CASE REPORT
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Primary Sclerosing Mucoepidermoid Carcinoma with Eosinophilia of the Thyroid: Description of a Case and Review of the Literature

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Primary sclerosing mucoepidermoid carcinoma with eosinophilia (SMECE) of the thyroid gland is a very rare disease. We present the clinical and histopathologic findings of a 37-year-old woman recently diagnosed with SMECE of the thyroid gland. The patient, clinically euthyroid, who presented with a neck swelling since last 2 years along. Fine needle aspiration cytology suggested thyroid papillary carcinoma. Total thyroidectomy, central neck dissection and right selective neck dissection were performed. Although SMECE is considered to be a relatively slow growing and non-aggressive tumor, occasional metastasis does occur. We report an additional case of SMECE, with metastasis to regional lymph nodes. Physicians should be aware of extended operation, including total thyroidectomy and/or neck node dissection for metastatic lesion of the neck node. More standardized treatment is likely to evolve in the future.

Key Words: Mucoepidermoid, Carcinoma, Eosinophilia, Thyroid gland

Introduction

Sclerosing mucoepidermoid carcinoma with eosinophilia (SMECE) of the thyroid gland was first described by Chan et al.[1)] in 1991 as a new distinctive low-grade carcinoma of the thyroid gland generally occurring in the background of Hashimoto's thyroiditis. Since this initial report, another 21 additional cases have been described in the literature as small case studies and as individual case reports. SMECE tends to affect women between the ages of 32 and 74.[1)] In contrast; conventional mucoepidermoid carcinoma (MEC) of the thyroid gland affects a slightly younger age group and may affect men (2:1).[2)] Most SMECE cases manifested a relatively indolent clinical course despite significant contiguous adenopathy and soft-tissue extension of the tumor. Metastasis has been described as an unusual manifestation of this new clinical entity.[3,4)] Because of the rarity of SMECE, definitive management remains elusive. We report a case of a 37-year-old woman who was diagnosed with SMECE in the setting of lymphocytic thyroiditis and treated surgically with total thyroidectomy and right selective neck dissection. The purpose of this paper is to present a case, review the pertinent literature, and provide insights into treatment options.

Case Report

A 37-year-old woman had presented with a palpable neck mass for 2 years. She had no previous history of neck irradiation. Family history was negative for thyroid disease. Clinical examination revealed a

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firm, non-tender mobile mass with smooth surface measuring 4×3 cm. Thyroid function test revealed normal free T4, T3, thyroid stimulating hormone (TSH) levels, and thyroglobulin levels. Other laboratory investigations revealed no abnormalities. Ultrasonography of the neck revealed a hypoechoic mass with extracapsular invasion at the right thyroid gland, measuring 4.7×1.9 cm and suggestive metastatic lymphadenopathy at the right supraclavicular area. Neck computed tomography also showed a right thyroid mass and metastatic right supraclavicular lymph node (Fig. 1). A positron emission tomography (PET) scan didn't show any distant metastatic disease; however, the suspicious metastatic uptake was seen in the right supraclavicular lymph nodes (Fig. 2).

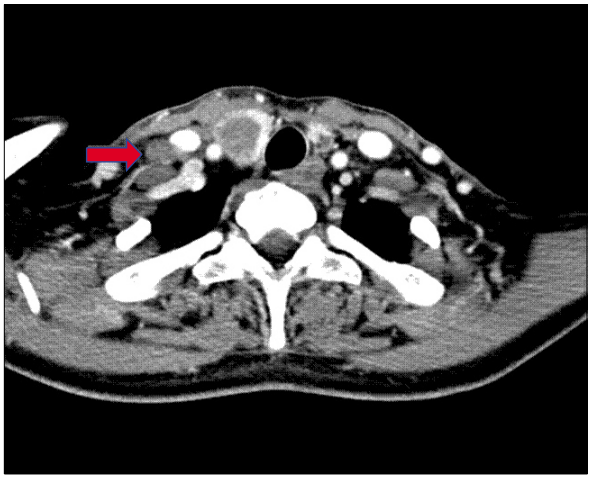

Fig. 1. Neck computed tomography with contrast enhancement demonstrating tumor invasion of the right thyroid lobe. A right supraclavicular lymph node metastasis is present (arrow).

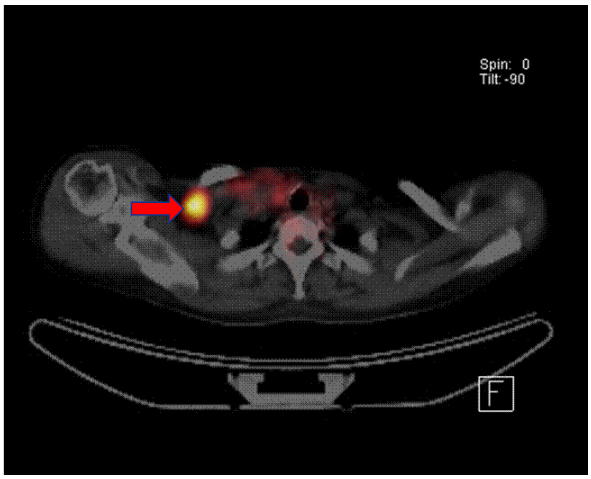

Fig. 2. 18F-fludeoxyglucose (FDG) positron emission tomography (PET) scan shows a metastatic lymphadenopathy at right supraclavicular area (arrow).

In October 2012, the patient underwent total thyroidectomy and right selective neck node dissection. She diagnosed SMECE and lymphocytic thyroiditis on the right thyroid and metastasis of right level VI and the right supraclavicular lymph node. Grossly, a well-defined, ovoid and firm mass (4.0×4.0×2.0 cm) was present in the mid portion to lower pole. The cut surface of the mass was homogenously solid and yellowish white without hemorrhage or necrosis. The mass abutted the thyroid capsule. The tumor nodule had ill-defined border and adjacent thyroid reveals lymphocytic thyroiditis (Fig. 3). The cells were characterized by anastomosing compact cords and nests of epidermoid cells, accompanied by extensive sclerosis and by infiltration of eosinophils, lymphocytes and plasma cells (Fig. 4). A well-formed squamous pearl was contained. And mucocytes compressed by globules of mucin was interspersed in epidermoid cells (Fig. 5). The patient was given concurrent chemoradiotherapy with carboplatin. The last follow-up of the patient was in April 2017, when she showed no evidence of tumor.

Discussion

MEC is a rare primary thyroid tumor with indolent

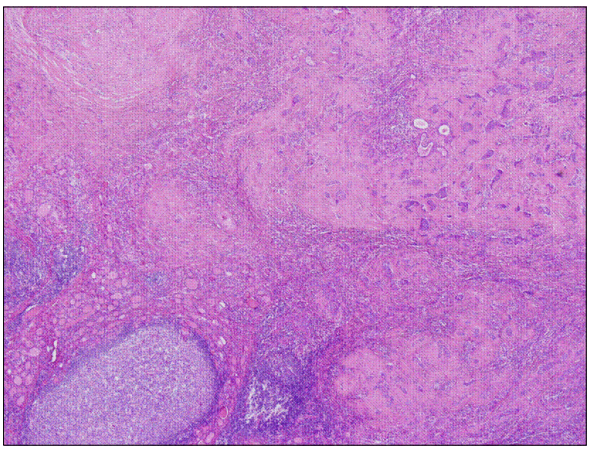

Fig. 3. The tumor nodule has ill-defined border and adjacent thyroid reveals lymphocytic thyroiditis (H&E staining, ×40).

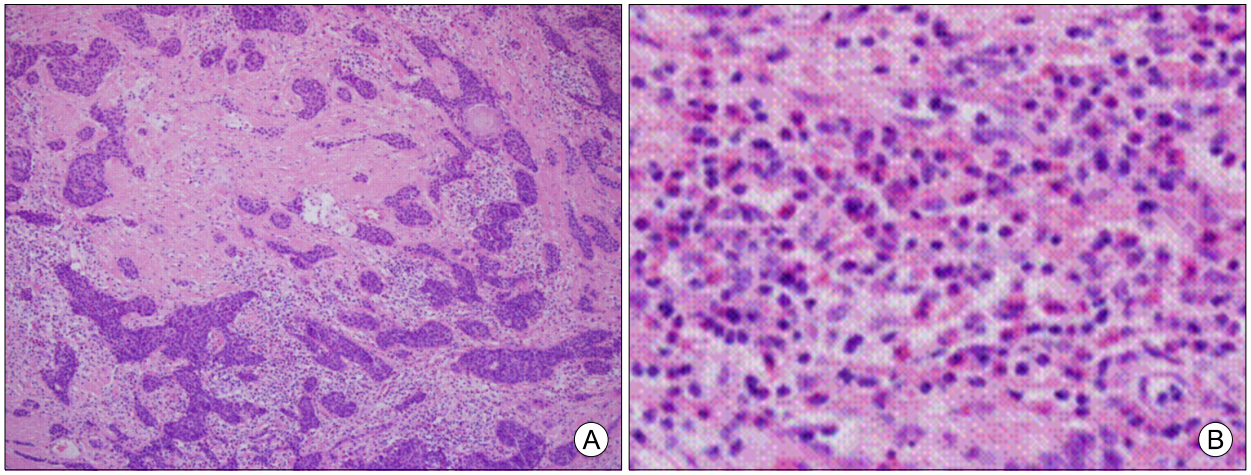

Fig. 4. The tumor is characterized by anastomosing compact cords and nests of epidermoid cells, accompanied by extensive sclerosis and by infiltration of eosinophils, lymphocytes and plasma cells (A: H&E staining, ×100; B: inlet, ×400).

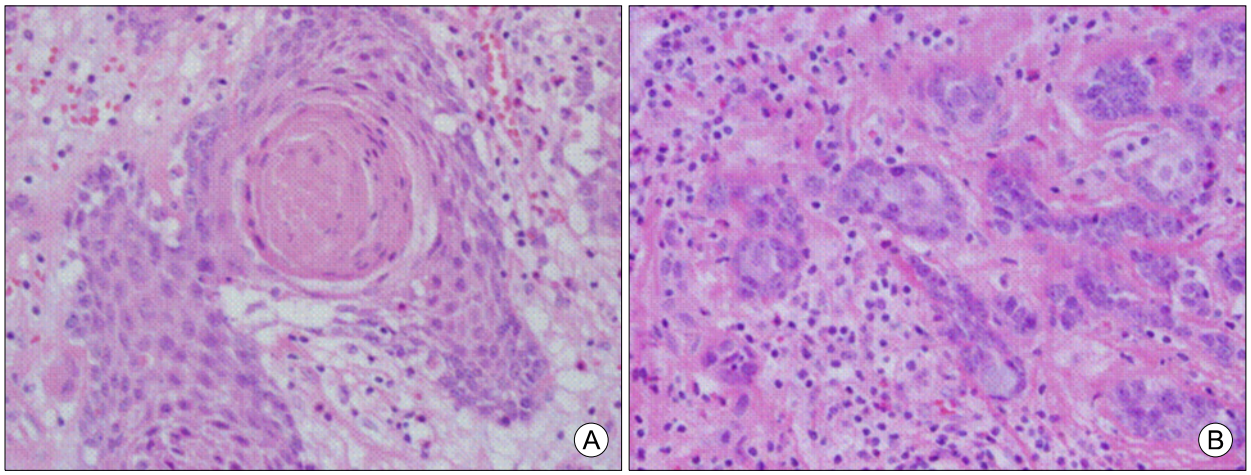

Fig. 5. (A) Tumor contains a well-formed squamous pearl. (B) Mucocytes compressed by globules of mucin is interspersed in epidermoid cells (H&E staining, ×400).

biologic potential. Two types of tumors have been described under this category: MEC and SMECE. The MEC shows both squamous and glandular differentiation in a background of a noninflamed gland, whereas SMECE is characterized by extensive sclerosis, squamous and glandular differentiation, a concomitant inflammatory infiltrate rich in eosinophilia.

MEC is usually a malignancy of the salivary glands, although it has been reported in other locations.[5-10] In 1991, Chan et al.[1] described 8 cases of a new distinct entity, which he called SMECE. It rarely occurs in the thyroid gland with fewer than 30 cases reported to date (Table 1). This was then compared with the conventional MEC of the thyroid gland by Sim et al.[4] He compared 10 cases of SMECE with 23 cases of MEC of the thyroid gland. He compared the clinical and histopathological features of both entities and suggested that SMECE should be separated from MEC as a distinct entity because it has characteristic morphologic features as described earlier that differ from conventional MEC of the thyroid gland. Pathologically, SMECE is characterized by sclerosis, mucin, and squamous features with eosinophilic infiltrate surrounded by desmoplastic stroma.[4,11-17] It is often associated with Hashimoto's thyroiditis.[1] Immunohistochemistry of most cases of SMECE described by Chan et al.[1] were positive for carcinoembryonic antigen and cytokeratin. This was duplicated

Table 1. Literature review of sclerosing mucoepidermoid carcinoma with eosinophilia of the thyroid gland

No.	Reference	Year	Age	Sex	Operation	Other treatment	Extrathyroidal extension or metastasis
1	Chan et al.[1]	1991	35	F	Total thyroidectomy	External radiation	Ext. into perithyroidal tissue, nerves and esophagus
2	Chan et al.[1]	1991	64	F	Left lobectomy		None
3	Chan et al.[1]	1991	71	F	Total thyroidectomy	External radiation	Ext. into perithyroidal soft tissue
4	Chan et al.[1]	1991	61	F	Left lobectomy		None
5	Chan et al.[1]	1991	43	F	Total thyroidectomy	External radiation	Adherent to trachea; tumor recurred in trachea
6	Chan et al.[1]	1991	46	F	Total thyroidectomy		Nodal metastasis and ext. into perithyroidal soft tissue
7	Chan et al.[1]	1991	69	F	Total thyroidectomy		Ext. into perithyroidal tissue; adherence to trachea and esophagus
8	Chan et al.[1]	1991	69	F	Total thyroidectomy		None
9	Wenig et al.[14]	1995	46	M	Isthmusectomy		None
10	Wenig et al.[14]	1995	46	F	Total thyroidectomy		None
11	Wenig et al.[14]	1995	44	F	Left lobectomy		None
12	Sim et al.[4]	1997	70	F	Total thyroidectomy	Chemotherapy recommended	Trachea, bilateral lung mets. developed right humeral head mets.
13	Sim et al.[4]	1997	69	F	Thyroidectomy with multiple surgeries		Tracheal and esophageal involvement
14	Geisinger et al.[3]	1998	39	F	Right thyroidectomy followed completion thyroidectomy		Perithyroidal tissue ext. then developed lung nodules and pleural effusion
15	Geisinger et al.[3]	1998	61	M	Total thyroidectomy	RAI then combined chemotherapy	Mediastinal ext. then 2 year later had T-spine mets. and liver mets.
16	Chung et al.[15]	1999	57	F	Total thyroidectomy then laryngectomy and esophagectomy	RT	Lymph nodes and esophageal involvement
17	Cavazza et al.[21]	1999	32	F	Total thyroidectomy		None
18	Solomon et al.[16]	2000	39	F	Total thyroidectomy	RT	Tracheal involvement
19	Baloch et al.[17]	2000	38	F	Total thyroidectomy		Ext. to skeletal muscles and lymph nodes
20	Baloch et al.[17]	2000	47	F	Right thyroidectomy		None
21	Baloch et al.[17]	2000	73	F	Right thyroidectomy		None
22	Baloch et al.[17]	2000	64	F	Right thyroidectomy		None
23	Sharma et al.[22]	2003	55	F	N/D	N/D	N/D
24	Shehadeh et al.[19]	2004	38	F	Total thyroidectomy with modified radical neck dissection then right neck and supraclavicular lymph node dissection and posterior neck surgery	RAI and concurrent chemo/RT	Perithyroidal ext., right axillary adenopathy, lung nodule
25	Hunt et al.[23]	2004	37	F	N/D	N/D	N/D
26	Hunt et al.[23]	2004	57	F	N/D	N/D	N/D
27	Hunt et al.[23]	2004	64	M	N/D	N/D	N/D

Table 1. Continued

No.	Reference	Year	Age	Sex	Operation	Other treatment	Extrathyroidal extension or metastasis
28	Kanat et al.[24]	2004	74	F	N/D	N/D	N/D
29	Das et al.[25]	2008	65	F	Subtotal thyroidectomy		Lymph node
29	Kim et al.[20]	2014	72	F	Total thyroidectomy with central compartment and bilateral compartment lateral neck dissection	RT	Trachea, esophagus, right recurrent laryngeal nerve invasion then 3 months later had liver, lung, bone mets.
30	Our Case	2014	37	F	Total thyroidectomy with central compartment node dissection and right selective neck dissection	Concurrent chemo/RT	Right lateral lymph nodes and right supraclavicular lymph node

Ext.: extension, F: female, M: male, mets.: metastasis, N/D: no data, RAI: radioactive iodine, RT: radiotherapy

in most of the cases that were subsequently described in the literature.[1,3,4,14,16,17] Thyroglobulin was negative except in 2 cases described by Wenig et al.[14] In all the cases, there was no immunoreactivity with calcitonin. The pathological differential diagnosis of SMECE includes primary or metastatic squamous carcinoma, papillary carcinoma with squamous metaplasia, conventional MEC, and medullary carcinoma.[17] Squamous differentiation in papillary carcinoma is not infrequent. Bondeson et al.[18] have also described papillary carcinoma of the thyroid gland with mucoepidermoid features in which there was immunoreactivity with thyroglobulin.

The most common presenting symptom is a painless neck mass or cold nodule on thyroid scan.[19] Symptoms secondary to locoregional extension such as hoarseness have been described. The average age of patients in the literature was 54 years with the majority of the patients being women.[19] The first man to be reported with SMECE was in a case series of 3 patients reported by Wenig et al.[14] in which the patient was unfortunately lost to follow-up after having surgery. The second male patient reported by Geisinger et al.[3] had spine and liver metastasis.

Generally, the SMECE can behave in a slowly growing manner and even in the presence of extension outside the thyroid gland can be associated with prolonged survival. This tumor tends to involve the adjacent perithyroidal tissues extensively including adipose tissue and skeletal muscles. In some cases it may extend more widely into the larynx,[15] trachea,[1,4,16,20] and esophagus.[1,4,15,20] Although the growth of this tumor is usually slow, Chan et al.[1] and subsequently Geisinger et al.[3] described 2 cases of rapidly growing tumors. Rare cases of lung and other distant metastases are reported.[3,4,20]

The eosinophilia, which is an important diagnostic clue to this lesion, remains unexplained, but it is likely that the tumor produces a cytokine that serves as a chemoattractant to eosinophils.[1,3,4,15,16,21] Whether this feature is responsible for the indolent behaviour of this lesion even in cases with extrathyroidal extension remains to be determined.

A limited number of cases preclude definitive recommendations regarding the proper treatment of MEC. The treatment that has been described in all cases varied from thyroid lobectomy to total thyroidectomy with modified radical neck dissection in addition to radiotherapy, chemotherapy, and iodine ablation.[1,3,4,14,16,17] Most of the patients in the Chan et al.[1] series had total thyroidectomy with no obvious difference in survival compared with patients having lobectomy. Wenig et al.[14] treated 2 patients with total and subtotal thyroidectomy (right lobectomy) with no evidence of disease of 8 and 13 years, respectively. The use of chemotherapy in this disease has not been shown to have a definitive role. Geisinger et al.[3] used chemotherapy in 2 patients. The first case received 13 courses of cisplatin and etoposide after a recurrence in the paratracheal area and in the lung. He described a period

of 28 months without progression but did not mention the percentage of response of the tumor to chemotherapy. Four and a half years after the initial diagnosis, the patient was receiving weekly doxorubicin, however, pulmonary metastasis progressed. The second case received a single course of combined chemotherapy without elaboration on the subsequent course of the disease. Radioactive iodine ablation has been attempted in some cases with a short progression-free survival as described by Geisinger et al.[3] who used iodine ablation for residual dis ease in a 61-year-old patient. She developed new cervical mass 3 months after the ablation.

External-beam radiation was used in 3 patients initially described by Chan et al.[1] after total thyroidectomy with NED from 3 to 5 years. And distant metastasis to the liver, lung, and bone were described by Kim et al.[20] after radiation therapy for three months. Concurrent chemoradiotherapy was not used in the cases that were described in this review; however, our patient showed very good response in the majority of the areas that were irradiated with concurrent carboplatin.

In conclusion, SMECE appears to be a uniquely distinct disease with especially aggressive behaviour as in our case, having noncontiguous multiple lymph nodes and visceral metastasis. SMECE is biologically aggressive as our case shows by virtue not merely of its local lymph node metastatic pattern but the involvement of noncontiguous lymph nodes, progressive local soft-tissue involvement, and distant visceral metastatic sites. Because this has significant prognostic implications, we believe this entity is biologically unique requiring accurate pathologic classification. More standardized treatment is likely to evolve in the future, with current management of patients with SMECE being surgical. Treatment of metastatic disease is certainly not well defined; however, with more familiarity with this neoplasm, this may well change.

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