case report

Sclerosing mucoepidermoid carcinoma of the thyroid gland: cytohistological findings of a case

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Mucoepidermoid carcinoma is an extremely rare thyroid neoplasm with only a handful of cases reported so far.[3,4,23,25,26] Although it has been considered a low-grade carcinoma, rare high-grade cases have also been described.[4,25] A sclerosing variant of thyroid mucoepidermoid carcinoma associated with eosinophilia (SMEC) has also been reported.[1-3,7-9,11,19-22] Overall, the histogenesis of mucoepidermoid carcinomas in the thyroid is unclear and remains under debate. Authors hypothesize whether they originate from solid cell nests, the ultimobranchial body remnants, or from follicular cells. The first option is favored by most,[3,11,13,20] based upon the histological and immunohistochemical similarities between these neoplasms and ultimobranchial body remnants. The cytological and histological features of a new case of SMEC diagnosed on core biopsy (CB) and treated with radical surgery are reported here. The tumor showed the expected mucoepidermoid histology, but showed intense atypia, prominent inflammatory infiltrate and extensive desmoplasia. To the best of our knowledge, there are very few reports describing the cytological findings of this entity.[5,11]

CASE

A 65-year-old man presented a diffuse neck swelling of rapid onset. Clinical symptoms started two months earlier and included neck pain, increasing breathing difficulties and slight fever. Physical and radiological studies revealed the tumor affected almost the whole thyroid gland and showed bilateral satellite nodules interpreted as node metastases. Serum tumor markers were negative and thyroid hormones were under normal limits. Ultrasound-guided CBs of the thyroid gland and lymph nodes were performed for diagnostic purposes using 18G BioPince needles. One month after the histological diagnosis, a total thyroidectomy with radical bilateral neck dissection was performed. Surgical resection also included a tumor implant observed in the esophagus wall. The patient died of disseminated metastatic seed 10 months after the diagnosis.

PATHOLOGICAL DATA

CB samples were immersed in cooled serum to delay autolysis and were immediately submitted to the pathology lab. Our routine procedure with this material has been previously described,[15] and included an imprint cytology stained with haematoxylin-eosin, cytocentrifugates of the transport serum stained by Papanicolaou technique, and conventional formalin fixation and paraffin embedding of cores for histology. The following commercially available antibodies were used: High molecular weight 34βE12 cytokeratin (Dako, dilution 1:50), EMA (Dako, 1:100), cytokeratin 19 (Dako, 1:100), p63 (Dako, 1:50), calcitonin (Biogenex, prediluted), TTF-1 (Dako, 1:50), thyroglobulin (Novocastra, 1:50), and HBME-1 (Dako, prediluted). Total thyroidectomy and radical bilateral neck dissection material was submitted "in fresh" to the pathology lab and processed following routine methods. The pathological staging was based on the 2002 TNM/AJCC classification.[12]

Core biopsy findings: CB material included a whitish 10 mm in length tissue core of the thyroid gland and two 7 and 8 mm in length cores of two adjacent lymph nodes, right and left respectively. Cytological imprints showed a high grade neoplasm composed of large epithelial cells arranged in irregular poorly cohesive nests (Figure 1). Lymphoid inflammatory infiltrate was prominent and the tumor. Tumor cells showed large cytoplasm with occasional vacuolization.

Normal thyroid and lymph nodes were not sampled

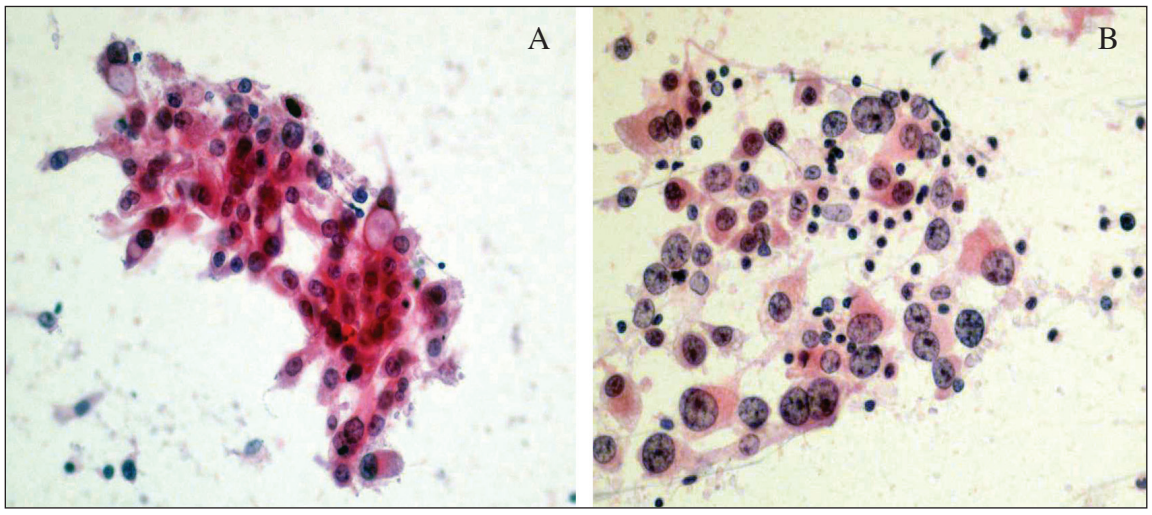

Figure 1. Tumor cells are grouped in irregular nests with low cohesiveness. Mucinous vacuolization (A) and inflammatory background (B) are occasionally seen (Hematoxylin & Eosin, ×250 and ×400).

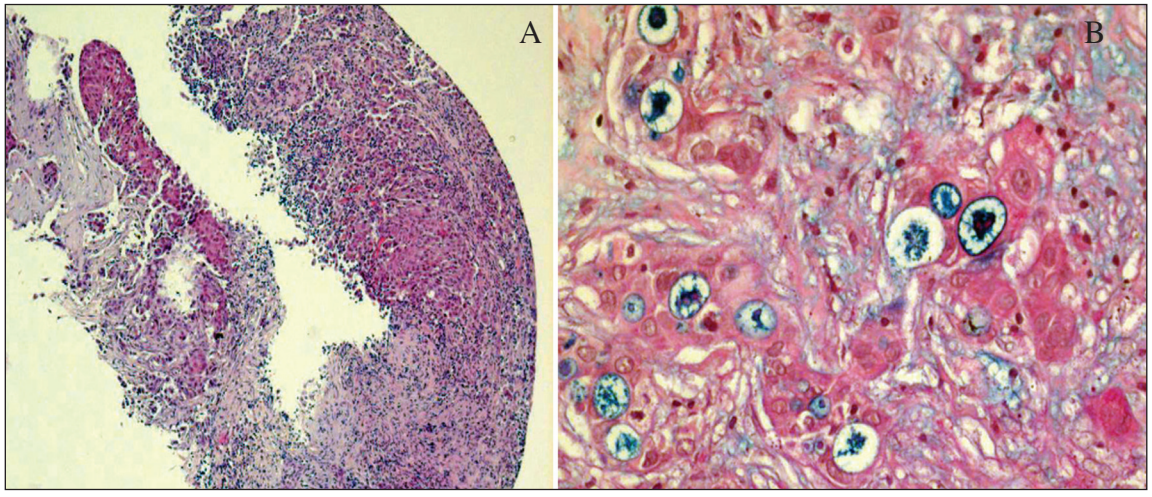

Figure 2. Core biopsy specimen showing solid tumor nests accompanied by inflammatory infiltrate within a sclerosing stroma (A) (Hematoxylin & Eosin, ×25). High power view showing foci of mucin production (B) (Alcian blue, ×400).

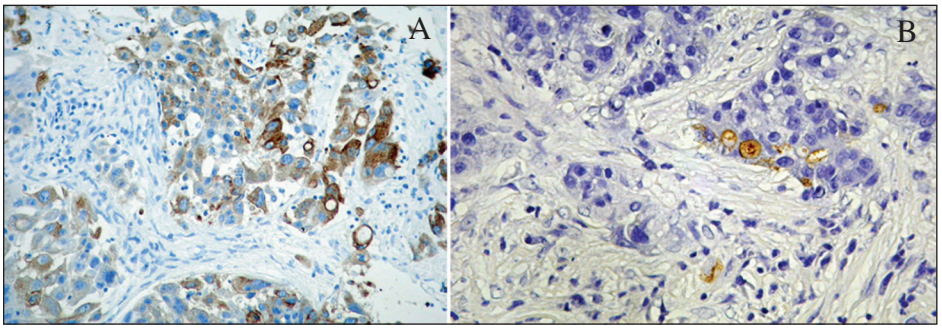

Figure 3. Diffuse cytoplasmic immunostaining with cytokeratin 19 (A) (×400) and focal membrane immunostaining with HBME-1 (B) (×400) are seen in tumor cells.

in core specimens. In fact, the whole obtained material consisted of a sclerotic tissue infiltrated by a malignant epithelial neoplasm (Figure 2). The tumor was arranged in odd-shaped solid nests composed of large squamous-like cells with atypical nuclei and mitoses. Keratinization was not detected. Tumor nests also contained indeterminate cells and small cysts and intracytoplasmic vacuoles showing intense Alcian-blue positive material (Figure 2). The stroma was sclerotic and contained dispersed lymphocytes and plasma cells. Eosinophils were only very rarely seen. Solid tumour islands showed diffuse positive immunostaining with 34βE12 cytokeratin, cytokeratin 19 (Figure 3) and p63. EMA and HMBE-1 (Figure 3) were focally positive enhancing the cytoplasmic membranes in vacuoles. TTF-1, thyroglobulin and calcitonin were negative.

Surgical specimen findings: The thyroid gland was firm and diffusely enlarged, weighted 110.3 g, and measured 12×9×6.5 cm. The cut surface showed a whitish tumor invading the right and left lobes. Focal extracapsular extension was seen on naked eye in the right lobe. Radical bilateral neck dissection included 21 lymph nodes, three of them showing macrometastases. Histologically, the tumor showed a similar histology and immunophenotype described in the CB. Scattered necrotic foci were focally seen. Perithyroid soft tissues, fat and muscle, were invaded in the right side. A total of 15 lymph nodes, right and left sided, presented metastatic seed, 7 of them showing extracapsular extension. The nodule identified in the esophageal wall was a tumor implant.

DISCUSSION

Mucoepidermoid carcinoma is an infrequent tumor mainly reported in the salivary glands, although it has been found in other sites.[10] It rarely occurs in the thyroid gland, where only a handful of single cases and a short series have been published so far.[3,26] The histological features of this tumor are well established and similar regardless of location. Thus, squamoid, intermediate and mucin-producing cells are the classical cellular components of this tumor, with quantitative as well as qualitative differences, and diverse arrangements, depending on the tumor grade and differentiation. Papillary carcinoma has been occasionally found in the literature forming part of the tumor.[5,17] Quite typically the tumor pursues an indolent behavior,[3] although an aggressive clinical course has been demonstrated in some cases.[4,25]

SMEC is a rare variant of mucoepidermoid carcinoma first reported in the thyroid by Chan et al[8] in the context of Hashimoto's thyroiditis. SMEC has also been occasionally reported in the salivary glands.[24] Since the first report, less than 20 cases have been reported in the literature.[1-3,7-9,11,19-22] The limited accumulated experience with this tumor shows a female predominance and a relatively benign clinical course despite the frequent presence of lymph node and soft tissue involvement. However, as with classical mucoepidermoid carcinoma, metastatic disease and aggressive clinical behavior have occasionally been reported.[11,20,21]

Although rare, SMEC is a well-defined entity. Most of the previously reported cases are low-grade tumors. The two previous cytological reports[5,11] describe paucicellular epithelial neoplasms composed of small nests of monomorphic bland cells showing some evidence of mucin production. Histologically, these tumors are composed of sheets of cells with squamoid features and duct-like structures encased in a desmoplastic stroma percolated by variable amounts of inflammatory cells, typically including eosinophils.[3] Foci of mucinous material, and even mucous secreting cells, are also evident. Psammoma bodies and clear cells[1] can occasionally be present. High-grade tumors[9,20,22] or typical low-grade cases with partial secondary high-grade transformation[3,6] have also been described. Metastases reproduce the typical histological pattern.

By immunohistochemistry, thyroglobulin and calcitonin are consistently negative, and this finding speaks against a follicular or C-cell origin. TTF-1 is positive in 50% of the cases.[1] Solid cell nests, structures considered to represent the ultimobranchial body remnants in the thyroid, were very soon proposed as the most plausible origin for this tumor based on the histological similarities between them. This idea is most widespread now[3,20] and has been supported by Hunt et al[13] in a recent immunohistochemical study in which both small cell nests and SMEC, share a constant p63 positive staining. However, the occasional associations of SMEC either with Hashimoto's thyroiditis,[8,21] or with follicular-derived neoplasms like papillary carcinoma,[3] led to some authors to favor a follicular cell origin.[2,26]

The differential diagnosis of SMEC includes squamous cell carcinoma, papillary carcinoma, particularly the sclerosing variant,[14] conventional mucoepidermoid carcinoma,[3] medullary carcinoma, and even nonneoplastic conditions associating squamous metaplasia and prominent inflammation.[18] On the other hand, as reported by Solomon et al,[22] the prominent inflammatory infiltrate accompanying this tumor, often rich in eosinophils, may mimic Hodgkin's disease in lymph node metastases. Secondary tumors must also be eventually considered in the differential diagnosis, but metastases from distant tumors, or contiguous extension

from tumors of the larynx or other neighboring organs, are quite infrequent in the thyroid gland.

In conclusion, SMEC is a significantly well-established morphological entity and therefore its occasional development in the thyroid gland should always be kept in mind. Interestingly, ultrasound-guided core biopsy provided in this case representative tumor fragments for making the complete histopathological diagnosis, thus proving the usefulness of this technique in the initial approach of thyroid masses. Despite the fact that SMEC has been traditionally considered a low-grade neoplasm in the thyroid, the occasional reporting of highly aggressive cases advises a cautious attitude in the management of these tumors, especially those presenting cytological atypia and/or non-organ confined disease at diagnosis.

REFERENCES

1. Albores-Saavedra J, Gu X, Luna MA Clear cells and thyroid transcription factor I reactivity in sclerosing mucoepidermoid carcinoma of the thyroid gland. Ann Diagn Pathol. 2003;7: 348-353.
2. Arezzo A, Patetta R, Ceppa P, Borgonovo G, Torre G, Mattioli FP Mucoepidermoid carcinoma of the thyroid gland arising from a papillary epithelial neoplasm. Am Surg 1998;64: 307-311.
3. 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: 802-807.
4. Bhandarkar ND, Chan J, Strome M A rare case of mucoepidermoid carcinoma of the thyroid. Am J Otolaryngol 2005;26:138-141.
5. Bondeson L, Bondeson AG Cytologic features in fine-needle aspirates from a sclerosing mucoepidermoid thyroid carcinoma with eosinophilia. Diagn Cytopathol 1996;15: 301-305.
6. Cameselle-Teijeiro J, Febles-Perez C, Sobrinho-Simoes M Cytologic features of fine needle aspirates of papillary and mucoepidermoid carcinoma of the thyroid with anaplastic transformation. A case report. Acta Cytol 1997;41: 1356-1360.
7. Cavazza A, Toschi E, Valcavi R, Piana S, Scotti R, Carlinfante G, Gardini G Sclerosing mucoepidermoid carcinoma with eosinophilia of the thyroid: description of a case. Pathologica 1999;91: 31-35.
8. Chan JK, Albores-Saavedra J, Battifora H, Carcangiu ML, Rosai J 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: 438-448.
9. Chung J, Lee SK, Gong G, Kang DY, Park JH, Kim SB, Ro JY. Sclerosing mucoepidermoid carcinoma with eosinophilia of the thyroid glands: A case report with clinical manifestations of recurrent neck mass. J Korean Med Sci 1999;14: 338-341.
10. Fletcher CDM, ed., Diagnostic Histopathology of Tumors, 3rd Edition, Churchill Livingstone Elsevier, Philadelphia, 2007
11. Geisinger KR, Steffee CH, McGee RS, Woodruff RD, Buss DH The cytomorphologic features of sclerosing mucoepidermoid carcinoma of the thyroid gland with eosinophilia. Am J Clin Pathol 1998;109: 294-301.
12. Greene FL, Page DL, Fleming ID, Fritz AG, Balch CM, Haller DG, and Morrow M eds. AJCC Cancer Staging Handbook. Sixth Edition TNM Classification of Malignant Tumors. Springer, New York, 2002. p. 89-98
13. Hunt JL, LiVolsi VA, Barnes EL. p63 expression in sclerosing mucoepidermoid carcinomas with eosinophilia arising in the thyroid. Mod Pathol 2004;17: 526-529.
14. Lam AKY, Lo CY Diffuse sclerosing variant of papillary carcinoma of the thyroid: A 35-year comparative study at a single institution. Ann Surg Oncol 2006;13:176-181.
15. Lopez JI, del Cura JL, Zabala R, Bilbao FJ Usefulness and limitations of ultrasound-guided core biopsy in the diagnosis of musculoskeletal tumours. APMIS 2005;113: 353-360.
16. Miller RT, Estran C Heat-induced epitope retrieval with a pressure cooker. Appl Immunohistochem 1995;3: 190-193.
17. Miranda RN, Myint MA, Gnepp DR Composite follicular variant of papillary carcinoma and mucoepidermoid carcinoma of the thyroid. Report of a case and review of the literature. Am J Surg Pathol 1995;19: 1209-1215.
18. Musso-Lassalle S, Butori C, Bailleux S, Santini J, Franc B, Hofman P A diagnostic pitfall: nodular tumor-like squamous metaplasia with Hashimoto's thyroiditis mimicking a sclerosing mucoepidermoid carcinoma with eosinophilia. Pathol Res Pract 2006;202: 379-383.
19. Sharma K, Nigam S, Khurana N, Chaturvedi KU Sclerosing mucoepidermoid carcinoma with eosinophilia of the thyroid. A case report. Indian J Pathol Microbiol 2003;46: 660-661.
20. Shehadeh NJ, Vernick J, Lonardo F, Madan SK, Jacobs JR, Yoo GH, Kim HE, Ensley JF Sclerosing mucoepidermoid carcinoma with eosinophilia of the thyroid: A case report and review of the literature. Am J Otolaryngol2004;25: 48-53.
21. Sim SJ, Ro JY, Ordonez NG, Cleary KR, Ayala AG Sclerosing mucoepidermoid carcinoma with eosinophilia of the thyroid: report of two patients, one with distant metastasis, and review of the literature. Hum Pathol 1997;28: 1091-1096.
22. Solomon AC, Baloch ZW, Salhany KE, Mandel S, Weber RS, LiVolsi VA Thyroid sclerosing mucoepidermoid carcinoma with eosinophilia. Mimic of Hodgkin disease in nodal metastases. Arch Pathol Lab Med 2000;124: 446-449.
23. Steele SR, Royer M, Brown TA, Porter C, Azarow KS Mucoepidermoid carcinoma of the thyroid gland: A case report and suggested surgical approach. Am Surg 2001;67: 979-983.
24. Urano M, Abe M, Horibe Y, Kuroda M, Mizoguchi Y, Sakurai K, Naito K Sclerosing mucoepidermoid carcinoma with eosinophilia of the salivary glands. Pathol Res Pract 2002;198: 305-310.
25. Vazquez Ramirez F, Otal Salaverri C, Argueta Manzano O, Galera Ruiz H, Gonzalez-Campora R Fine needle aspiration cytology of high grade mucoepidermoid carcinoma of the thyroid. A case report. Acta Cytol 2000;44:259-264.
26. Wenig BM, Aldair CF, Heffess CS Primary mucoepidermoid carcinoma of the thyroid gland: a report of 6 cases and a review of the literature of follicular-derived tumor. Hum Pathol 1995;26: 1099-1108.