DOI: 10.30928/2527-2039e-20202820

PRIMARY MUCOEPIDERMOID CARCINOMA OF THE THYROID

CARCINOMA MUCOEPIDERMOIDE PRIMÁRIO DE TIREOIDE

Alexandre Andrade Sousa[1]; Carolina Belfort Resende Fonseca[1]; Gustavo Meyer de Moraes[1]; Patrícia Salomé Gouvêa Braga[2]; Tiago Vencato da Silva[3]; Igor Lima Fernandes[3].

RESUMO

Introdução: O carcinoma mucoepidermoide (CME) é geralmente encontrado nas glândulas salivares, mas há relatos de envolvimento primário de outros órgãos. O primeiro caso dessa neoplasia na topografia da tireoide foi descrito em 1977. Atualmente, há 53 casos relatados na literatura, incluindo os dois casos relatados neste estudo. O MEC da tireoide é raro e geralmente tem um bom prognóstico. **Descrição do caso**: Neste estudo, apresentamos o relato de dois casos clínicos de CME da tireoide: uma variante não esclerosante e uma variante esclerosante com eosinofilia. Ambos ocorreram em mulheres com diagnóstico prévio de tireoidite de Hashimoto. **Discussão:** Considerando o pequeno número de casos publicados, uma revisão completa da literatura de todos os casos publicados foi realizada e relacionada à nossa experiência. Os tumores raros da glândula tireoide devem sempre ser considerados como um possível diagnóstico nos nódulos tireoidianos de Bethesda III.

Descritores: Neoplasias da Glândula Tireoide. Carcinoma. Carcinoma Mucoepidermoide. Glândula Tireoide.

ABSTRACT

Introduction: Mucoepidermoid carcinoma (MEC) is usually found in the salivary glands, but there have been reports of the primary involvement of other organs. The first case of this neoplasm in thyroid topography was described in 1977. Currently, there have been 53 cases reported in the literature, including the two cases reported in this study. Thyroid MEC is rare and usually has a good prognosis. **Case description**: In this study,we present a report of two clinical cases of thyroid MEC: a nonsclerosing variant and a sclerosing variant with eosinophilia. Both occurred in women who had a previous diagnosis of Hashimoto's thyroiditis. **Discussion**: Considering the small number of published cases, a complete literature review of all published cases was performed and was related to our experience. Rare tumors of the thyroid gland should always be considered as a possible diagnosis in Bethesda III thyroid nodules.

Keywords: Thyroid Neoplasms. Carcinoma. Carcinoma, Mucoepidermoid. Thyroid Gland.

INTRODUCTION

Mucoepidermoid carcinoma (MEC) is a malignant epithelial neoplasm characterized by the presence of epidermoid cells and cells producing mucin and is usually found in the salivary glands. In the literature, there have been descriptions of other organ involvement, such as the larynx, trachea, thyroid, breast, bones and esophagus[1-3]. In 1977, Rhatigan et al. described a thyroid neoplasm with squamous and glandular differentiation, establishing the structure for a category of mucoepidermoid carcinoma in the gland[3]. Thyroid MEC is rare and More prevalent in women. The average of the patients is 47 years, ranging from 10 to 91 years (Table 1). Hashimoto's thyroiditis occurs in 40% of cases and previous radiation from the neck in childhood has been documented in some cases described[1,4]. The prognosis is good in most cases, including when it comes to thyroid MEC. Lymph node involvement was described in 40% of all cases and distant metastases occurred in less than 16% (Table 1). Due to the rarity of neoplasms in thyroid topography, we describe in this study two cases of thyroid MEC; one was a sclerosing variant with eosinophilia, which is even rarer than the nonsclerosing variant[4,5].

[1]Faculdade de Medicina da UFMG, Departamento de Cirurgia - Belo Horizonte – MG - Brasil.
[2]Hospital Biocor Instituto, Patologia - Nova Lima - Minas Gerais – MG – Brasil.
[3]Bacchi Pathology Laboratory, Patologia - Botucatu - São Paulo – Brasil.

Table 1. Literature review of mucoepidermoid carcinoma of the thyroid[1,7-11].

All cases published in the literature - 53 cases	**N**
Sex – *53 cases described*	
Male	21 (39.6%)
Female	32 (60.4%)
Age– *53 cases described*	
Age range (years)	10 to 91
Average (years)	48.6
Disease extension – *46 cases described*	
Extrathyroid disease	11 (23.9%)
Metastasis	
Lymph nodes – *51 cases described*	21 (41.1%)
Distant – *45 cases described*	7 (15.5%)
Management – *45 cases described*	
Total thyroidectomy	29 (64.4%)
Subtotal thyroidectomy	12 (26.6%)
Radiotherapy	2 (4.4%)
Chemotherapy	1 (2.2%)
Radiotherapy and chemotherapy	1 (2.2%)
Follow-up time - *53 cases described*	
Variation	10 days – 22 years
Average	31 months
Patient status at follow-up – *40 cases described*	
Alive without disease	26 (65%)
Alive with disease	4 (10%)
Died of the disease	10 (25%)

CASE DESCRIPTION

Case 1

In 64-year-old female smoker with hypothyroidism, a nodule in the left lobe of the thyroid was detected. Ultrasound of the thyroid showed signs of chronic thyroiditis and a left lobe nodule measuring 1.5 cm x 1.0 cm x 0.6 cm with irregular margins and microcalcifications that was hypoechoic. Fine-needle aspiration puncture (FNAB) of the nodule revealed an amorphous smear that was slightly hemorrhagic, contained clusters of follicular cells with a Hürthle pattern, ovoid and pleomorphic nuclei, delicate chromatin and inconspicuous nucleoli in addition to squamous cells without atypia, polyhedral crystals and cellular debris. FNAB was compatible with dense thyroid cyst content, Bethesda class III. She underwent total thyroidectomy and left cervical-mediastinal lymphadenectomy.

In the macroscopic analysis of the surgical specimen, a thyroid measuring 6.5 cm x 5.5 cm x 2.0 cm and weighing 42.0 g was observed that was covered by a thin capsule and contained a grossly nodular, brown and firm lesion that measured 1.1 cm on the major axis and was located in the left lobe. The rest of the thyroid tissue showed a multinodular appearance and was light brown and firm. Ten lymph nodes with dimensions between 0.1 cm and 0.8 cm were isolated in the adipose tissue of the cervical-mediastinal lymphadenectomy.

Microscopy revealed a thyroid neoplasm consisting of cells with broad eosinophilic cytoplasm that were sometimes mucosecretory, had rounded and hyperchromatic nuclei, formed cystic areas filled with dense keratin, and had infiltrative blocks in the periphery. The morphological elements were compatible with an epithelial neoplasm and suggestive of mucoepidermoid carcinoma of the thyroid. There was an absence of extrathyroidal neoplastic extension and an absence of metastases in 10 (ten) regional lymph nodes. The surgical margins were clear.

Complementary exams with histochemistry (PAS – periodic acid-Schiff) and immunohistochemistry (cytokeratin AE1/AE3; TTF1 - thyroid/lung transcription factor 1; and p63 protein) corroborated the anatomopathological diagnosis of primary thyroid mucoepidermoid carcinoma (nonsclerosing variant, WHO 2017).

Case 2

In a 52-year-old female patient with hypothyroidism and nodular goiter, biopsy (FNAB) revealed Bethesda class III and Hashimoto's thyroiditis. She underwent total thyroidectomy.

In the anatomopathological study, macroscopy showed a thyroid measuring 4.5 cm x 3.5 cm x 1.0 cm and weighing 8.0 g. The gland had a nodular, light brown and firm tumor measuring 1.2 cm located on the isthmus. The rest of the thyroid tissue exhibited pale and irregular areas of increased consistency.

In histological analysis, the thyroid presented an epithelial neoplasm characterized by the proliferation of atypical polyhedral cells with squamous differentiation next to mucosecretory cells forming nests, trabeculae and small cysts. The stroma was sclerotic and infiltrated by lymphocytes, plasmocytes and eosinophils. The adjacent thyroid tissue exhibited changes consistent with Hashimoto's thyroiditis. There was no extrathyroidal neoplastic extension. The surgical margins were clear (Figure 1 and Figure 2).

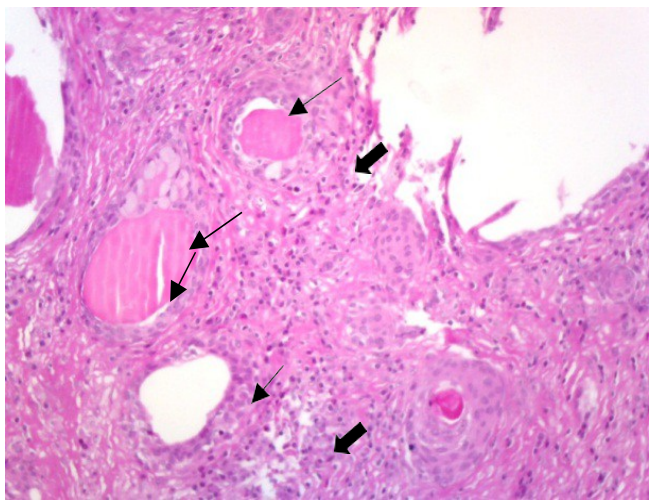

Figure 1. Mucoepidermoid carcinoma (MEC) showing mucinous tumor cells forming mucin-containing cysts. Hematoxylin-eosin (HE) photo micrografia, original magnification x 1.

Complementary exams of histochemistry (PAS - periodic acid-Schiff) and immunohistochemistry (cytokeratin AE1/AE3; cytokeratin 19; TTF1 - thyroid/lung transcription factor 1; and p63 protein) confirmed the suggested diagnosis of sclerosing mucoepidermoid carcinoma with thyroid eosinophilia (WHO 2017).

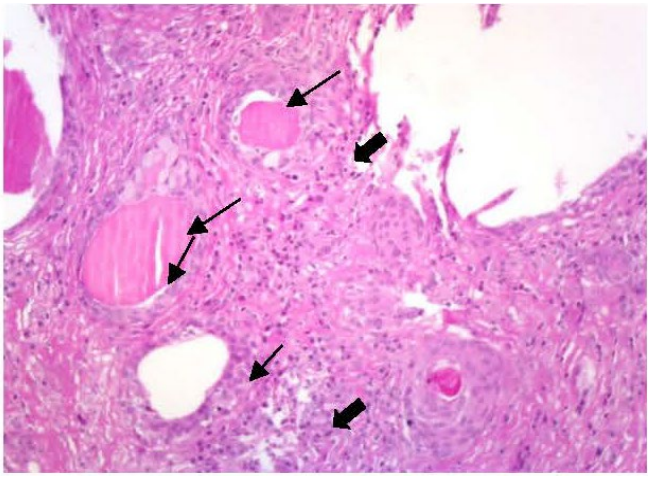

Figura 2. MEC showing intermediate cells nest (double arrow) with squamoid differentiation on the periphery (single arrow) and dense granulomononuclear inflammatory cells infiltrate. HE photo micrografia, original magnification x 100.

DISCUSSION

MEC is a malignant epithelial neoplasm characterized by the presence of epidermoid cells and cells that produce mucin. MECs occur most commonly in the salivary gland. However, in the literature, there are descriptions of other organ involvement, including the thyroid[1,2]. MEC is responsible for less than 0.5% of thyroid neoplasms, and the first case was described by Rhatigan et al. in 1977[1,3].

Thyroid MECs are more prevalent in women (2:1), and the average age of the patients is 47 years, ranging from 10 to 91 years (Table 1). Hashimoto's thyroiditis occurs in 40% of cases, and previous radiation of the neck in childhood has been documented in some cases[1,4]. Such characteristics were present in both cases reported by our team. The etiology is unknown, and the metaplastic derivation of follicular cells is more likely than hypotheses of ectopic salivary gland and remaining thyroglossal duct[6].

Our patients were being treated for hypothyroidism. The literature also describes the possibility of euthyroid individuals. Metastases to regional lymph nodes are described in 40% of cases (Table 1), which did not occur in our experience, probably due to the early diagnosis and approach of suspected thyroid nodules. Distant metastases are rare, occur in less than 16% of cases, and occur mainly in the lungs and bones (Table 1)[6].

Thyroid MEC presents with squamous and glandular differentiation, establishing the structure for a type of mucoepidermoid carcinoma in the gland 3 with two histopathological variants (WHO, 2017): the nonsclerosing variant and sclerosing variant with eosinophilia[5]. These are differentiated by the presence or absence of an intensely fibrotic stroma[5,7]. In immunohistochemical analysis, MECs were positive for keratins, TTF1, thyroglobulin, PAX8, and p63. P-cadherin expression and E-cadherin abnormalities can also be seen in epidermoid areas[5,6]. In our experience, there was positivity for cytokeratins, TTF1 and p63, and the sclerosing variant with eosinophilia also showed positivity for cytokeratin 19, which did not occur in the nonsclerosing variant.

Total thyroidectomy is an important part of treatment for thyroid MEC and was performed by our team in both cases. Prophylactic neck dissection of level VI and VII was performed by the team in one case. Despite being a controversial measure, it is not refuted by the medical literature. The decision to perform prophylactic neck dissection was corroborated by the ultrasound results of intermediate suspicion. Radiotherapy and chemotherapy are mentioned in the literature as adjuvant therapies in advanced cases[1,7,8] and were not used in the treatment of our patients.

Finally, MEC is a neoplasm with a low degree of malignancy, indolent behavior, and a good prognosis in most cases. As stated, distant metastases are rare. Mortality due to tumor progression occurs in approximately 25% of patients and is usually associated with advanced age and poor differentiation and a late diagnosis[6]. Both patients reported by our team are undergoing clinical follow-up, with no signs or symptoms of disease.

Considering the rarity of this type of tumor in the thyroid gland, we believe that the diagnosis is always performed in the postoperative period when the surgical specimen is evaluated with histopathological examination. For this reason, it is important that the surgeon always considers the possibility of rare thyroid neoplasms for patients with preoperative Bethesda III cytopathological results.

Table 1 describes the literature review of all cases published to date.

CONCLUSION

Primary Mucoepidermoid Carcinoma of the thyroid is a rare malignant neoplasm, corresponding to less than 0.5% of all malignancies that affect the gland[1]. In this present study, two cases of different histopathological variants of this neoplasm in thyroid topography were reported. Both cases showed a favorable evolution, with no signs of lymph node involvement or distant metastasis.

REFERENCES

1. Le QV, Ngo DQ, Ngo QX. Primary Mucoepidermoid Carcinoma of the Thyroid: A Report of a Rare Case with Bone Metastasis and Review of The Literature. Case Rep Oncol 2019;12: 248-59.
2. Morais EF, Silva LP, Mororó ABG, Pinto EP, Taylor AM, Pinto LP et al. Intraosseous maxillary mucoepidermoid carcinoma: a rare case report. J. Bras. Patol. Med. 2019;55:540-9.
3. Rhatigan RM, Roque JL, Bucher RL. Mucoepidermoid carcinoma of the thyroid gland. Cancer 1977;39:210-4.
4. Raveendran Nair AKA, George NA, Kumar R, Sreekumar A, Jayasree K. Sclerosing mucoepidermoid carcinoma with eosinophilia of thyroid gland: Not so indolent a neoplasm?. Indian J Pathol Microbiol. 2018;61:242-4.
5. DeLellis RA, Lloyd RV, Heitz PU, Eng C, eds. World Health Organization Classification of Tumours. Pathology and Genetics of Tumours of endocrine organs. IARC Press: Lyon 2004.
6. Cameselle-Teijeiro J, Albores-Saavedra J, Baloch ZW, Sobrinho-Simões M, Wenig BM. Mucoepidermoid carcinoma. In: Lloyd RV, Osamura RY, Klöppel G, Rosai J, eds. WHO Classification of tumours of endocrine organs. 4th ed. Lyon: IARC Press; 2017. p. 117-8.
7. França SR, Caldas D, Junior AV, Oliveira CAB. Carcinoma mucoepidermóide de tireoide: relato de caso e revisão da literatura. Arq Bras Endocrinol Metab. 2006;50:968-76;
8. Sukumar JS, Sukumar S, Purohit D, Welch BJ, Balani J, Yan S, et al. Activating BRAF mutation in sclerosing mucoepidermoid carcinoma with eosinophilia of the thyroid gland: two case reports and review of the literature. J Med Case Rep. 2019;13: 385.
9. Baloch ZW, Solomon AC, LiVolsi VA. Primary mucoepidermoid carcinoma and sclerosing mucoepidermoid carcinoma with eosinophilia of the thyroid gland: a report of nine cases. Mod Pathol. 2000;13:802-7.
10. Jayakody NS, Faoury M, Fraser LR, Jogai S, Patel NN. Composite poorly differentiated mucoepidermoid carcinoma of the thyroid and follicular variant of papillary thyroid carcinoma. Report of a case and review of the literature. J Surg Case Reports. 2019;4:1–4;
11. Wiles AB, Kraft AO, Mueller SM, Powers CN. Sclerosing mucoepidermoid carcinoma with eosinophilia of the thyroid: Case report of a rare lesion with novel genetic mutation. Diagn Cytopathol. 2019;47:589-93.

Received in: 17/05/2020
Accepted for publication: 04/06/2020
Conflict of interest: no.

Mailing address:
Alexandre Andrade Sousa
E-mail: alexandradeccp@gmail.com