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CASE REPORTS

Giant multifocal thyroid tumor

Claudiu NISTOR, MD, PhD[a]; Mihnea DAVIDESCU, MD[b]; Adrian CIUCHE, MD[a]; Ovidiu RUS[b]; Augustin TUDOSE, MD[c]; Florina VASILESCU MD[d]; Teodor HORVAT, MD, PhD, Professor of Thoracic Surgery[b]

[a]Military Clinical Central and Emergency Hospital – Thoracic Surgery Department, Bucharest, Romania
[b]Thoracic Surgery Department, "Prof. Dr. Al. Trestioreanu" Oncology Institute, Bucharest, Romania
[c]Military Clinical Central and Emergency Hospital – Anaesthesia and Intensive Care Department, Bucharest, Romania
[d]Military Clinical Central and Emergency Hospital – Pathology Department, Bucharest, Romania

ABSTRACT

Thyroid carcinomas are the most common type of endocrine neoplasia. They represent approximately 1% of all new cancer diagnoses each year, and the rate of new cases is increasing.

We report the case of a 54 year old man admitted to our department for a giant right anterolateral cervical tumor, measuring about 15 cm in diameter, diagnosed by fine-needle biopsy as follicular thyroid carcinoma. We performed a total thyroidectomy and the histological evaluation established the diagnosis of follicular variant of papillary thyroid carcinoma.

The paper refers to the etiopathogenesis, clinical symptoms, diagnosis treatment and prognosis of well-differentiated thyroid carcinoma.

Key words: thyroid carcinoma, papillary carcinoma, follicular variant, giant tumor

INTRODUCTION

Thyroid carcinoma is the most common type of endocrine neoplasia. They represent approximately 2% of all new cancer diagnoses each year (1), and the rate of new cases has been increasing in the last decades (2). Thyroid carcinomas are divided histologically into: papillary carcinoma, follicular carcinoma, medullary carcinoma and anaplastic carcinoma. Papillary carcinoma is the most common thyroid malignancy, representing nearly 80% of all cases (3). The most common morphological subgroups of papillary carcinoma are represented by: pure papillary thyroid carcinoma and its follicular variant, the later making up 23-41% of all papillary neoplasias (4). ❑

Address for correspondence:
Mihnea Davidescu, MD, 19 Sfantul Elefterie, District 5, Bucharest, Romania
email address: mihneadav@gmail.com

CASE PRESENTATION

We present the case of a 54-year-old man, residing in an iodine sufficient area, who was admitted to the Thoracic Surgery Department of the Emergency Central Military Hospital with a firm, painless right anterolateral cervical tumor, measuring about 15 cm in diameter (FIGURE 1). The tumor appeared two years before as a small nodule, which gradually grew to this giant size.

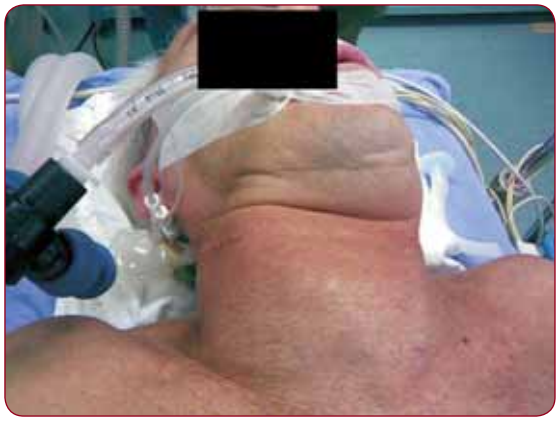

FIGURE 1. Giant right anterolateral cervical tumor – preoperative aspect

A fine needle biopsy performed two months prior to the patient's admission to our clinic indicated a diagnosis of follicular thyroid carcinoma.

Blood laboratory tests showed normal levels of T3 – 0,9 ng/ml (0.49-20.2ng/ml) and T4 – 44nmol/ml (44-108nmol/ml) and a slightly decreased TSH level of 0.49 μU.I./ml (0.54 – 5.7 μU.I./ml). Bronchoscopy revealed left lateral deviation of the trachea without infiltration and indirect laryngoscopy showed vocal cords of normal aspect and mobility.

Thyroid ultrasonography described a grossly enlarged right thyroid lobe occupied by a 3.9/3.2 cm, hypoechogenic macronodule with microcalcifications and intranodular hypervascularity which displaced the trachea and a hypoechogenic micronodular left lobe with another nodule of 1.1/0.3 cm.

Computed tomography revealed a highly vascular cervical tumor originating from the thyroid gland which compressed the right carotido-jugular vascular bundle and displaced the trachea and esophagus to the left (FIGURE 2).

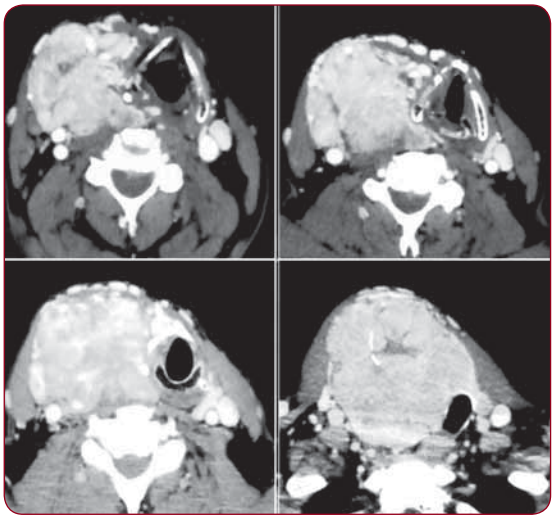

FIGURE 2. CT – A highly vascular thyroid tumor

We performed a Kocher cervicotomy and found the right thyroidian lobe greatly increased in size and entirely occupied by a firm, polylobular tumor of 14/8/6 cm, with ill-defined margins; the left lobe was slightly enlarged and polynodular. The tumor was very well vascularized, posing great technical difficulties during the dissection. The small vessels, but with great vascular flow, were sealed with LigaSure. The infiltrated external jugular vein was dissected and ligated. Afterwards the large vascular pedicles were ligated and divided starting with the right thyroid lobe (FIGURE 3). Resection of the left, smaller lobe, which proved adherent to the surrounding tissues, made up the second stage of the operation. Thus, total thyroidectomy was performed with the preservation of the recurrent laryngeal nerves and of the parathyroid glands (FIGURE 4).

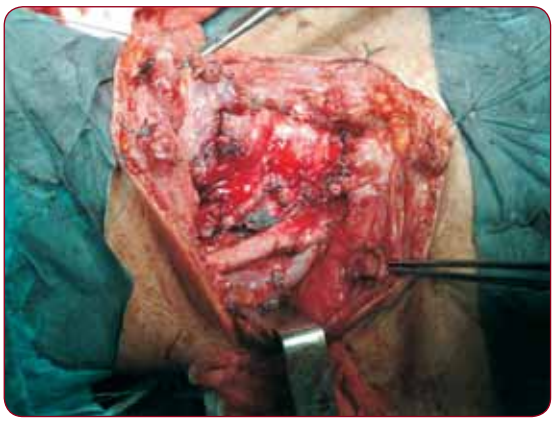

FIGURE 3. Intraoperative view after removal of the specimen.

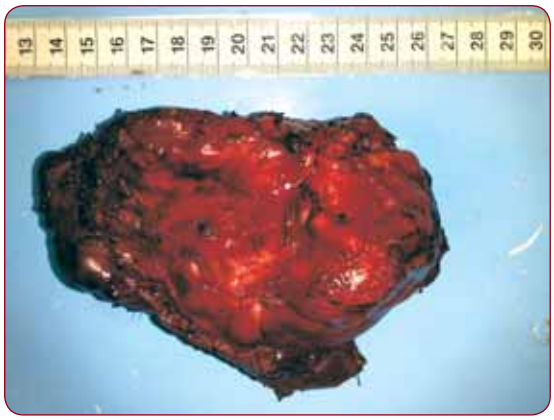

FIGURE 4. Surgical specimen

The tissue specimens were fixed in formalin, embedded in paraffin, sectioned at 4 microns, and stained with hematoxilin eosin.

On microscopic examination the right thyroid lobe presented tumoral nodules composed of small to medium sized, irregularly-shaped follicles. They contained a variable amount of hypereosinophilic and scalloped colloid and were lined by cuboidal cells with the characteristic nuclei of papillary thyroid carcinoma: enlarged, clear and ground glass appearence (FIGURES 5, 6). There was no evidence of papillary structures and psammoma bodies. Areas of capsular and vascular invasion were present (FIGURES 7, 8). All these microscopic findings were characteristic of the follicular variant of papillary thyroid carcinoma diagnosis.

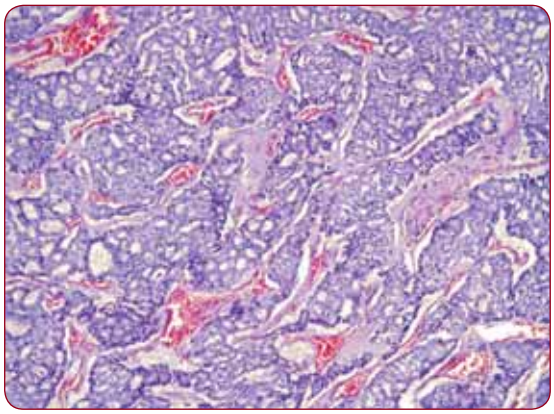

FIGURE 5. Hematoxilin-eosine stain, Ob. 10x. Follicular variant of papillary thyroid carcinoma of the right lobe.

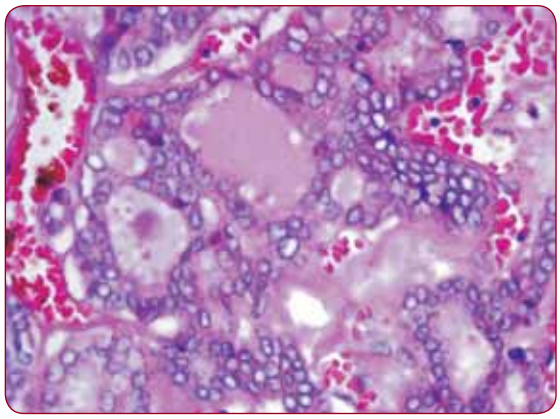

FIGURE 6. Hematoxilin-eosine stain, Ob. 40x. Follicular variant of papillary thyroid carcinoma of the right lobe – clear nuclei with longitudinal grooves.

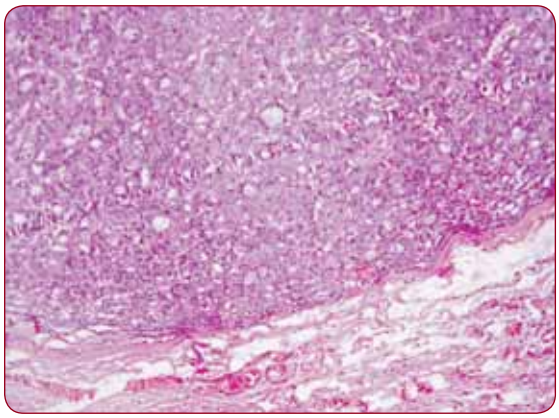

FIGURE 7. Hematoxilin-eosine stain, Ob. 10x. Capsular invasion

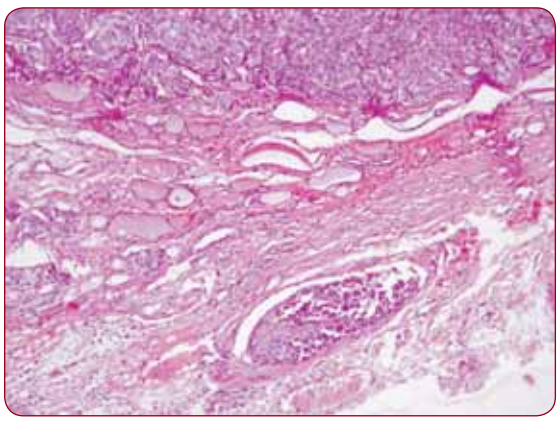

FIGURE 8. Hematoxilin-eosine stain, Ob. 10x. Intravascular carcinomatous invasion.

The left thyroid lobe presented papillary microcarcinoma, measuring 1cm in diameter, and showed papillary structures covered by epithelial

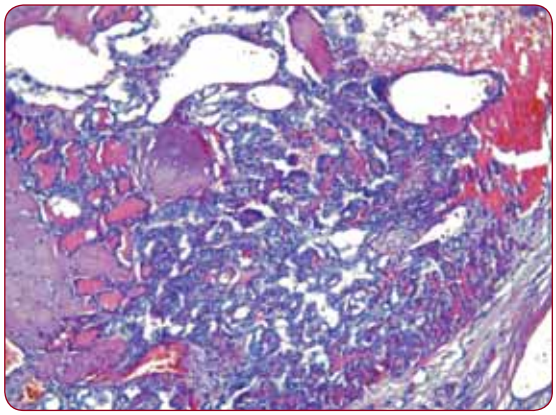

FIGURE 9. Hematoxilin-eosine stain, Ob. 10x. Occult papillary carcinoma of the left thyroid lobe.

cells with the characteristic nuclear features described above, and a hyalinized stroma (FIGURE 9).

Postoperatively the patient had normal phonation and an uneventful recovery. He was discharged 3 days after surgery. Thyroid-suppression therapy and radioiodine treatment were recommended.

Unfortunately the patient failed to present at follow-up. ❑

DISCUSSIONS

Although thyroid nodules are frequently encountered during routine palpation of the neck or during echography (1 in 5 adults) (1), the incidence of thyroid cancers is relatively low, accounting for only 1.5% of all cancers in adults and 3% in children (5) and the mortality rate hovering under 0,5% (1).

Papillary carcinoma and follicular carcinoma are considered well-differentiated thyroid carcinomas, together they adding up to 95% of all thyroid cancers. Although low dietary intake of iodine does not increase the overall incidence of thyroid cancers, it does increase the ratio of follicular carcinomas to papillary carcinomas. The latter's incidence drops from 85% to 55% in this setting (1).

The mean age at presentation, for the patients with papillary carcinoma, is 34-40 years old. It is three times more frequently encountered in women.

Of the etiological factors responsible for thyroid carcinomas the most documented is radiation exposure. This was observed in children exposed to radiation after the nuclear bombings in Hiroshima and Nagasaki during World War II and later after the accident at Chernobyl. An increased incidence was also observed in patients who received radiation therapy for benign disorders (acne, adenotonsillar hypertrophy, cervical tuberculosis) in the first half of the 20th century (5), or for other cervical neoplasias. Radiation exposure from imaging studies does not appear to increase the risk of developing thyroid cancers (3), (5). Radioiodine therapy or high-dose external-beam radiation therapy does not appear to increase the risk of papillary thyroid carcinoma. A family history of polynodular goiter is associated with a two fold increase in the risk of thyroid cancer and a family history of thyroid carcinoma can be correlated with a threefold increase (1).

Although it has well-differentiated characteristics, papillary carcinoma may invade surrounding structures: the trachea, producing symptoms and signs ranging from hemoptysis to airway obstruction, the recurrent laryngeal nerve, producing dysphonia and the esophagus, producing dysphagia (3). Papillary carcinoma has a propensity to invade lymphatics with the development of lymph node metastases, while distant metastases rarely occur (5). It frequently presents as a multifocal process. The follicular variant of papillary thyroid carcinoma has a similar evolution, with multiple tumor foci present in both lobes, lymphatic invasion and nodal metastases and rare hematogenous spread (6). Multifocality in papillary microcarcinoma is reported in 20% to 47% of cases (7).

In our case the carcinoma was also multicentric with a large tumor entirely occupying the right thyroid lobe and tumor nodules in the left lobe. A special aspect of this case was the giant size reached by the tumour, suggesting dedifferentiation to anaplastic carcinoma although no such features were found on the histopathological examination; we also did not find cervical adenopathies. Molecular analysis of multifocal papillary thyroid carcinoma, including microcarcinomas, can be used to separate independent nodules from intrathyroid metastasis of thyroid carcinoma (7).

In the follicular variant of papillary thyroid carcinoma the papillary architecture is absent, though the specific nuclear features of papillary thyroid carcinoma – empty ground-glass appearance with nuclear grooves and pseudoinclusions – are preserved (4,8).

Thyroid carcinoma most commonly manifests as a painless thyroid nodule or tumor.

Some patients may present with dysphonia if the recurrent laryngeal nerve is involved, dyspnea in tracheal involvement, dysphagia if the esophagus is compressed or invaded. Usually, the patients do not present signs of hyper or hypothyroidism.

Ultrasonography is the imaging study of choice in the evaluation of thyroid nodules. It is a noninvasive, inexpensive study, it can identify nodules up to 2-3 mm in diameter, as well as microcalcifications and it may be used to guide a fine-needle aspiration biopsy. However, the drawback of this imaging modality, is its limited ability to distinguish between malignant and benign nodules. The presence of intranodular microcalcifications, a hypoechogenic pattern without posterior attenuation, the absence of a peripheral halo, intranodal hypervascularity, irregular borders and regional lymphadenopathy are all ultrasonographic features suggestive of malignancy (1,2).

The fine-needle aspiration biopsy (FNAB) is considered the best first-line diagnostic procedure for thyroid nodules. The technique is easy to perform, inexpensive and it causes few complications. In uninodular lesions the sensitivity of the procedure is 80%, the specificity is near 100% and the false-negative and false-positive rates are less than 6% (5). Although FNAB is considered the most accurate diagnostic procedure for papillary carcinoma, its accuracy in subtyping the variants of papillary carcinoma, especially the follicular variant, is doubtful. Tissue architecture has the most important role in establishing a differential diagnosis between papillary carcinoma subtypes but it can be destroyed during sampling or the obtained specimen may be too small (8). Total thyroidectomy is recommended when cytology raises any suspicion of papillary thyroid carcinoma (2).

In our case the preoperative cytologic diagnosis obtained by FNAB was that of follicular thyroid carcinoma but the postoperative histological diagnosis was that of the follicular variant of papillary thyroid carcinoma. Although cytology alone can not distinguish between malignant and benign follicular nodules (only a quarter of the patients with follicular cytology actually had a cancer) (9) in our patient the probability of a carcinoma was high because of the giant size of the tumor.

Computed tomography or magnetic resonance imaging can be used to evaluate local extension in large tumors or to assess the presence of distal metastases. They are not routinely indicated (2). The use of iodinated contrast agents should be avoided in patients with possible thyroid carcinoma, as it may interfere with the postoperative radioiodine therapy.

Thyroid scintigraphy allows the determination of the functional status of thyroid nodules: hyperfunctioning nodules, also called "hot" nodules because they pick up radioiodine, make up to 90% of cases and have a low risk of malignancy; whereas nonfunctional "cold" nodules make up for the rest 10%. 5-8% of the latter harbor malignancy (1). Therefore, radioiodine scans are not helpful in the routine evaluation of thyroid nodules, their role being replaced by the fine-needle aspiration biopsy. They are useful to confirm the functional nature of a nodule when TSH is low or undetectable (2) and in the postoperative evaluation of residual thyroid tissue, tumor recurrence or the appearance of metastasis.

The thyroid function tests are not specific for thyroid cancer. The Determining the serum thyroid-stimulating hormone (TSH) concentration allows evaluation of hyper-, hypo- or normo-thyroidism. Low TSH values are indicative of autonomously functioning nodules, which are typically benign. However, the benign or malign character of a nodule cannot be determined on the basis of TSH levels.

A preoperative laryngoscopy is performed in order to evaluate the mobility of the vocal chords. Bronchoscopic evaluation is mandatory if tracheal involvement is suspected.

Surgical excision is the main therapy for well-differentiated thyroid carcinoma. However, there is no consensus about the extent of resection. Total thyroidectomy is the procedure with the most supporters. It reduces the risk of local recurrence, it facilitates postsurgical radioiodine therapy and follow-up and has low morbidity (2). The presence of lymph node metastases calls for cervical lymphadenectomy. Routine lymphadenectomy is not indicated because postoperative radioiodine therapy effectively treats lymphatic micrometastases (3).

Giant thyroid tumors pose great surgical problems because of the proximity of large vessels and other important structures and of the compression and dislocation of the trachea, esophagus and recurrent laryngeal nerves. As the tumor was highly vascularized the use of the LigaSure device greatly reduced operating time.

Patients receive postsurgical suppressive levothyroxine therapy in order to inhibit TSH production and to prevent hypothyroidism. Well-differentiated thyroid carcinomas are TSH sensitive and take up iodine. Low serum TSH levels lead to a reduction of tumoral growth and recurrence rates. TSH levels must be maintained around 0.1 mU/L (2).

Radioiodine is taken up and concentrated in normal or malignant thyroid tissue, this process is at the basis of metastasis and recurrence detection by scintigraphy and of radioiodine treatment. Radioiodine therapy is indicated 4-6 weeks after surgery. A hypothyroid state must be induced to obtain high TSH levels, over 30 mUI/L, which will stimulate iodine uptake by thyroid tissue. Replacement with thyroxine (T4) will be discontinued for 4 weeks, or for 2 weeks in the case of triiodothyronine (T3). An alternative is the use of recombinant human TSH (Thyrogen) (10). The use of whole-body scanning before ablation is controversial because of the stunning effect on the subsequent uptake of therapeutic radioiodine and the fact that the postirradiation scan is much more sensitive than the diagnostic one (2). A post-ablation scan must be performed 3–5 days later because it may reveal initially inapparent metastases. Thyroid hormone replacement therapy is reinstated after radioablation. All patients with well-differentiated thyroid carcinoma should receive radioiodine therapy with the exception of those under 21 years of age, without previous percutaneous radiation to the neck and unifocal microcarcinoma (less than 1cm in diameter) (1), (10).

The patients will be monitored every 6-12 months postoperatively with serum thyroglobulin measurements with or without radioiodine scanning. Thyroglobulin is a useful marker of tumor recurrence, but only after total thyroid ablation. As in postoperative scintigraphy, thyroglobulin determination is performed at high TSH values (11). Levels under 1ng/ml in the absence of serum antithyroglobulin antibodies suggest complete remission (12). The development of new ultrasensitive assays with a cut-off value of 0.1 ng/ml permits the evaluation of the thyroglobulin levels without TSH stimulation but at the cost of a lower specificity (12).

Recurrences are treated with surgical excision whenever possible or with radioiodine. External-beam radiotherapy is not routinely indicated in patients with locally invasive tumors (13). It may be used for dedifferentiated tumors that do not concentrate iodine. Chemotherapy is reserved for progressive tumors which show no response to other treatment modalities (12).

Prognostic factors in well-differentiated thyroid carcinomas are:

- age: patients under 45 years of age have a better prognosis,
- sex: the mortality rate is twice as high in men as for women,
- stage of the disease: tumor size of more than 4cm, lymph node metastasis (14) or distant metastasis, invasion of surrounding tissues worsen the patient's prognosis.

The survival rate of patients with papillary thyroid carcinoma is at least 95% with aggressive treatment (5). ❑

INSTEAD OF CONCLUSION

The presented case is special due to the giant size of the tumor, the long period of time (two years) between the emergence of the tumor and hospital presentation, which allowed reaching of this tumor volume, worsened the patient's prognosis and caused great surgical difficulties. This once more emphasizes the necessity and importance of a better medical education of the general population in order to make consulting a physician at the first signs of disease – and not in very advanced stages, as it often happens – more likely.

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