# Sclerosing Mucoepidermoid Carcinoma with Eosinophilia of the Thyroid with High-Grade Transformation

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*Transformação de Alto Grau em Carcinoma Mucoepidermoide Esclerosante com Eosinofilia da Tiroide*

Transformación de Alto Grado en Carcinoma Mucoepidermoide Esclerosante con Eosinofilia de Tiroides

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ABSTRACT

**Introduction:** Sclerosing mucoepidermoid carcinoma with eosinophilia of the thyroid is a rare malignant neoplasm, typically associated with chronic lymphocytic thyroiditis. It usually presents as a painless, slowly enlarging unilateral thyroid nodule, frequently mimicking a benign lesion. **Case report:** A 77-year-old woman presented a large fast-growing thyroid mass. Fine-needle aspirates rendered a diagnosis of atypia of undetermined significance. Histopathology revealed proliferation of solid and pseudoangiomatous nests of cells showing predominant squamous differentiation, with focal mucinous cells, in a sclerotic and eosinophil-rich stroma. Areas of high-grade morphology were observed. The tumor was diffusely positive for AE1/AE3, CK5/6, p63, and p40, and focally positive for CK7, CEA, and TTF1. Ki-67 was heterogeneous. The final diagnosis of sclerosing mucoepidermoid carcinoma with eosinophilia with high-grade transformation was established. Next generation sequencing panel showed high levels of *NTRK1* expression and copy number alterations on *VHL* gene *locus* of chromosome 3, with no other mutations or fusions known to occur in thyroid cancer. The patient had a local recurrence of the high-grade component, followed by lung and skull metastasis, and died from the disease. **Conclusion:** The current case is remarkable due to the high-grade transformation and aggressive clinical course. The features discussed herein intend to help the further characterization of sclerosing mucoepidermoid carcinoma with eosinophilia of the thyroid, especially its molecular background.
**Key words:** Thyroid Neoplasms/complications; Carcinoma, Mucoepidermoid; Thyroid Nodule; Immunohistochemistry.

RESUMO

**Introdução:** O carcinoma mucoepidermoide esclerosante com eosinofilia da tireoide é uma neoplasia maligna rara, tipicamente associada à tireoidite linfocítica crônica. Frequentemente se apresenta como um nódulo tireoidiano unilateral indolor e de crescimento lento, podendo simular uma lesão benigna. **Relato do caso:** Mulher de 77 anos apresentou uma grande massa tireoidiana de crescimento rápido. A punção aspirativa por agulha fina levou ao diagnóstico de atipia de significado indeterminado. A histopatologia revelou proliferação de ninhos celulares sólidos e pseudoangiomatosos, apresentando diferenciação escamosa predominante, com células mucinosas focais, em um estroma esclerosante e rico em eosinófilos. Foram observadas áreas de morfologia de alto grau. O tumor apresentou-se difusamente positivo para AE1/AE3, CK5/6, p63 e p40, e focalmente positivo para CK7, CEA e TTF1. O Ki-67 foi heterogêneo. Foi estabelecido o diagnóstico final de carcinoma mucoepidermoide esclerosante com eosinofilia com transformação de alto grau. O painel de sequenciamento de última geração mostrou altos níveis de expressão de *NTRK1* e alterações no número de cópias no *locus* do gene *VHL* do cromossomo 3, sem outras mutações ou fusões conhecidas no câncer de tireoide. A paciente apresentou recorrência local do componente de alto grau, seguida de metástases pulmonares e cranianas, e faleceu em decorrência da doença. **Conclusão:** O presente caso merece atenção em razão da transformação de alto grau e do curso clínico agressivo. As características aqui discutidas têm como objetivo auxiliar na caracterização mais aprofundada do carcinoma mucoepidermoide esclerosante com eosinofilia da tireoide, especialmente seu perfil molecular.
**Palavras-chave:** Neoplasias da Glândula Tireoide/complicações; Carcinoma Mucoepidermoide; Nódulo da Glândula Tireoide; Imuno-Histoquímica.

RESUMEN

**Introducción:** El carcinoma mucoepidermoide esclerosante con eosinofilia de la tiroides es una neoplasia maligna poco frecuente, típicamente asociada a la tiroiditis linfocítica crónica. A menudo se presenta como un nódulo tiroideo unilateral indoloro y de crecimiento lento, y puede simular una lesión benigna. **Informe del caso:** Mujer de 77 años presentó una gran masa tiroidea de crecimiento rápido. La punción aspirativa con aguja fina condujo al diagnóstico de atipia de significado indeterminado. La histopatología reveló proliferación de nidos celulares sólidos y pseudoangiomatosos, con diferenciación escamosa predominante y células mucinosas focales, en un estroma esclerosante y rico en eosinófilos. Se observaron áreas de morfología de alto grado. El tumor se presentó difusamente positivo para AE1/AE3, CK5/6, p63 y p40, y focalmente positivo para CK7, CEA y TTF1. El Ki-67 fue heterogéneo. Se estableció el diagnóstico final de carcinoma mucoepidermoide esclerosante con eosinofilia y transformación de alto grado. El panel de secuenciación de última generación mostró altos niveles de expresión de NTRK1 y alteraciones en el número de copias en el locus del gen VHL del cromosoma 3, sin otras mutaciones o fusiones conocidas en el cáncer de tiroides. La paciente presentó recidiva local del componente de alto grado, seguida de metástasis pulmonares y craneales, y falleció a causa de la enfermedad. **Conclusión:** El presente caso merece atención debido a la tranformación de alto grado y a su curso clínico agresivo. Las características aquí discutidas tienen como objetivo contribuir a una caracterización más detallada del carcinoma mucoepidermoide esclerosante con eosinofilia de la tiroides, especialmente su perfil molecular.
**Palabras clave:** Neoplasias de la Tiroides/complicaciones; Carcinoma Mucoepidermoide; Nódulo Tiroideo; Inmunohistoquímica.

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## INTRODUCTION

First described in 1991[1], sclerosing mucoepidermoid carcinoma with eosinophilia (SMECE) of the thyroid is a rare malignancy developing in a background of chronic lymphocytic thyroiditis[1]. With less than 100 cases reported to date[2], SMECE is currently classified by the World Health Organization as a thyroid tumor of uncertain histogenesis[2,3].

SMECE most commonly affects middle-aged euthyroid or hypothyroid women, arising as a painless, slow-growing nodular lesion in a unilateral thyroid lobe, usually mimicking a non-malignant lesion[4,5]. Histologically, it is characterized by strands, nests, and cords of squamous and mucous tumor cells admixed in a sclerotic stroma with dense lymphoplasmacytic infiltration and eosinophils[2,5,6].

The molecular background of SMECE is yet to be stablished, as well as prognostic and predictive indicators[2]. Regional lymph node metastases are seen in around 40% of patients[2], and 10-13% may develop distant metastases[7,8]. Long-term follow-up is advised[2] and high-grade transformation has been barely reported.

This report provides imaginological, histological, immunohistochemical, and molecular features of a rare case of SMECE of the thyroid with high-grade transformation. Ethical approval was obtained (CAAE (submission for ethical review): 02839212.4.0000.5149), in compliance with Directive 466/12[9] of the National Health Council (CNS).

## CASE REPORT

A 77-year-old woman presented to the head and neck surgeon in February 2024 complaining of a large, fast-growing goiter at the front of her neck. Clinical examination revealed a solid, lobulated nodule measuring 9.0 x 8.0 cm in the left lobe of the thyroid. She had a medical history of hypothyroidism and took Puran T4 (100 mcg/ daily), Omeprazole, and Zolpidem. Blood tests revealed the following results: D vitamin 21.8, thyroid-stimulating hormone (TSH) 0.01, free T4 1.47, calcium 1.27, parathyroid hormone (PTH) 58.8, and calcitonin 2.0, indicating subclinical hyperthyroidism. Doppler ultrasound of February 2024 showed an enlarged thyroid with heterogeneous parenchyma, and a well-defined, lobulated, hypoechoic nodule containing echogenic foci, with peripheral blood supply. The nodule measured 8.0 x 6.5 x 4.0 cm, with a volume of 110.6 $cm^3$, occupying the entire left lobe of the gland (TI-RADS 5). A contrast-enhanced computed tomography scan of March 2024 revealed an enlarged left thyroid lobe with heterogeneous texture, internal calcifications, and contralateral tracheal displacement, shown in Figure 1a.

Fine-needle aspirates (FNA) revealed a hemorrhagic background with numerous epithelioid cells arranged in both cohesive and loose collections, showing mild anisocytosis and nuclear pleomorphism, as well as prominent nucleoli, portrayed in Figure 1b. A small number of isolated lymphocytes and some multinucleated giant cells were also observed. The diagnosis was of atypia of undetermined significance (AUS-Nuclear), based on the Bethesda system, being established in March 2024.

In April 2024, the patient underwent a left lobectomy and left cervico-mediastinal lymphadenectomy. The surgery was uneventful, no surgical drain was placed, and the patient had a one-day hospital stay. She experienced left vocal cord paresis that improved 40 days after surgery.

The gross examination of the tumor revealed a firm, solid, whitish lesion with calcifications, measuring 6.8 x 5.1 x 4.8 cm, without gross invasion of strap muscles, portrayed in Figure 1c. Histopathology is shown in Figure 2 and revealed proliferation of solid and pseudoangiomatous nests of cells showing squamous differentiation, areas of keratinization and focal mucinous cells, in a fibrotic stroma with abundant eosinophils. Additional findings included foci of high-grade morphology, with nuclear pleomorphism, high mitotic index (10 per $2mm^2$) and tumor necrosis. There was perineural invasion, infiltration into the perithyroidal adipose connective tissue, lack of vascular invasion or gross invasion of strap muscles. There was a metastasis in one perithyroidal lymph node with no neoplastic involvement in the left cervico-mediastinal lymph nodes. The lesion was staged pT3a pN1a.

Immunohistochemical analysis presented in Figure 3 showed diffuse positivity for AE1/AE3, CK5/6, p63, and p40 and focal positivity for CK7, CEA, and TTF1. Ki-67 was heterogeneous, ranging from 05% up to 90% in high-grade areas. Thyroglobulin, PAX8, calcitonin, chromogranin, synaptophysin, CD5, and CD117 were negative. The final diagnosis of SMECE with high-grade transformation was established in May 2024. The patient was referred for adjuvant radiotherapy (6000 cGy on tumor bed and 5000 cGy on draining cervical lymph nodes), delivered from July to August 2024, with no adverse effects. The tumor underwent molecular testing with a next generation sequencing panel, which showed high levels of *NTRK1* expression and copy number alterations on *VHL* gene locus of chromosome 3, with no other mutations or fusions known to occur in thyroid cancer.

In January 2025, the patient presented an ulcerated lesion in the anterior region of the neck, measuring 2.0 x 1.7 cm, shown in Figure 1d, which was submitted



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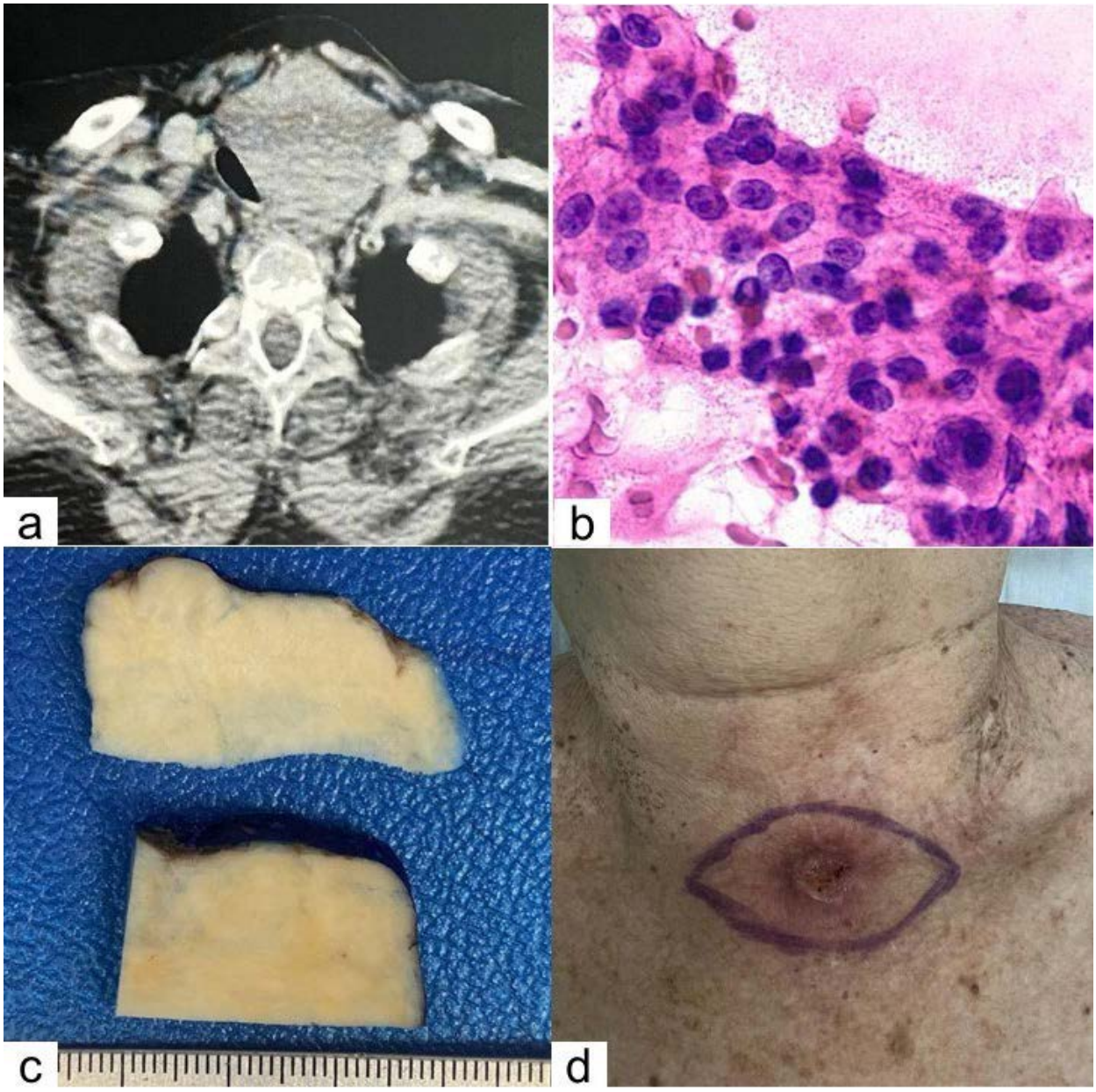


**Figure 1. a:** Contrast-enhanced computed tomography scan revealing an enlarged left thyroid lobe with heterogeneous texture, internal calcifications, and contralateral tracheal displacement; **b:** FNA conventional smears show cohesive atypical epithelial tumor cells with squamoid appearance and prominent nucleoli (H&E, 40x); **c:** Solid, lobulated and whitish tumor on gross evaluation; **d:** Recurrence in the anterior region of the neck (January 2025)

to surgical excision. Histopathology (February 2025) demonstrated relapse of the high-grade component, composed of carcinoma with squamous differentiation, evident nuclear pleomorphism, brisk mitotic activity (24 mitosis per $mm^2$), and abundant coagulative necrosis. Immunohistochemistry was positive to p63, p40, and CK5/6. Computed tomography evidenced multiple nodules on lungs, suggesting metastatic disease. The patient underwent chemotherapy with carboplatin and paclitaxel from February to September 2025 with almost complete resolution of lung disease. In October 2025, skull computed tomography evidenced multiple nodules and edema in occipital region. The patient underwent palliative care and died in November 2025.

## DISCUSSION

SMECE of the thyroid was classified as a thyroid tumor of uncertain histogenesis in the 5th classification of tumors of the World Health Organization[2]. There are assumptions that SMECE of the thyroid originates from ultimobranchial body remnants due to their similarity in immunophenotypic characteristics, such as positivity for the p63 marker and thyroglobulin negativity. Additionally,

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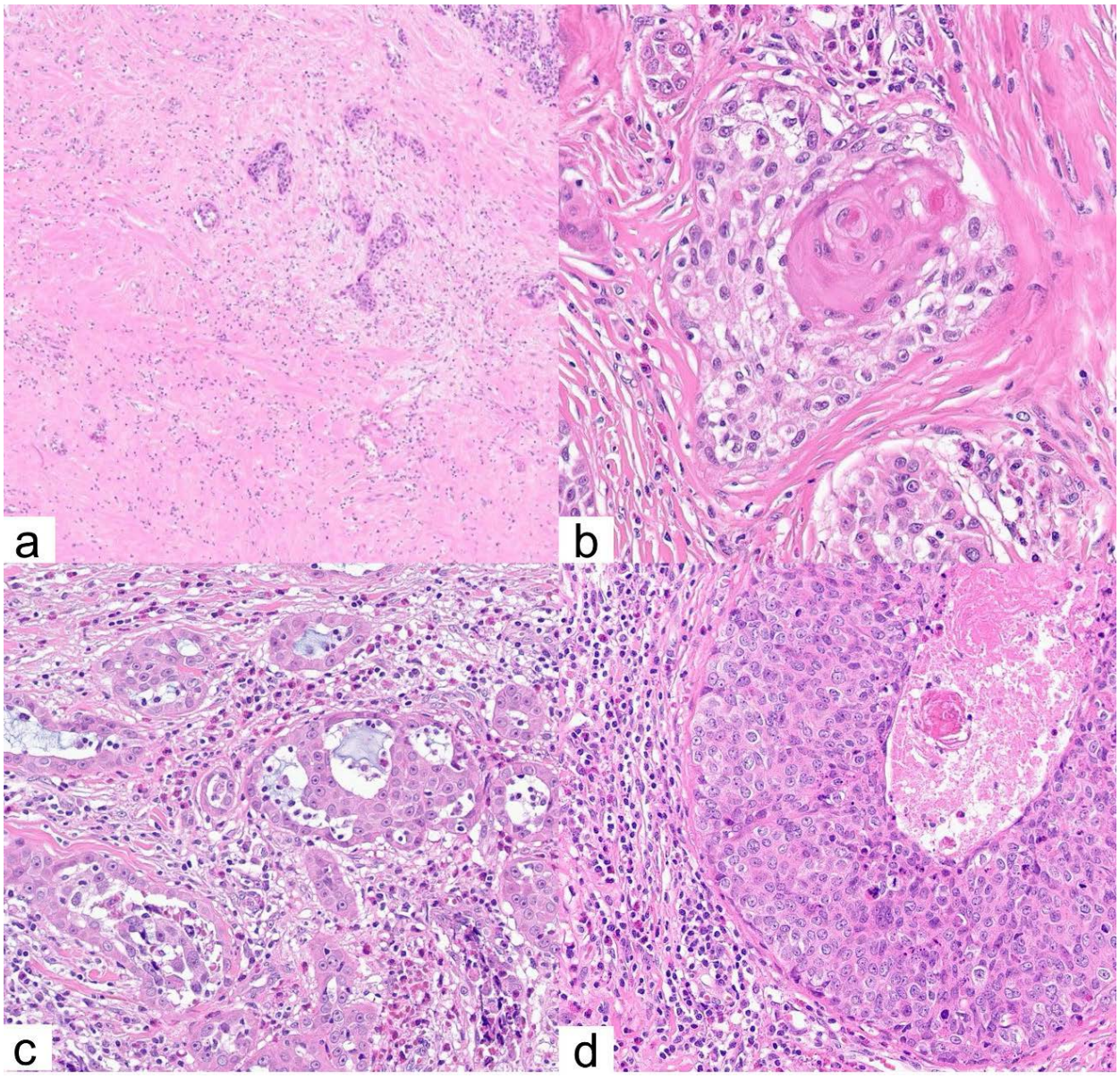


**Figure 2. a:** Tumor nests infiltrating abundant sclerotic stroma (H&E 4x); **b:** Squamous differentiation with keratin pearl formation (H&E 20x); **c:** Tumor cells exhibiting solid and pseudoangiomatous architectures with intraluminal mucin secretion, in an inflammatory stroma containing abundant eosinophils, lymphocytes and plasma cells (H&E 20x); **d:** High-grade areas with marked nuclear atypia, abundant mitosis and tumor necrosis, while retaining eosinophils-rich stroma (H&E 20x)

SMECE typically lacks common genetic alterations found in salivary gland-type carcinomas of the thyroid, such as the fusion genes *ETV6::NTRK3* and *CRTC1* or *CRTC3::MAML2*, as well as mutations or gene fusions typically observed in differentiated thyroid tumors, like *BRAF*$^{V600E}$ and *RAS*[3]. Of importance, the molecular landscape of SMECE is yet to be determined[2], and a recent case report identified nonsynonymous mutations in genes including *KIF20A, SDHB, PHKB, ABCA1, PIK3C2A, PHGDH, FZD8, NCOR2* and *TTK*, among others[10]. The current case showed high levels of *NTRK1* expression, and further investigation on SMECE eligibility for targeted therapy with TRK inhibitors is warranted.

The age range for the occurrence of thyroid SMECE is variable, ranging from the 3rd and 4th decades to the 8th and 9th decades of life[11,12], with a mean age of 55 years[2]. As in the current case, a notable female predilection is reported (>90%), with a female:male ratio of 13:1[2]. Studies[7,13] reported SMECE to be a hypoechoic, well-defined mass in a unilateral thyroid lobe upon ultrasonography, as observed in the present case.

Diagnosis of SMECE can be challenging due to its rarity and usually unspecific findings in FNA, which may include squamous-appearing cells, intracellular mucin vacuoles, rare keratin pearls, oval nuclei, small nucleoli, rare nuclear inclusions, and variable amounts of



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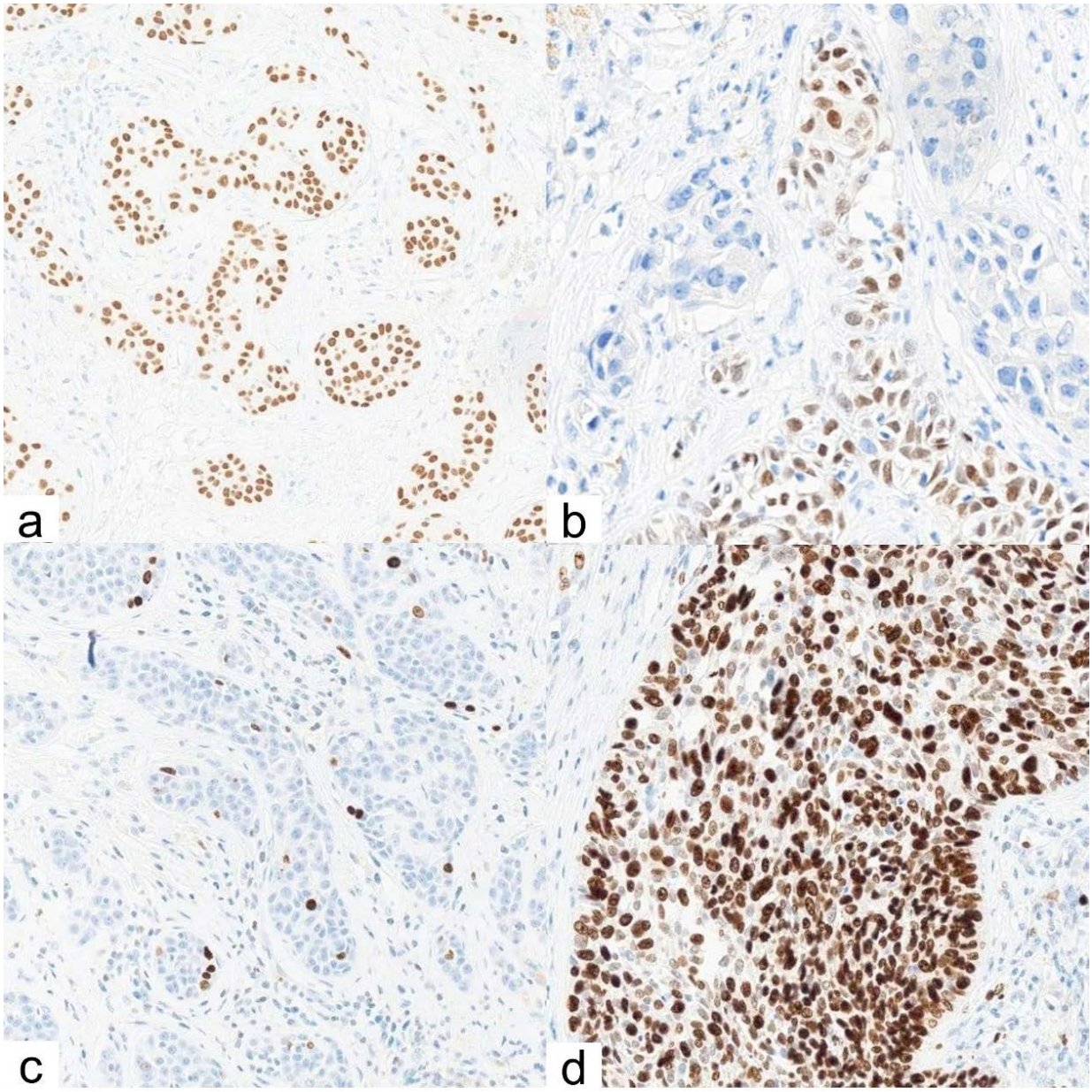


**Figure 3.** Tumor cells exhibiting p40 positivity (**a** – 10x), TTF1 heterogeneous positivity (**b** – 14x), Ki67 with low proliferation index in conventional SMECE areas (**c** – 10x) and high proliferation index in high-grade areas (**d** – 10x)

cytoplasm[4,14]. As expected, the FNA features of the present case were not confirmatory of SMECE.

In most cases, histological examination is essential for the diagnosis of SMECE, showing a carcinoma composed by mucous and squamous cells in a sclerotic stroma containing an intense lymphocytic infiltration. Eosinophils are always present, varying from few to numerous[2,4,15]. Although squamous and mucous cells are found in both SMECE and mucoepidermoid carcinoma of the thyroid, the presence of the sclerotic stroma with abundant inflammatory infiltrate favors SMECE diagnosis[3,15].

Immunohistochemistry can be supportive for the diagnosis. AE1/AE3 cytokeratin evidences the epithelial origin, as well as CK7 in the luminal cells and CK5/6 in the basal cells. p63 and p40 evidences the squamous differentiation. Focal and weak TTF1 positivity is reported in around 50% of SMECE[2]. Thyroglobulin and PAX8 are usually negative[2], although a previous study[12] reported 2/6 SMECE with focal thyroglobulin expression and another study[6] reported 1/9 cases with weak staining for PAX8. The expected negativity for calcitonin and CD117, chromogranin and synaptophysin, and CD5 excluded medullary thyroid, neuroendocrine, and thymic carcinomas, respectively.

SMECE of the thyroid typically occurs in a background of chronic lymphocytic thyroiditis[3,6,13]. In addition, SMECE

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can occur concomitantly with other lesions, such as anaplastic thyroid carcinoma[16], parotid basal cell adenoma[14] and papillary carcinoma[2,15]. SMECE of the thyroid prognosis remains controversial; some studies classify it as a low-grade neoplasm, while others suggest distinct prognostic stages due to its potential for locoregional or distant metastasis[7,12]. Therefore, long-term follow-up is advised for SMECE patients[2]. In the present case, despite infiltration into the perithyroidal adipose connective tissue, neither gross extrathyroidal extension nor vascular invasion were reported, but the patient developed a cutaneous recurrence of the high-grade component and lung and skull metastasis upon follow-up, dying from the disease.

## CONCLUSION

Due to the high-grade transformation and aggressive clinical course, this case contributes to the characterization of thyroid SMECE. Future research should address the molecular background of the tumor and eligibility for targeted therapy.

### CONTRIBUTIONS

Patrícia Carlos Caldeira and Alexandre Andrade Sousa contributed substantially to the conception and design of the study, acquisition, analysis and interpretation of the data, writing, editing and critical review with intellectual contribution. Hyago Portela Figueiredo and Beatriz Fuga Rossi Teixeira contributed to the analysis, investigation, writing, critical review and editing. Natália Santos Barcelos contributed to the writing, critical review and editing. All the authors approved the final version for publication

### DECLARATION OF CONFLICT OF INTEREST

There is no conflict of interest to declare.

### DATA AVAILABILITY STATEMENT

All the content underlying the text of the article is included in the manuscript.

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## REFERENCES

1. Chan JK, Albores-Saavedra J, Battifora H, et al. Sclerosing mucoepidermoid thyroid carcinoma with eosinophilia: a distinctive low-grade malignancy arising from the metaplastic follicles of Hashimoto's thyroiditis. Am J Surg Pathol. 1991;15(5):438-48.
2. WHO Classification of Tumours Editorial Board. Endocrine and neuroendocrine tumours. 5th ed. Lyon (FR): World Health Organization; 2025.
3. Jung CK, Bychkov A, Kakudo K. Update from the 2022 world health organization classification of thyroid tumors: a standardized diagnostic approach. Endocrinol Metab (Seoul). 2022;37(5):703-18. doi: https://doi.org/10.3803/EnM.2022.1553
4. Ames E, Campbell MJ, Afify A, et al. Sclerosing mucoepidermoid carcinoma with eosinophilia: cytologic characterization of a rare distinct entity in the thyroid. Diagn Cytopathol. 2018;46:632-5. doi: https://doi.org/10.1002/dc.23914
5. Le HT, Nguyen TPX, Hirokawa M, et al. Primary thyroid mucoepidermoid carcinoma (MEC) is clinically, prognostically, and molecularly different from sclerosing MEC with eosinophilia: a multicenter and integrated study. Endocr Pathol. 2023;34(1):100-11. doi: https://doi.org/10.1007/s12022-022-09741-1
6. Shah AA, La Fortune K, Miller C, et al. Thyroid sclerosing mucoepidermoid carcinoma with eosinophilia: a clinicopathologic and molecular analysis of a distinct entity. Mod Pathol. 2017;30(3):329-39. doi: https://doi.org/10.1038/modpathol.2016.180
7. Lam H, Saoud C, Faquin WC, et al. Cytopathology of primary sclerosing mucoepidermoid carcinoma with eosinophilia of the thyroid: a multi-institutional case series and review of literature. J Am Soc Cytopathol. 2024;13(1):33-41. doi: https://doi.org/10.1016/j.jasc.2023.10.003
8. Salem J, Shamil E, Folkes L, et al. Sclerosing mucoepidermoid carcinoma with eosinophilia of the thyroid: demonstrating the natural progression of a rare and misunderstood disease. BMJ Case Rep. 2021;14(7):e241086. doi: https://doi.org/10.1136/bcr-2020-241086
9. Conselho Nacional de Saúde (BR). Resolução nº 466, de 12 de dezembro de 2012: Aprova as diretrizes e normas regulamentadoras de pesquisas envolvendo seres humanos [Internet]. Diário Oficial da União, Brasília, DF. 2013 jun 13 [acesso 2026 abr 22]; Seção 1:59. Disponível em: https://www.gov.br/conselho-nacional-de-saude/pt-br/atos-normativos/resolucoes/2012/resolucao-no-466.pdf/view
10. Song N, He X, Duan T, et al. Sclerosing mucoepidermoid carcinoma with eosinophilia of the thyroid: clinicopathological characterization and whole-exome sequencing insights. Oral Oncol. 2025;163:107259. doi: https://doi.org/10.1016/j.oraloncology.2025.107259



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11. Chambers M, Nosé V, Sadow PM, et al. Salivary-like tumors of the thyroid: a comprehensive review of three rare carcinomas. Head Neck Pathol. 2021;15(1):212-24. doi: https://doi.org/10.1007/s12105-020-01193-5

12. Quiroga-Garza G, Lee JH, El-Naggar A, et al. Sclerosing mucoepidermoid carcinoma with eosinophilia of the thyroid: more aggressive than previously reported. Hum Pathol. 2015;46(5):725-31. doi: https://doi.org/10.1016/j.humpath.2015.01.012

13. Nam JH, Han CW, Kim NI, et al. The cytological features of sclerosing mucoepidermoid carcinoma with eosinophilia of the thyroid gland: a case report. Cytopathology. 2020;31:593-7. doi: https://doi.org/10.1111/cyt.12889

14. Noor M, Russell DK, Israel AK, et al. Thyroid sclerosing mucoepidermoid carcinoma with eosinophilia in conjunction with parotid basal cell adenoma: cytologic, histologic, and molecular features. Diagn Cytopathol. 2021;49(7):E262-8. doi: https://doi.org/10.1002/dc.24701

15. Baloch ZW, Asa SL, Barletta JA, et al. Overview of the 2022 WHO Classification of Thyroid Neoplasms. Endocr Pathol. 2022;33(1):27-63. doi: https://doi.org/10.1007/s12022-022-09707-3

16. Mao R, Shi L, Yan W, et al. Anaplastic thyroid carcinoma combined with sclerosing mucoepidermoid carcinoma with eosinophilia: a case report. Medicine (Baltimore). 2020;99(42):e22783. doi: https://doi.org/10.1097/MD.0000000000022783

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