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Original contribution

Sclerosing mucoepidermoid carcinoma with eosinophilia of the thyroid: more aggressive than previously reported

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Summary Sclerosing mucoepidermoid carcinoma with eosinophilia (SMECE) of the thyroid is a rare traditionally "low-grade" tumor that predominantly occurs in women. Approximately 50 cases have been reported in the literature. It arises in a background of Hashimoto thyroiditis and is characterized by nests of epidermoid and mucin-secreting cells located within an eosinophil-rich sclerotic stroma. Herein, we outline the clinicopathological and immunohistochemical characteristics of 6 cases of thyroid SMECE. All tumors were detected in women (age, 36-89 years; average, 59 years), and all patients underwent total thyroidectomies. Clinicopathological findings included extensive tumor invasion into the adjacent soft tissues, trachea, pharynx, and esophagus. Of 6 specimens, 5 had positive surgical margins. Cervical lymph node metastases were seen in 4, and distant metastases were in 3 patients. Immunohistochemically, all tumors were positive for CK19, galectin 3, and p63 and negative for calcitonin, calponin, S-100, and smooth muscle actin. Interestingly, 2 tumors also showed faint focal staining for thyroglobulin, and 2 others had focal positivity for thyroid transcription factor 1. Together, galectin 3 and CK19 expression supported the malignancy of these lesions, and p63 expression raised the possibility that these tumors originated from the ultimobranchial body. In summary, SMECE tumors in our series exhibit a clear female predominance with aggressive behavior and appear to arise from pluripotent solid cell nests. A correct diagnosis is crucial to providing SMECE patients with the appropriate treatment options, and we recommend a closer follow-up schedule than previously considered.

1. Introduction

Sclerosing mucoepidermoid carcinoma with eosinophilia (SMECE) of the thyroid gland is a rare disease, with

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approximately 50 cases reported in the literature [1-15]. SMECE has a distinct histologic pattern, consisting of a poorly circumscribed tumor that contains nests of epidermoid and mucin-secreting epithelial cells located in a densely sclerotic, eosinophil-rich stroma. These tumors typically arise in a background of lymphocytic or Hashimoto thyroiditis and, despite their name, bear minimal morphological resemblance to salivary gland or thyroid mucoepidermoid carcinomas (MECs). Early SMECE reports characterized them as low-grade tumors [1,16-19], although recent evidence suggests that they can exhibit a locally aggressive behavior with regional lymph node involvement and occasional distant metastasis [2,3,5-8,11,12]. Most clinical SMECE reports describe the disease in women, but at least 1 case has been recorded in a man [3]. The objective of the present study is to provide additional clinicopathological and immunohistochemical characterization from 6 cases of SMECE of the thyroid.

2. Materials and methods

This study was approved by Houston Methodist Hospital and MD Anderson Cancer Center institutional review boards. Pathology files contained at the Houston Methodist Hospital, Houston, Texas, were searched and yielded 2 SMECE cases. Four additional cases collected from 1993 to 2003 were retrieved from the Department of Pathology at The University of Texas MD Anderson Cancer Center of Houston, Texas. None of these cases had been previously reported, and clinical information and paraffin-embedded tissue blocks were available for all.

Tissue sections for routine hematoxylin and eosin staining and for immunohistochemical studies were cut, deparaffinized, rehydrated, and incubated with primary antibodies against p63 (4A4, 1:100; LabVision, Fremont, CA), smooth muscle actin (SMA) (1A4, 1:5; Biogene, Kimbolton, Cambridgeshire, UK), calponin (1:400; Dako, Glostrup, Denmark), S-100 protein (15E2E2, 1:2500; Dako), galectin 3 (9C4, 1:250; Vector, Carpinteria, CA), calcitonin (1:5000; Dako), thyroglobulin (2H11 and 6E1, 1:2000; LabVision), and thyroid transcription factor 1 (TTF-1) (8G763/1, 1:10; Dako), estrogen receptor (ER) (6F11, 1:50; Novocastra Lab, Newcastle, UK), and progesterone receptor (PR) (1A6, 1:30, Neomarkers, Fremont, CA).

3. Results

The main clinicopathological findings are summarized in Table 1.

3.1. Clinical findings

All tumors were detected in women (age, 36-89 years; median age, 59 years) who presented with neck masses and were referred to the treating institution for further management. Because archival pathology reports did not include gross description in 2 cases (cases 2 and 5), some relevant information was not available.

Total thyroidectomies were performed in all patients, although 2 patients initially received subtotal thyroidectomy but subsequently underwent complete thyroidectomies after histologic diagnosis. In addition, cervical lymph node dissections were performed in 4 patients: 2 cases with bilateral neck dissection, 1 case with right neck dissection and selective left neck dissection, and 1 case with right neck dissection.

All tumors presented as a single mass, with 4 cases involving a single lobe (2 right, 1 left, and 1 not known), and the remaining 2 cases involving the entire thyroid gland. Tumor sizes ranged from 2.4 to 10 cm, and multiple regional lymph node metastases were identified in all 4 neck-dissected cases. Distant metastases were identified in 3 patients: case 5 had metastasis in the upper mediastinal ("thymus") lymph node, case 2 had a tissue-confirmed lung metastasis, and case 6 had a metastatic lesion that was strongly suggested by radiologic studies, but histologic evaluation was not performed.

Subsequent to thyroidectomy, 5 of 6 patients were treated with radiotherapy. Five patients died within 8 years of diagnosis and treatment, although the exact cause of death is unknown.

3.2. Pathologic findings

Gross pathology findings were available in 4 cases. On cut sections, all tumors exhibited a predominantly tan-white cut surface with firm consistency, with 2 tumors exhibiting homogeneous cut surfaces, and the others being variegated in appearance. In addition, 1 case contained a tan-white nodule with gritty yellow material and another displayed multiple small mucous-filled cystic spaces.

When examined by light microscopy, all primary and metastatic tumors had similar histologic findings. Specifically, the lesions had an ill-defined infiltrative border and contained tumor cell nests and sheets, separated by fibrotic and sclerotic stroma (Fig. 1A). Tumor cells had epithelial appearance with moderate eosinophilic cytoplasm, prominent intercellular junctions, intracellular cytoplasmic keratinization, and keratin pearl formation. Tumor nuclei were round to ovoid with prominent nucleoli. Tumor also displayed areas of focal glandular differentiation with cystic spaces that contained mucinous secretions or single or groups of cells containing mucin vacuoles (Fig. 1B and C), and background fibrotic and sclerotic stroma exhibited eosinophilic infiltrates of varying intensity (Fig. 1D). Lymphovascular invasion was frequently observed (Fig. 1A).

Nuclear features representative of papillary thyroid carcinoma, including nuclear pseudoinclusions or grooves, were not observed in these neoplastic cells. In the background, associated lymphocytic and/or Hashimoto thyroiditis were observed in 4 cases (Fig. 1A). In the other