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Modern diagnosis and treatment of papillary thyroid cancer

Bardychevskiy Dmytro¹, Yuzvenko Violetta², Tovkai Oleksandr²

¹O. Bohomolets National Medical University, Kyiv, Ukraine

²Ukrainian Scientific and Practical Center of Endocrine Surgery, Transplantation of Endocrine Organs and Tissues of MoH of Ukraine, Kyiv, Ukraine

Address for correspondence:

Bardychevskiy Dmytro

E-mail: dimabardichevskii@gmail.com

Abstract: thyroid cancer is the most common malignant tumor of the endocrine glands, accounting for 1% of all cases of malignant neoplasms. According to the National Cancer Registry, 24,626 patients with thyroid cancer were identified in Ukraine for the period from 2014 to 2021, of which 4,556 were men (18.5%) and 20,070 were women (81.5%). Treatment of papillary thyroid cancer combines three methods: surgery, the use of radioiodine therapy, and hormone replacement therapy with levothyroxine drugs. The aim of this work, based on the example of a clinical case, was to analyze the patient's route, methods of diagnosis, and treatment of a thyroid neoplasm in accordance with current guidelines and recommendations. This clinical case highlights the importance of early diagnosis of TG diseases, namely papillary thyroid cancer. The patient turned to the clinic of the Ukrainian Scientific and Practical Center for Endocrine Surgery, Transplantation of Endocrine Organs and Tissues of MoH of Ukraine with complaints of an increase in the front surface of the neck and deterioration of the general condition for a long time. After analyzing the complaints, the patient was sent for a comprehensive examination, where an ultrasound of the TG revealed a mass, cytological examination confirmed a thyroid papillary cancer, grade 6. After undergoing preparation, the patient was referred for surgical intervention, namely extrafascial thyroidectomy. Combined treatment was carried out (operative intervention and treatment with the drug I¹³¹), and a suppressive dose of levothyroxine was prescribed, followed by dose correction and dynamic supervision by an endocrinologist. The described clinical case testifies to the high quality of diagnosis and treatment of a patient with thyroid papillary cancer in the conditions of a highly specialized endocrinological center. This approach fully meets the international requirements for the treatment of thyroid cancer. Despite the difficult epidemiological situation in Ukraine and the state of war, the patient was promptly referred to the Ukrainian Scientific and Practical Center for Endocrine Surgery, Transplantation of Endocrine Organs and Tissues, where she received the necessary assistance in full.

Keywords: [hormone replacement therapy](#), [papillary carcinoma](#), [thyroglobulin](#), [thyroidectomy](#), [thyroid gland](#).

Introduction

According to the data obtained during the GLOBOCAN study of morbidity and mortality from malignant neoplasms, in 2020, in the structure of oncological diseases, malignant neoplasms of the thyroid gland (TG) are in ninth place and occupy 8.6% of the total number (Pizzato M, Vaccarella S, 2022; Sung H, Bray F, 2020). Thyroid cancer (TC) is the most common malignant tumor of the endocrine glands, which accounts for 1% of all cases of malignant neoplasms (Megwalu UC, Moon PK, 2022). Diagnosis of TC remains a difficult problem. The standard method of preoperative diagnosis of TC after ultrasound examination (ultrasound) is fine-needle aspiration puncture biopsy (FNA) with a cytological examination (Smith T, Kaufman CS, 2021). FNA allows to assess the risk of malignant potential and determines clear indications for operative treatment. However, the result depends on the accuracy of getting into the focus and has certain limitations, in particular, in the differential diagnosis of follicular tumors of the TG, assigned to the diagnostic category III-V according to the Bethesda classification (Kiernan CM, Solórzano CC, 2017). Similar cytological findings occur in about 10-40% of cases and require surgical interventions for diagnostic purposes, although only in 10-15% of cases a malignant process is confirmed during a histological examination. (Mon SY, Hodak SP, 2018).

In Ukraine, up to 3,000 cases of TC have registered annually, and the mortality rate reaches 10-12 people per 1 million population, which is twice as high as the average statistical indicators in the world. According to the National Cancer Registry, in Ukraine for the period from 2014 to 2021, 24,626 patients with TC were identified, of which 4,556 were men (18.5%) and 20,070 were women (81.5%). On average, 3078.25 ± 136.15 people were diagnosed per year. The incidence rate among women is 3.8 times higher than among men. The average incidence rate in Ukraine for 2014-2021 was 6.5 per 100,000 population (Kurochkin A, Moskalenko Yu, 2022).

The study of histological types of malignant neoplasms of the TG showed that the papillary variant of the TC is the most often observed (70.5-81.9%). The share of follicular TC ranges from

12.8 to 19.2%. Medullar cancer occurs much less often – in 1.5-4.6% of cases, while undifferentiated and squamous cell carcinoma is extremely rare (0.2-3.3% of cases) (Kurochkin A, Moskalenko Yu, 2022; Tovkai, O. A., YI Komisarenko, 2022). The prognosis of TC is generally favorable, and the relapse rate is in the range of 5 to 20% (Ulisse S, Ferent IC, 2021).

The results of researches in recent years indicate that the increase in the incidence of papillary TC is partially related to the increase in the number of preventive examinations (Olson E, Silberstein PT, 2019).

Treatment of papillary TC combines three methods: surgery, the use of radioiodine therapy, and hormone replacement therapy with levothyroxine drugs (Nguyen QT, Plodkowski RA, 2015).

Therefore, it is important to use modern diagnostic methods aimed at establishing and confirming the diagnosis in order to identify thyroid neoplasms to choose the right treatment tactics and the fastest recovery of the patient.

Aim

The purpose of this work, based on the example of a clinical case, was to analyze the patient's route, methods of diagnosis, and treatment of a thyroid neoplasm according to current instructions and recommendations.

Clinical case description

Patient K., 57 years old, applied for a consultation at the Ukrainian Scientific and Practical Center for Endocrine Surgery, Transplantation of Endocrine Organs and Tissues of MoH of Ukraine with complaints of pain and swelling in the right side of the neck, swallowing disorders, shortness of breath with minor physical exertion, dizziness. These complaints have arisen in the last three months. There is no family history of thyroid pathology and oncological pathology. Objectively: at the time of examination, the general condition of the patient is relatively satisfactory. The patient has a normosthenic physique, the skin is pale pink and moist. Blood pressure 135/80 mm Hg, heart rate 85 in 1 min. Breathing is vesicular, wheezing is absent. There is no peripheral edema. The TG is not enlarged on palpation, dense consistency.

The patient was examined by an endocrinologist, and directed to laboratory tests to clarify the function of the TG, ultrasound of the

TG, and ultrasound of the vessels of the head and neck. An ultrasound of the brachiocephalic arteries revealed extravasal compression of the internal jugular vein on the right, so multispiral computed tomography (MSCT) of the mediastinal organs was recommended.

Ultrasound of the TG revealed its typical location, without sealing of the capsule. An isoechoic formation of a non-homogeneous echo structure measuring 5x12 mm is visualized in the right lobe of the TG. In the upper pole, on the dorsal surface of the right lobe, a formation measuring 7x12 mm, irregular in shape, with clear borders is localized. The echo structure of the formation is heterogeneous due to small calcifications. In general, thyroid tissue is isoechoic, the echostructure is heterogeneous due to small hydrophilic areas. Additional formations along the vascular-nerve bundle are not identified. Thyroid volume according to Brunn: right lobe 8.91 cm³, left lobe 3.94 cm³. In the lower pole of the right lobe, there is an accumulation of macrocalcifications up to 7 mm in size. In the upper third of the collector to the right to the middle of the sternocleidomastoid muscle, altered lymph nodes with microcalcifications of 24 and 28 mm in size were found.

MSCT of the neck and chest with intravenous contrast revealed signs of a neoplasm of the right lobe of the TG without extrathyroidal spread, multiple small hypovascular foci in both lobes of the TG, and lymphadenopathy of neck nodes of secondary genesis. In the mediastinum and parenchyma of both lungs, volumetric, focal, and fresh infiltrative changes were not detected.

Laboratory data: complete blood count corresponds to the reference values, ionized calcium (Ca²⁺) – 1.21 mmol/l (reference values 1.13-1.32 mmol/l), thyroid stimulating hormone (TSH) – 0.46 μIU/mL (0.3-4.2 μIU/mL), free thyroxine (fT₄) – 1.09 ng/dL (0.89-1.76 ng/dL), free triiodothyronine (fT₃) – 4.06 pg/ml (2,3-4.2 pg/mL), antibodies to thyroid peroxidase (AT-TPO) – 25.8 IU/mL (< 50 ml), parathyroid hormone – 38.5 pg/mL (16-46 pg/mL), calcitonin – less than 2 pg/mL (< 5.89 pg/mL).

After the studies, the patient underwent FNAB of thyroid formations, followed by immunocytochemical studies. Cytological

conclusion: node of the right lobe of the TG (12 mm) – papillary cancer, class 6, DAPIV – 12. DAP(dipeptidyl-aminopeptidases IV) is a cellular enzyme actively involved in oncogenesis of the thyroid gland, and the cytochemical study of DAP IV is considered as a marker of cell malignancy (Fig. 1). In the lymph nodes of the neck of the third collector on the right, metastasis of papillary TC, 26 mm in size. Class 6. DAP 12 (Fig. 2).

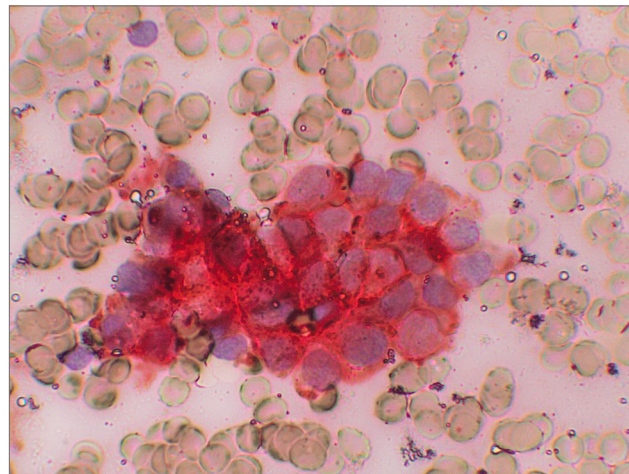


Figure 1. Cytochemical activity study DAPIV – 12

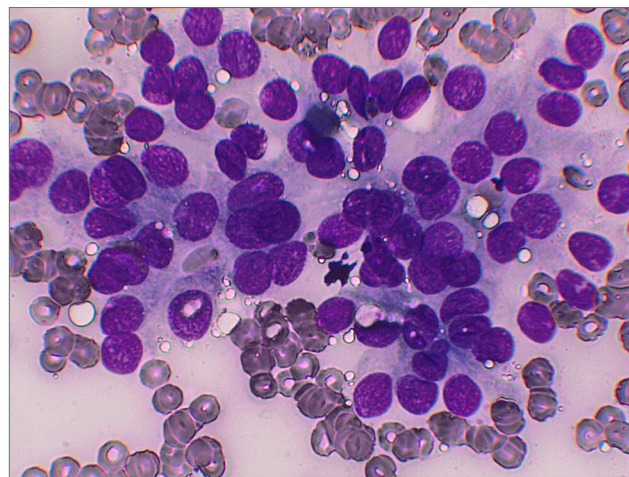


Figure 2. The structure of atypical cells that are suspicious for papillary TC. The May–Grünwald stain

The patient was diagnosed with multinodular goiter. Suspicion of papillary cancer (15.0 mm) of the right lobe of the TG, signs of extraorganic invasion (into the trachea, right laryngeal nerve, vessels), metastasis to level VI lymph nodes (2/21, d = 10.0-18.0 mm), II-V level on the right (5/20, d = 1.0-25.0 mm).

The patient was transferred to the surgical department of the Ukrainian Scientific and Practical Center for Endocrine Surgery, Transplantation of Endocrine Organs and Tissues of MoH of Ukraine for planned surgical intervention. Extrafascial thyroidectomy, central and right-sided modified neck dissection, and lymphadenectomy were performed. Intraoperative histological express examination revealed metastases of papillary cancer in 2-5 lymph nodes on the right. During the surgical intervention, an invasion into the reverse laryngeal nerve on the right was detected, and reinnervation of the nerve was performed.

In the postoperative period, the patient showed signs of phonation disturbance. The postoperative wound healed by primary intention. In the postoperative period, calcium D3 was prescribed at a dose of 1500 mg/day, vitamin D 4000 IU once a day, and B vitamins (B1, B6, B12). After the treatment, there was a positive trend.

Considering the size of the tumor, extra organ invasion, and presence of metastases, the patient is referred for further treatment with radioactive iodine treatment. For a month, the patient followed a diet with a low iodine content and did not receive levothyroxine preparations.

A month after surgery and before treatment with radioactive iodine (I^{131}), an examination was carried out. TSH level was 82.4 μ IU/mL (reference values 0.3-4.2 μ IU/mL), thyroglobulin – 0.98 ng/mL, antibodies to thyroglobulin – 552.0 IU/mL, Ca^{2+} – 1.24 mm/L.

The patient received treatment with I^{131} with a total dose of 5180.0 MBq for five days. Whole body scintigraphy with I^{131} revealed an accumulation of a radiopharmaceutical (RP) in the projection of the thyroid bed on the left and the upper third of the neck along the midline of the neck (d. Thyroglossus).

After combined therapy (surgery and treatment with I^{131}), the patient has prescribed a suppressive dose of levothyroxine 125 mcg/day, followed by dose adjustment after 6-8 weeks. Upon re-examination, the patient noted the presence of positive dynamics, the phonation function was restored, and there were no complaints of pain and swelling of the neck, impaired swallowing, shortness of breath, and dizziness.

The woman was prescribed lifelong replacement therapy with thyroid hormone preparations (levothyroxine) at a dose of 125 mcg/day, followed by dose adjustment. It was recommended to study the level of TSH, thyroglobulin, antibodies to thyroglobulin, parathyroid hormone, ionized calcium, and ultrasound of the thyroid bed and neck after 2 months. In the future, the patient undergoes a mandatory annual oncological examination in highly specialized centers with an examination by endocrinologists.

Discussion

This clinical case makes it possible to understand the need for prompt examination of patients. The woman was examined in full according to the recommendations of the European Thyroid Association (Lebbink CA, Krude H, 2022).

In clinical practice, there are cases of unjustified surgical treatment of thyroid nodules without verification of their structure. In this case, there are operational risks, and the need to take replacement therapy throughout the patient's life.

Ultrasound of the TG is used not only as a method for detecting and describing formations of the TG and a way to monitor the implementation of FNA of suspicious nodes but also to visualize the spread of the oncological process. Ultrasound is performed to identify cervical lymph nodes suspicious for metastatic disease. Based on the data obtained, the volume of surgical intervention is determined (Tovkai, Zemskov, 2022). As noted in the American Thyroid Association guidelines for patients with thyroid nodules and differentiated TC, ultrasound is the first-line imaging modality for individuals with suspected or proven TC (Yeh MW, Bernet VA, 2015).

The generally recognized "gold standard" for the treatment of differentiated TC is total thyroidectomy, supplemented by dissection of the lymphatic collectors, followed by radioiodine ablation of the residual thyroid tissue (Yeh MW, Bernet VA, 2015). It has been proven that this approach significantly reduces the recurrence rate, mortality rates, and also allows monitoring of patients by the level of thyroglobulin in the blood and/or antibodies to it regarding the possible occurrence of metastases, which in most cases are effectively treated with radioactive iodine (Ostafichuk M, Tarashchenko Y, 2022).

In the future, patients with TC are recommended periodic outpatient monitoring with the determination of relevant indicators.

The described clinical case testifies to the high quality of diagnostics and treatment of a patient with papillary TC in a highly specialized endocrinological center. This approach fully meets international requirements for the treatment of TC. Despite the difficult epidemiological situation in Ukraine and the state of war, the patient was timely referred to the Ukrainian Scientific and Practical Center of Endocrine Surgery, Transplantation of Endocrine Organs and Tissues, where she received the necessary assistance in full.

Conclusion

An integrated approach in accordance with international recommendations contributes to the prompt diagnosis of papillary TC and the determination of patient treatment tactics, which positively affects the duration and quality of life. Adequate treatment improves the quality of life and achieves positive long-term results.

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This study did not receive external funding.

Conflict of interest

The authors declare that there is no conflict of interest and no financial interest in the preparation of this article.

Consent for publication

The authors obtained consent to publish this work from a patient relevant to this manuscript.

ORCID ID and author contributions

[0000-0002-9812-943X](https://orcid.org/0000-0002-9812-943X) (C, D) Dmitry Bardichevsky

[0000-0002-5562-4406](https://orcid.org/0000-0002-5562-4406) (A, B, C, F) Yuzvenko Violetta

[0000-0002-1329-279X](https://orcid.org/0000-0002-1329-279X) (B, E, F) Tovkai Oleksandr

A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of article

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Сучасна діагностика та лікування папілярного раку щитоподібної залози

Бардичевський Дмитро¹, Юзвенко Віолетта², Товкай Олександр²

¹Національний медичний університет імені О.О. Богомольця, Київ, Україна

²Український науково-практичний центр ендокринної хірургії, трансплантації ендокринних органів і тканин МОЗ України, Київ, Україна

Address for correspondence:

Bardychevskiy Dmytro

E-mail: dimabardichevskii@gmail.com

Анотація: рак щитоподібної залози (РЩЗ) – найпоширеніша злоякісна пухлина ендокринних залоз, яка становить 1% від всіх випадків злоякісних новоутворень. За даними Національного реєстру раку, в Україні за період з 2014 по 2021 рік виявлено 24626 хворих на РЩЗ, з них 4556 чоловіків (18,5%) і 20070 жінок (81,5%). Лікування папілярного РЩЗ поєднує в собі три методи: хірургічний, використання радіоїодтерапії та замісної гормональної терапії препаратами левотироксину. Метою даної роботи на прикладі клінічного випадку було проведення аналізу маршруту пацієнта, методів діагностики та лікування новоутворення щитоподібної залози згідно з діючими настановами та рекомендаціями. Даний клінічний випадок висвітлює важливу значущість ранньої діагностики захворювань щитоподібної залози, а саме папілярного раку ЩЗ. Пацієнтка звернулась в клініку Українського науково-практичного центру ендокринної хірургії, трансплантації ендокринних органів і тканин МОЗ України зі скаргами на збільшення передньої поверхні шиї та погіршення загального стану протягом тривалого часу. Проаналізувавши скарги, пацієнтка була направлена на комплексне обстеження, де при УЗД ЩЗ було виявлено утворення, цитологічним дослідженням підтверджено папілярний РЩЗ, клас 6. Після проходження підготовки, пацієнтка направлена на оперативне втручання, а саме екстрафасціальну тиреоїдектомію. Проведено комбіноване лікування (оперативне втручання та лікування препаратом I¹³¹), призначено супресивну дозу левотироксину з подальшою корекцією дози та динамічним наглядом ендокринолога.

Описаний клінічний випадок свідчить про високу якість діагностики, лікування пацієнтки з папілярним РЩЗ в умовах високоспеціалізованого ендокринологічного центру. Такий підхід повністю відповідає міжнародним вимогам до лікування РЩЗ. Попри складну епідеміологічну ситуацію в Україні, воєнний стан, пацієнтка була своєчасно скерована до Українського науково-практичного центру ендокринної хірургії, трансплантації ендокринних органів і тканин, де отримала необхідну допомогу в повному обсязі.

Ключові слова: екстраорганна інвазія, папілярний рак, радіоїодтерапія, тиреоглобулін, тиреоїдектомія, щитоподібна залоза.



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