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Rare Metastases in Thyroid Cancer

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Abstract: Introduction: Papillary thyroid carcinoma is the most common endocrine malignancy worldwide, with a rate of regional metastasis in more than 50% of patients and distant metastasis up to 10%, the most frequent being lung and bone, with the appearance of extremely rare skin lesions, in which the overall survival prognosis decreases at 5 years when these lesions are present, even more so in patients over 45 years of age. Clinical case: We present a 64-year-old female patient with classic papillary thyroid carcinoma of 1-year evolution, with atypical findings such as intratumoral hemorrhage observed when performing fine-needle aspiration puncture, requiring drainage until the time of surgery due to persistence of bleeding. Additionally, the patient also developed a metastatic lesion in the neck region, located 2 cm below the primary tumor and the puncture area, which was histologically confirmed. The treatment used was tumor and metastatic surgical resection, along with right cervical and level VI dissection, followed by postoperative radioactive iodine ablative therapy, achieving satisfactory results. Discussion: After the development of cutaneous metastasis from thyroid carcinoma, patient survival ranges from 1 month to 7 years, with a mean of 19 months. The exact mechanism of this metastatic spread remains unclear, although current hypotheses suggest that both lymphatic and hematogenous dissemination may contribute to this pattern of neoplastic proliferation.

Key words: papillary carcinoma; metastasis; skin; hemorrhage

1. Introduction

Thyroid cancer is well known for representing the highest percentage of malignant neoplasms of the endocrine system. According to the American Cancer Society (2024), an estimated 44,020 new cases are expected in the U.S., with a higher incidence in the female sex and an estimated 2,170 deaths. In Latin America, incidence rates range from 0.01% to 0.5% per 100,000 inhabitants, with Argentina having the highest prevalence [1, 2]. Fortunately, more than 90% correspond to differentiated thyroid carcinomas, of which papillary carcinoma is the most common, with an overall 5-year survival rate of more than 90% to 95% [3, 4]. Slow and progressive growth has been described, with a less aggressive development than the rest of these neoplasms, with regional metastasis, known as cervical lymph node dissemination, occurring in more than 50%. However, distant metastases are usually sporadic, occurring in 5-10% of cases, and are extremely rare in the skin,

since the most common sites of distant dissemination are the lung and bone. The 3.5-year survival prognosis decreases to 50%, and is even more associated with patients over 45 years of age [5]. In addition to this unusual finding of cutaneous metastasis, bleeding differentiated thyroid tumors at the time of diagnosis have not been described. This finding is reported in degenerative nodules with intranodular hemorrhage, which is attributed to altered blood supply and subsequent infarction and necrosis [6].

These tumors are generally asymptomatic and usually present with signs and symptoms when they reach a significant tumor size. They present with airway compression symptoms such as dysphagia or dysphonia secondary to vocal cord paralysis. These symptoms are determined during preoperative laryngoscopy to occur in 0% to 8% of patients with thyroid cancer and are associated with locally advanced disease. Approximately 10% to 15% of cases exhibit extrathyroidal extension, with the most commonly involved anatomical sites being: prethyroid muscles (53%), recurrent laryngeal nerve (47%), trachea (30%), esophagus (21%), and larynx (12%). Thus, we present an unlikely clinical case due to its clinical presentation and biological behavior.

2. Clinical Case

A 64-year-old female patient from Mérida - residing in Caracas, Capital District, worked as an administrator. She had a history of infiltrating, ulcerated, moderately to well-differentiated adenocarcinoma of the right colon, treated with oncologic resection and adjuvant chemotherapy in 2016 (currently disease-free). With no significant medical history or tobacco use, she now presents with a progressive, painless, right cervical mass (related to the thyroid gland) persisting for 1 year, accompanied by sporadic dysphonia. She is being evaluated in the head and neck oncologic surgery consultation at La Trinidad Teaching Medical Center in March 2024. Physical examination revealed a 6 × 7 cm, irregularly bordered, well-defined, indurated mass in the anterior cervical region, mobile on swallowing, with overlying skin discoloration (Figures 1 and 2). Ultrasound identified bilateral inferior jugular lymph nodes - rounded, with loss of fatty hilum, measuring 0.5 - 1.2 cm (Figure 3). Additionally, a < 0.5 cm papule was noted 3 cm caudal to the primary lesion, along with mild dysphonia. Chest X-ray showed no abnormalities (Figure 4). Contrast-enhanced neck CT revealed a 6 cm (CC - cephalocaudal) × 6 cm (T - transverse) × 5.5 cm (AP - anteroposterior) heterogeneous space-occupying lesion in the right thyroid lobe, containing linear hyperdense areas suggestive of vascular involvement (Figure 5). The arterial phase showed irregular and heterogeneous uptake, with severe displacement of the trachea and esophagus to the left (Figure 6-7), as well as displacement of the carotid artery and internal jugular vein without erosion of the thyroid cartilage. Multiple lymphadenopathy images were observed at lymph node levels II, III, and V on the right, ranging from 1 to 1.5 cm (Figure 8).

In view of the clinical and imaging findings, it was decided to perform ultrasound-guided fine needle aspiration, obtaining dark blood content (Figure 9), which was sent for cytology and cell block (Figure 10). This was complemented by a biopsy with a 16G Trucut needle of the solid component. Given the persistence of blood content, a decision was made to place a Blake #19 drain, although the output of blood content persisted. The results were unsatisfactory due to necrotic content. Calcitonin levels were requested, which were found to be 2.0 pg/ml (within normal ranges). The patient was taken to the operating table where the drain was removed (Figures 11-12), and a peri-drainage skin resection was performed + total thyroidectomy + cervical dissection of levels II, III, IV, V on the right + bilateral level VI dissection (Figure 13) + skin resection of the indurated area located lower than the incision area + extemporaneous biopsy, which was positive for malignancy. Intraoperative findings revealed a 7 × 5 cm thyroid tumor with irregular borders that macroscopically involved the entire right thyroid lobe. The lesion demonstrated mixed cystic and solid components (Figure 14) and demonstrated adhesions to without frank invasion of the trachea, common carotid artery, and internal jugular vein. Multiple brownish

lymph nodes (1 cm in diameter) were identified in right levels IV and VI. Significant tracheal deviation to the left was observed secondary to mass effect from the tumor. Additionally, a 0.3 cm indurated subcutaneous nodule with well-circumscribed borders was noted 3 cm inferior to the cervicotomy incision site (Figure 15). The patient progressed satisfactorily in the postoperative period (Figure 16), and histopathological results were received, concluding:

- Total thyroidectomy: classic papillary carcinoma occupying 80% of the gland, with areas of necrosis and extensive recent and old hemorrhage measuring 5 × 4 cm, without capsule infiltration, angiolymphatic invasion, moderate stromal desmoplasia with areas of hyalinization and dystrophic calcifications, and resection margins free of lesions.
- Right lymph node dissection: 2/14 lymph nodes with metastatic papillary carcinoma.
- Level VI lymph node dissection: 8/8 lymph nodes with metastatic papillary carcinoma.
- Neck skin: Metastatic papillary carcinoma, completely resected.

Based on the findings, the patient's MACIS score was 10.62 points. According to AMES criteria, the case was classified as high-risk with stage IVB disease (Figure 17). Nuclear medicine evaluation was requested, where the decision was made to administer 100 mCi of radioactive iodine. The patient was kept under continuous surveillance and remained free of locoregional and distal disease.

Figure 1. Physical examination.

Figure 2. Tumor on physical examination.

Figure 3. Cervical ultrasound - inferior jugular nodes.

Figure 4. Poster-anterior chest X-rays.

Figure 5. Contrast-enhanced CT scan of the neck, axial section - right thyroid lobe tumor.

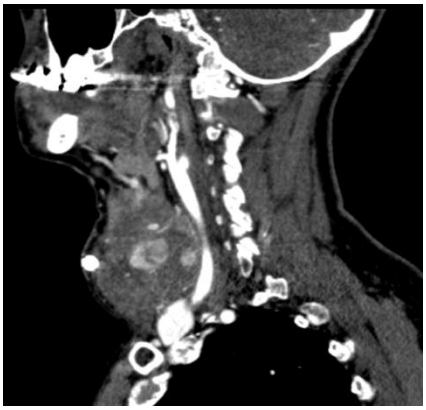

Figure 6. Compression of the right carotid artery.

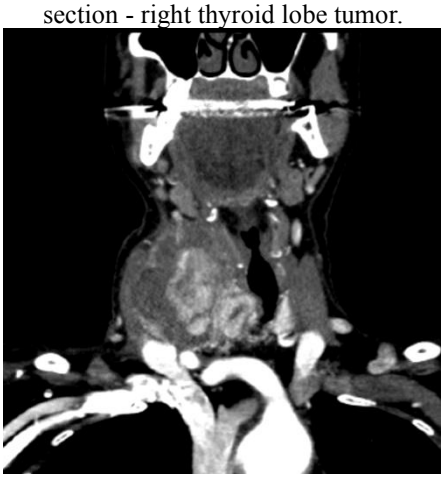

Figure 7. Contralateral displacement of the trachea.

Figure 8. Bilateral jugular lymph nodes.

Figure 9. Blood secretion from fine needle aspiration puncture.

Figure 10. Cytology sample and cell block.

Figure 11. Cervical drainage.

Figure 12. Cervical drain removal.

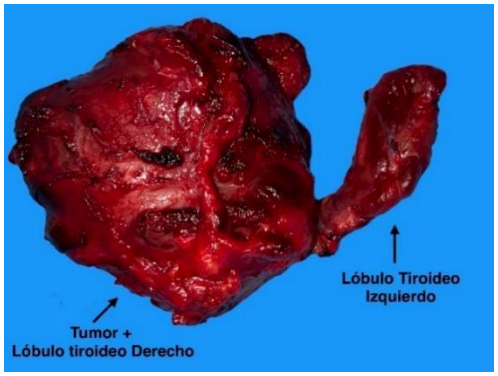

Figure 13. Surgical specimen.

Figure 14. Right cervical dissection.

Figure 15. Resection of microscopic cutaneous metastasis.

Figure 16. Immediate postoperative period.

TNM	T3a(m)N1bM1
Stage	IVB
MACIS (7 high risk)	10.62
AMES (≤ 4 low risk; ＞ 4 high risk)	11.2
AMES	High risk

Figure 17. Risk according to the American Thyroid Association.

3. Discussion

Although mortality rates associated with papillary thyroid carcinoma appear to have remained stable in recent decades, with a survival rate for localized papillary carcinoma (> 99.5%) and regional metastasis (99%), it is noteworthy that when distant metastasis occurs, the survival rate decreases significantly to 74% [1], especially considering the rare metastatic nature of the skin, as it is commonly associated with breast, lung, melanoma, and other cancers. In contrast, some cases have been reported where the most common anatomical location in skin associated with thyroid carcinoma is the scalp [3-8]. However, the real challenge facing these patients is not only the presence of the lesion itself, but also the high level of clinical suspicion due to its resemblance to benign cutaneous lesions. Physical examination is crucial for diagnosis and treatment. As presented in this clinical case, the lesion was practically imperceptible both during clinical examination and imaging studies, with a clinical presentation that can go unnoticed.

Dahl et al. established that survival after the development of cutaneous metastasis from thyroid carcinoma ranges from 1 month to 7 years, with a mean of 19 months. In a systematic review of rare metastases in patients with differentiated thyroid carcinoma, the mean overall survival of 94 patients from 77 studies was 60 months [10], compared to the publication of Jee et al., in which the overall survival was 58.3 months [11]. The mechanism underlying this dissemination route remains poorly understood. While some hypotheses suggest that lymphatic and hematogenous spread

may account for this behavior in neoplastic proliferation [3], others propose it could result from needle seeding during fine needle puncture. However, in this particular case, the lesion was located distant from the resected puncture area adjacent to the tumor specimen [13]. Some theories describe genetic mutations associated with the aggressive behavior presented, such as mutation of the BRAF V600E gene or mutation of the tyrosine kinase receptor, without reaching a certain conclusion of the pathogenetic mechanism, but it is expected that in the future specific strategies for genetic analysis can be developed, in order to establish targeted therapies that improve disease-free survival rates.

Recently, Jiang W. et al. described that platelet-activating factor acetyldihydrolase 1B3 (PAFAH1B3), known as an autocrine growth factor involved in cell reproduction processes and a proinflammatory and angiogenic lipid mediator, was deregulated in some carcinomas, potentially triggering tumor development, progression, and more aggressive behavior in papillary thyroid carcinoma.

Optimal treatment should be based on complete surgical resection of the lesion and radioiodine, with or without radiotherapy, with rigorous clinical, biochemical, and imaging follow-up every 3 months for the first 3 years, to detect early recurrences [14]. However, the prognosis of these patients is difficult to predict, as it is usually associated with the stage of the primary thyroid tumor, simultaneous distant metastases in other organs, and refractoriness to radioactive iodine therapy. In addition, the atypical behavior of intratumoral hemorrhage is an interesting finding, and may be related to the marked growth of this tumor over the past year; however, it is usually associated with pain and symptoms of compression, which were not present in this patient. The mechanism by which bleeding occurs in malignant tumors is not well described, although in benign nodules, spontaneous intranodular hemorrhage is suggested to be associated with the rupture of small blood vessels located within the solid component of the lesion. A retrospective study of patients with benign partially cystic thyroid nodules, conducted between September 2017 and December 2019, related the presence of abundant blood supply, margin of the solid portion and spongiform content, associated with spontaneous intranodular hemorrhage [17]. Therefore, it is suggested that future multicenter and systematic studies should be increased to determine the origin of this finding, as well as to delve into the diagnosis, management, and treatment of extraordinary metastases of differentiated thyroid carcinoma, in order to increase overall survival and disease-free survival in our patients.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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