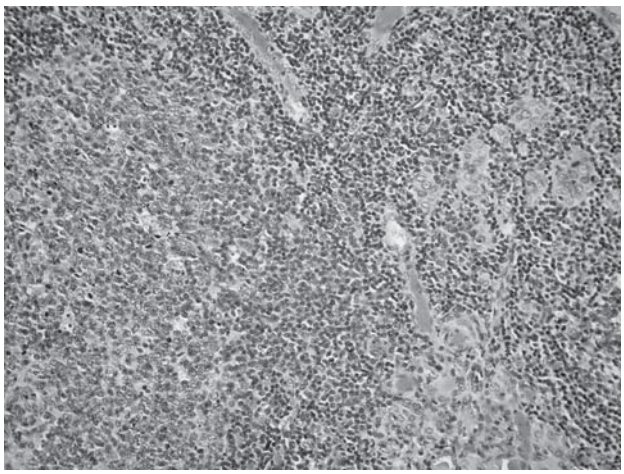

Figure 6. Warthin tumor-like papillary thyroid carcinoma (HβEx20)

The stalks of the papillae and the surrounding tissue showed a strong lymphocytic infiltration. The diagnosis of intrathyroid dissemination with lymphocytic (Hashimoto) thyroiditis was reached (Figure 6).

DISCUSSION

Apel et al coined the designation of this tumor in regard to its close resemblance to the papillary cystadenoma lymphomatosum or Warthin tumor of the salivary glands (1). These authors found that the epidemiologic features of this variant of papillary thyroid carcinoma are similar to the classic papillary carcinoma.

Fine needle aspirates (FNA) could show papillary fragments against background of lymphocytes, oncocytic and plasma cells. The nuclear features of tumor cells are generally those of classic papillary carcinoma, such as chromatin clearing, membrane thickening, grooves and pseudoinclusions and oncocytic nuclear characteristics such as coarse chromatin and prominent nucleoli. Such a pattern could suggest papillary carcinoma, lymphocytic thyroiditis or both (3). In our case the preoperative diagnosis based on FNA was that of papillary carcinoma and we indicated operative procedure with final histopathological diagnosis.

The macroscopic appearance of this variant of papillary carcinoma is, as in our case, usually white-yellowish, well circumscribed nodule, un-

encapsulated and confined to the thyroid gland. It may contain cystic-degenerative areas as we reported in our FNA findings, and its mean size reported in the literature was 15 mm (range 0.3-5 cm) (3). In our case there were two tumor nodules sized 13 mm and 9 mm, the second one diagnosed as the intrathyroid spread of the tumor cells.

The histological diagnosis of this variant of papillary carcinoma is based on the evidence of a morphological pattern of papillae lined by oncocytic cells admixed with lymphocytes and sparse plasma cells. The presence of lymphocytic infiltrate within the stalks of Warthin-like papillary carcinoma indicates a distinctive appearance to this tumor (3,7). Because of that the definitive diagnosis of this variant of papillary carcinoma could be reached as in our case only by histopathological findings. In our case, the definitive diagnosis was confirmed by intraoperative histology and final diagnosis added the diagnosis of lymphocytic thyroiditis and intraglandular spread of the disease.

Papillary carcinoma and its variants can exhibit different degrees of oncocytic metaplasia, predominantly Hurthle cell and tall cell variants of papillary carcinoma. Papillary Hurthle cell carcinoma are characterized by papillary architecture lined by oncocytic cells with nuclear features of papillary carcinoma but they usually lack lymphoplasmacytic infiltrate as seen in Wartin-like variant. The tall cell variant of papillary carcinoma is characterized by papillary growth, oncocytic elongated tumor cells and papillary nuclear features. Clinically, this variant behaves more aggressively and is associated with vascular invasion, lymph node metastases and tumor recurrence (7). Warthin-like variant of papillary carcinoma lacks elongated cells seen in tall cell variant, and has lymphocytic infiltrate. Hurthle cell lesions (benign and malignant) could have pseudopapillary pattern, which could be mistaken for a papillary Hurthle cell carcinoma but the nuclear features of papillary carcinoma must be present for the diagnosis of papillary carcinoma (4). The presence of oncocytic cells and lymphocytes can be seen in the aspirates from lymphocytic thyroiditis and some of these cells could show nuclear enlargement and chromatin clearing due to reactive changes and this may lead to false-positive diagnosis. However tumors arising in the background of lymphocytic thyroiditis usually show two cell populations in FNA: tumor cells with nuclear features of the papillary carcinoma and the background population of oncocytic cells, with small and large lymphocytes (7).

The role of immunohistochemistry in differential diagnosis with Hurthle cell and tall cell variant carcinoma is limited (3). In our case it was not necessary since the morphological pattern alone was clear enough for the confirmation of final diagnosis.

The neoplastic behaviour of Warthin tumor-like variant of papillary carcinoma seems to be similar or even better than the classical papillary carcinoma (2,3). The most reliable explanation for the low rates of lymph nodes involvement and favourable prognosis in this variant of papillary carcinoma is the presence of lymphatic cells in the tumor, which seems to restrain neoplastic progression (3). Both short and long term prognoses seem to be excellent, but if the tumor contains any part of dedifferentiated area that could have prognostic impact and change the biological behaviour to a more aggressive one (2,6). Because of that authors suggest that the large sized Warthin-like papillary tumors, more than 3 cm in diameter should be extensively sampled to exclude the presence of dedifferentiation (2). In the presented case, we excluded such an anaplastic change within the tumor and also lymph node metastases or vascular invasion. Nine months after surgery the patient is fine and disease-free.

CONCLUSION

This is a case of rare Warthin tumor-like variant of papillary thyroid carcinoma. Warthin tumor-like variant of papillary thyroid carcinoma is frequently associated with lymphocytic thyroiditis and has favourable prognosis. The tumor can be mistaken for Hurthle cell carcinoma and tall cell variant of papillary carcinoma both by FNA and histology but the lymphocytic infiltrate within the stalks of the tumor papillae in the histology specimens is a distinctive factor for its diagnosis than immunohistochemistry. The lymphocytic infiltration in these tumors and association with lymphocytic thyroiditis may suggest immunological impact for pathogenesis and prognosis of these tumors. More extensive long-term studies are required for better understanding of their biological behavior.

REFERENCES

1. Apel RL, Asa SL, LiVolsi VA. Papillary Hurthle cell carcinoma with lymphocytic stroma: „Warthin-like tumor“ of the thyroid. Am J of Surg Pathol. 1995;19:810-814.
2. Amico P, Lanzafame S, LiDestri G et al. Warthin tumor-like papillary thyroid carcinoma with a minor dedifferentiated component: report of a case with clinicopathologic considerations. Case Rep Med. 2010;2010:ID 495281, 5 pages,
3. Paliogiannis P, Attene F, Trogu F, Trignano M. Warthin-Like Papillary Carcinoma of the Thyroid Gland: Case Report and Review of the Literature. Case Rep in Oncol Med. 2012; 2012:ID 689291, 4 pages.
4. Baloch ZW, LiVolsi VA. Fine-needle aspiration cytology of papillary Hurthle cell carcinoma with lymphocytic stroma „Warthin-like tumor“ of the thyroid. Endocrine Pathol. 1998;9(4):317-323.
5. D'Antonio A, De Chiara A, Santoro M et al. „Warthin-like tumor of the thyroid gland: RET/PTC expression indicates it is variant of papillary carcinoma“. Histopathology 2000; 36(6):281-286.
6. Lam KY, Lo CY, Wei WI. „Warthin tumor-like variant of papillary thyroid carcinoma: a case with dedifferentiation (anaplastic changes) and aggressive biological behavior. Endocrine Pathol. 2005;16(1):83-89.
7. Baloch ZW and LiVolsi VA. Warthin-like papillary carcinoma of the thyroid. Arch Pathol Lab Med. 2000;124:1192-1195.

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