New insights into histopathological features of Warthin-like papillary thyroid carcinoma


Abstract. Background. The Warthin-like variant of papillary thyroid carcinoma (WLPTC) is a rare papillary thyroid carcinoma that is considered to be a subtype of the oncocyti variant. Purpose of the study: to present the diagnostic and clinical features, the oncological and surgical management of a patient with WLPTC as well as its discussion with other relevant studies. Materials and methods. We report a case of Warthin-like papillary thyroid carcinoma in a 31-year-old woman with Hashimoto thyroiditis. Results. The patient was admitted to the hospital with the presence of a node in the thyroid gland. Thyroid ultrasound showed a 24-mm nodule with oval shape and irregular contours in the left lobe. A fine-needle aspiration biopsy was performed, and a diagnosis of papillary thyroid carcinoma was made. The patient underwent thyroidectomy, bilateral modified and central neck dissection, lymphadenectomy. Histopathological examination suggested a WLPTC coexisting with chronic thyroiditis, metastases to the lymph nodes 2, 3, 4 on the left and 6 neck compartments. The patient underwent postoperative 131I ablation therapy. Conclusions. WLPTC is a recently described variant of papillary thyroid cancer that is frequently associated with lymphocytic thyroiditis. The correct cytological and histomorphological features are of utmost importance to render the diagnosis of WLPTC for better management. A surgical and postoperative treatment is identical to that in classic differentiated thyroid cancer, having a favorable outcome due to a low recurrence rate. A surgical management should be thyroidectomy and dissection of central neck compartment as well as lateral dissection in cases of suspicions for metastases in the lymph nodes or metastases confirmed preoperatively by a fine-needle aspiration biopsy. Keywords: Warthin-like variant of papillary thyroid carcinoma; papillary thyroid carcinoma; thyroid gland; rare thyroid malignancy

Introduction

Papillary thyroid cancer (PTC) is the most common malignant tumor of the thyroid gland [1]. Approximately 15 histological variants of PTC have been described with various biological behavior and prognosis [2, 3]. The Warthin-like variant of papillary thyroid carcinoma (WLPTC) is an uncommon and poorly understood tumor with approximately 80 cases reported in literature to date [4, 5], characterized by papillae lined by large oncocyti cells with cores having dense lymphoplasmacytic infiltrate [1, 6]. WLPTC was described in 1995 by Apel et al., who noticed in their series of 13 cases morphological resemblance to Warthin’s tumor of salivary glands origin [7]. The prognosis of WLPTC is the same or less aggressive than that of classical PTC [8–13].

The purpose of this study was to evaluate a WLPTC in a 31-year-old woman with a history of chronic thyroiditis. We aimed to present the diagnostic and clinical features as well as the oncological and surgical management of patient with WLPTC as well as its discussion with other relevant studies.

Materials and methods

A 31-year-old woman was admitted to department of surgery with chief complaints of the presence of a painless nodule in the thyroid gland. Hypothyroidism was detected and levothyroxine was prescribed at an initial dose of 125 µg/day (thyroid stimulating hormone (TSH) level 4.3 µIU/ml) with a gradual increase to 150 µg/day (TSH level 2.23 µIU/ml).
Ultrasound examination of the neck showed left thyroid lobe with hypoechoic nodule of 24 mm in greatest diameter, oval in shape, with irregular contours, vertical orientation (Thyroid Imaging Reporting and Data System 4). Ultrasound also showed features of the chronic thyroiditis such as heterogeneous echostructure of thyroid parenchyma due to presence of hydrophilic and fibrous-modified areas. The volume of the right lobe was 6.2 cm$^3$ and the left lobe was 7.3 cm$^3$. The capsule of the thyroid gland is not thickened.

Results

Fine needle aspiration biopsy (FNAB) showed a 24-mm left thyroid nodule with evidence of papillary thyroid carcinoma. A tumor composed of papillae lined by Hurthle cells having an abundant amount of granular eosinophilic cytoplasm and nuclear clearing and grooving with intranuclear cytoplasmic inclusions. The stalk of papillae showed dense lymphoplasmacytic infiltrate. Furthermore, the gland was affected by chronic lymphocytic thyroiditis (Fig. 1).

The patient underwent a total thyroidectomy as well as bilateral modified and central compartments neck dissection were performed. Histopathological analysis of the specimen confirmed the presence of PTC coexisting with chronic thyroiditis, as well as metastases to the lymph nodes of 2, 3, 4 on the left neck compartments and to the central neck compartment. The histopathology revealed a TNM for the patient as pT1bN1bM0, stage I.

At follow up of 6 weeks after the surgery, ultrasound examination of the thyroid bed and lymph nodes of the neck showed no signs of metastatic changes to the cervical lymph nodes. The level of plasma thyroglobulin was less than 0.04 ng/mL, thyroglobulin antibody (TgAb) 107 IU/ml (normal range < 0.4 IU/ml), TSH > 100 mIU/l. Considering the high risk of the PTC, the patient underwent radioactive iodine ablation therapy by I$^{131}$.

It is worth to mention, that scintigraphy did not show areas of pathological accumulation of I$^{131}$ neither in thyroid bed, nor in other body locations. At follow up of one year, the level of plasma thyroglobulin was less than 0.04 ng/ml, TgAb < 0.4 IU/ml (normal range < 0.4 IU/ml), TSH 0.08 mIU/l, as well as neck ultrasound showed no suspicious lymph nodes, indicating disease-free status. The study was performed in accordance using methodology that we described earlier [14–16].

Discussion

In this report we have showed a rare case of WLPTC. This variant of PTC was presented in 1995 by Apel et al. as papillary Hurthle cell carcinoma of the thyroid with lymphocytic stroma Warthin-like tumor of the thyroid [7]. To our best knowledge, WLPTC represents a rare variant of PTC, with approximately eighty cases have been reported in literature to date [7, 11, 12]. From the historical point of view, it is important to note that Apel et al. chose the name
Warthin-like tumor due to its histological resemblance to the Warthin tumor of the salivary gland [7].

The prevalence of WLPTC ranges from 0.2 to 1.9 % of all PTCs, which may be due to misclassification into oncocytic, classical or tall cell variants, or share some features of chronic lymphocytic thyroiditis [17–19]. WLPTC typically represents a tumor with a fast-growing feature as compared to classic PTC, and it is mainly diagnosed in females. However, patients diagnosed with WLPTC share similar demographic and clinical characteristics to those affected by PTC [9, 14, 20].

The macroscopic appearance of WLPTC is generally presented as white greyish, unencapsulated, well circumscribed nodule, and confined to the thyroid gland. It may contain hemorrhagic areas and zones of cystic transformations. The tumor size varies in range from 1.5 cm (range 0.3 to 5 cm) [21]. To our knowledge, only one paper has reported a WLPTC larger than 5 cm [3]. The color of the remaining thyroid parenchyma ranges from tan to red brownish and a variable number of nodules of different sizes may be present.

The clinical presentation is the same as that for other differentiated thyroid tumors: absence of signs and symptoms when the lesions are single, small, and deep; palpable masses, glandular swelling, and swallowing and/or phonatory alterations for larger, superficial, and/or multiple lesions, which is in line with other authors [22]. Signs, symptoms, and alterations in thyroid function related to thyroiditis or goiter may be also present. As showed in published series, features of CT imaging and ultrasound of WLPTC are similar to PTC. FNAB is a gold standard for early diagnosis of PTC and its variants [20, 23].

It is worth to mention the study showing FNAB features of WLPTC by Yousef et al., demonstrating the presence of groups of follicular cells and papillary fragments against a background of lymphocytes and plasma cells, which infiltrate the fibrovascular cores. The nuclear features are that of typical PTC which include enlargement of nucleus, clearing of chromatin, nuclear inclusions and grooves [23].

Though, FNAB might be a cytological challenge, because oncocytic cells might be admixed with lymphocytes, sharing similar characteristics between PTC and chronic lymphocytic thyroiditis [18, 24]. WLPTC is commonly accompanied by chronic lymphocytic thyroiditis in up to 80 % of all WLPTC cases [25]. Jun et al. reported 16 (0.2 %) WLPTC of 8,179 PTCs [18]. Vascular and capsular invasions are rare in WLPTC, in contrast to our study, showing presence of lymphovascular invasion with metastatic lymph nodes.

Differential diagnosis must be conducted with other variants of PTC with similar histopathology, such as Hurthle cell carcinoma and tall cell carcinoma. The Hurthle cell carcinoma usually lacks lymphoplasmacytic infiltrates and is rarely associated with lymphocytic thyroiditis [26]; the tall cell carcinoma is characterized by a papillary structure with elongated oncocytes, more than twice as high as their width, and tumor aggressiveness with more frequent vascular, nodular and capsular invasion [26].

In our case the preoperative diagnosis based on FNAB was PTC (category TB-RST 6) and thyroiditis, which is in line with the current guidelines [23, 27]. The role of immunohistochemistry in differential diagnosis with Hurthle cell and tall cell carcinomas is limited. We did not apply immunohistochemical investigation, because of limited laboratory resources which is common for Ukraine [27]. We hypothesized that the biological course of WLPTC might be similar to or even have a better prognosis than classic PTC due to association with benign thyroid disorder such as chronic lymphocytic thyroiditis as showed in our previous reports and other published series [27]. Lam et al. described a case of a 74-year-old Chinese woman diagnosed with a 3.5-cm WLPTC [28]. In this interesting case, Lam et al. presented a description of refusing any treatment by the patient at baseline, followed by palliative thyroidectomy after health worsened, and lethal outcome 15 months after the surgery. This case seems to have involved the natural evolution of thyroid carcinoma from well-differentiated to poorly differentiated entity with areas of WLPTC that remained untreated for a long time, rather than a typical WLPTC.

The most reliable explanation for the excellent prognosis, low rates of nodal involvement and a low recurrence rate in WLPTC is the presence of lymphatic tissue within the tumor, which seems to contrast and restrain neoplastic progression and dedifferentiation as suggested in published reports [28, 29].

The therapeutic plan for patients with WLPTC must be assessed after surgery. As the biological course of WLPTC is comparable to that of PTC, postoperative management should also be similar. Both ultrasound and ultrasound guided FNAB are excellent for the early diagnosis of primary tumor as well as for assessing cervical lymph node involvement, showed in this report, and in further planning of an appropriate management. The appropriate management for the WLPTC with lymph node metastases is thyroidectomy and dissection of neck compartments, followed by radioiodine ablation, suppressive TSH therapy and clinical surveillance every 6 months, which is in line with guidelines and our experience [27, 30, 31].

Conclusions

Warthin-like papillary thyroid carcinoma is a rare variant of PTC, which is frequently accompanied by chronic lymphocytic thyroiditis. Histopathologically, WLPTC resembles Warthin tumors of the salivary glands, with T and B lymphocytes infiltrating the stalks of papillae lined with oncocytic cells. A careful preoperative investigation should include ultrasound investigation of neck compartments to detect early signs of metastases to locoregional lymph nodes. A surgical management should be thyroidectomy and dissection of central neck compartment as well as lateral dissection in cases of suspicions for metastases lymph nodes or preoperatively confirmed metastases by FNAB.

References


3. Cherenko SM, Larin OS, Gorobeyko MB, Sichynava RM. Clinical analysis of thyroid cancer in adult patients exposed to ionizing radiation due to the Chernobyl nuclear accident: 5-year comparative


Accepted 04.09.2023

Vol. 19, No. 6, 2023

https://ije.zaslavsky.com.ua
Information about authors
Victoria Hoperia, MD, PhD, DSc, Professor, Department of Fundamental Medicine, Taras Shevchenko National University of Kyiv, Kyiv, Ukraine; https://orcid.org/0000-0002-1911-7984
Olena Mostiuk, Institute of Biology and Medicine, Taras Shevchenko National University of Kyiv, Kyiv, Ukraine; https://orcid.org/0000-0002-7486-762X
Andrii Dinets, MD, PhD, Associate Professor at the Department of Surgery, Institute of Biology and Medicine, Taras Shevchenko National University of Kyiv, Kyiv, Ukraine; https://orcid.org/0000-0001-9680-7519
Serhii Sheptukha, Scientific Department of Minimally Invasive Surgery, State Scientific Institution “Scientific and Practical Center of Preventive and Clinical Medicine” State Administration of Affairs, Kyiv, Ukraine; https://orcid.org/0000-0001-5553-5377
Olexandr Hubar, Scientific Department of Minimally Invasive Surgery, State Scientific Institution “Scientific and Practical Center of Preventive and Clinical Medicine” State Administration of Affairs, Kyiv, Ukraine; https://orcid.org/0000-0003-4486-2377
Maksym Gorobeiko, MD, PhD, Head of Department of Surgery, Institute of Biology and Medicine, Taras Shevchenko National University of Kyiv, Kyiv, Ukraine; https://orcid.org/0000-0003-1303-0076

Conflicts of interests. Authors declare the absence of any conflicts of interests and own financial interest that might be construed to influence the results or interpretation of the manuscript.

Authors' contributions. Victoria Hopper, Olena Mostiuk, Andrii Dinets — writing original draft, statistical analyses, supervision, review and editing, critical revision of the manuscript, final approval; Maksym Gorobeik — conceptualization, data curation, formal analysis, review and editing, writing original draft; Serhii Sheptukha — formal analysis, visualization, writing original draft, review and editing; Olexandr Hubar — data collection, writing the draft.

Хоперія В., Мостюк О., Дінець А., Шептуха С., Губар О., Горобейко М.
1 Інститут біології та медицини, Київський національний університет імені Тараса Шевченка, м. Київ, Україна
2 Інститут охорони здоров'я, Київський аграрний університет, м. Київ, Україна
3 Клініка Verum Expert, м. Київ, Україна

Нове уявлення про гістопатологічні особливості Warthin-подібної папілярної карциноми щитоподібної залози

Резюме. Актуальність. Warthin-подібна папілярна карцинома щитоподібної залози (WLPTC) є рідкісним варіантом папілярного раку щитоподібної залози, що вважається підтипом однокілатарного варіанта. Мета дослідження: представити діагностичні та клінічні особливості, онкологічні та хірургічні лікування пацієнтів із WLPTC, а також їх обговорення порівняно з іншими дослідженнями.

Матеріал та методи. У цій роботі проаналізовано випадок WLPTC, поєднаної з тиреоїдитом Хашімото, в 31-річної жінки.

Результати. Пацієнтку госпіталізували з приводу вузла щитоподібної залози. При ультразвуковому дослідженні в лівій частці щитоподібної залози виявлено утворення овальної форми розміром 24 мм з неправильними контурами. Виконано тонкоголкувальну аспіраційну пункційну біопсію цього вузла і встановлено діагноз папілярного раку щитоподібної залози. Хворій проведено тиреоїдектомію, двосторонню модифіковану та центральну дисекцію шиї, лімфаденектомію. При патогістологічному дослідженні виявлено WLPTC на тлі хронічного тиреоїдиту з метастазами в лімфатичні вузли 2, 3, 4 ліворуч і 6 колекторів шиї. Пацієнтті проведено післяоперативну обляшюю welfare-131.

Висновки. WLPTC є нещодавно описаним варіантом папілярної карциноми щитоподібної залози, який часто асоціюється з лімфоцитарним тиреоїдитом. Правильні гістологічні та гістоморфологічні ознаки є надзвичайно важливими при встановленні діагнозу WLPTC для кращого лікування. Хірургічне та післяоперативне лікування ідентично тому при класичному диференційованому раку щитоподібної залози; має сприятливий результат завдяки низькій частоті рецидивів. Хірургічне лікування повинно включати тиреоідектомію та дисекцію центрального відділу шиї, а також латеральну дисекцію у випадках підозри на метастази в лімфатичних вузлах або дооперативно підтверджених метастазів.

Ключові слова: Warthin-подібний варіант папілярної карциноми щитоподібної залози; папілярна карцинома щитоподібної залози; щитоподібна залоза; рідкісна злоякісна пухлина щитоподібної залози