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A Case of Sclerosing Mucoepidermoid Thyroid Carcinoma with Eosinophilia(SMECE)

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Sclerosing Mucoepidermoid Thyroid Carcinoma with Eosinophilia(SMECE) 1예

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= 국문초록 =

Sclerosing mucoepidermoid carcinoma with eosinophilia(SMECE)는 1991년 Chan 등[1]이 처음 보고한 이후로 현재까지 전세계적으로 단 17예 만이 보고된 매우 희귀한 갑상선 암종이다. 조직학적으로는 종양 내에 일부 점액성 세포와 증식된 상피성 세포들을 관찰할 수 있고, 조직내 호산구성 세포들이 자주 관찰된다. 대부분의 기질은 밀집된 섬유성 조직으로 구성되어 있으며, 하시모토 갑상선염이 동반되어 있는 것이 특징적이다. 종양의 악성도는 최초 보고인 Chan 등에 의하면 국소 재발 및 원격전이를 거의 하지 않는 예후가 좋은 암종으로 보고되었는데, 이후 여러 문헌에서 국소 침윤, 국소 재발, 원격 전이 및 사망이 발생하여 예후가 매우 불량했던 증례들을 보고한 바 있어 악성도에 대한 시각은 달라지고 있다.

본 저자들은 최근 병리적 진단이 매우 어려웠고, 국소침윤과 림프절 전이 소견을 보였으며, 수술 후 빠른 시일 내에 급속히 재발하였던 악성도가 매우 높은 sclerosing mucoepidermoid thyroid carcinoma with eosinophilia (SMECE) 1예를 경험하였기에 문헌고찰과 함께 보고하는 바이다.

중심 단어 : Sclerosing mucoepidermoid thyroid carcinoma with eosinophilia.

Sclerosing mucoepidermoid carcinoma with eosinophilia (SMECE) is a rare type of thyroid malignancy that was recognized recently. It is characterized by proliferation of squamoid tumor cells with a small portion of mucous cells typically in dense sclerotic stroma with prominent tissue eosinophilia and background Hashimoto's thyroiditis. So far 17 cases have been reported worldwide and some recent case reports indicated a somewhat aggressive clinical course in contrast to the original report[1] that emphasized an indolent course. Although SMECE has been established as a distinct entity it shares many histologic findings with mucoepidermoid carcinoma of the thyroid.

Herein we describe a case of SMECE that shows minimal tissue eosinophilia and no overt squamous differentiation thus causing a difficulty in pathologic diagnosis and showed a highly aggressive behavior.

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Case Report

This is a case of a 72-year-old woman who presented with a 2 month history of a palpable neck mass. The patient was referred to Severance Hospital of Yonsei University, Seoul, Korea after ultrasound and Fine needle aspiration of the neck had been performed at a local clinic under the impression of thyroid malignancy. The neck mass was described to have gradually increased in size over the 2

months but did not produce any pain, discomfort, dysphagia, dyspnea or hoarseness. The patient denied any symptoms of fatigue or weight loss. Her past medical history was unremarkable with no previous irradiation to the neck or the chest. The patient had no history of familial thyroid disease, autoimmune disease or other endocrine disorders. Palpation of the neck revealed a non-tender left thyroid mass extending to the right with no palpable nodes. The mass had a firm, irregular texture and was fixed to the sternocleidomastoid muscle. There was no bruit on auscultation. Physical examination of other systems was unremarkable. Neck ultrasound showed a 2.8×2.9cm irregular margined hypoechoic mass on the left thyroid with central 1.6cm-sized dense round rim of calcification. Findings of the right thyroid were insignificant. Neck computed tomography (CT) scan showed a left thyroid mass with huge calcification extending to the right thyroid (Fig. 1). There was no involvement of the surrounding nodes. Thyroid function tests revealed ; serum triiodothyronine (T3), 0.89 ng/dl, serum free throxine (T4), 0.96ng/dl, and serum thyroid stimulating hormone (TSH), 1.310microgm/dl. Chest X-ray, electrocardiogram, blood biochemical tests including serum calcium and phosphorous levels, were unremarkable.

Operative findings revealed a fixed, irregular, firm left thyroid mass extending behind the trachea, isthmus and the medial portion of the right thyroid. Left total thyroidectomy and isthmusectomy was initially performed due to the pathologist in charge of frozen section examination suggested the possibilities of diffuse sclerosing variant of papillary carcinoma and metastatic carcinoma. An immediate second operation was scheduled after making a diagnosis of sclerosing mucoepidermoid carcinoma with eosinophilia (SMECE) by reviewing the formalin-fixed, paraffin-embedded tissue sections and completion total thyroidectomy and central compartment node dissection was performed.

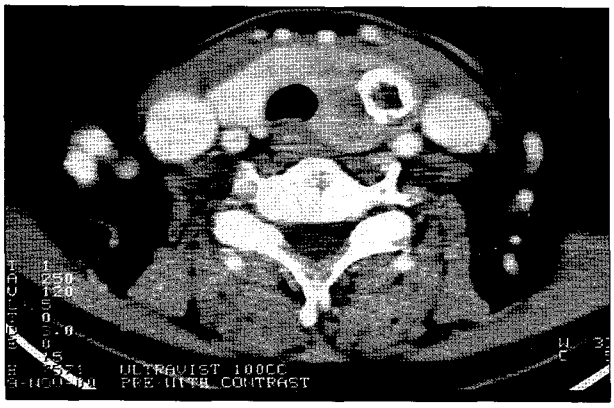

Fig. 1. A CT scan showing showed a left thyroid mass with huge calcification extending to the right thyroid.

The patient made an uneventful recovery and was discharged. However, 2 months after surgery, the patient presented with severe dypnea caused by a left side rapid growing tumor recurrence and she underwent emergent tracheostomy. We are planning a curative resection for recurrent tumor and an adjuvant therapy now.

Pathology

The left lobe of the thyroid weighs 21gm and it measures 5×3×2.5cm. Most of the lobe is replaced by an ill-defined firm, solid, and gray-white mass and there is a calcified, round, cystic mass measuring 1.8×1×1cm in its center. The calcified cystic mass is a follicular adenoma with cystic change and heavy calcification of the capsule. The thyroid parenchyma is diffusely infiltrated by malignant tumor cells having relatively abundant clear to amphophilic cytoplasm and vesicular nuclei. There is prominent sclerosis of the stroma and the tumor cells predominantly form cords, small islands, and pseudoangiomatous clefts (Fig. 2). Mucicarmine and Alcian blue stains revealed positive reaction in cytoplasm of some of the tumor cells. Although squamoid differentiation of the tumor cells mainly along the inner surface of the cords are noted focally (Fig. 3), definite evidence of squamous differetiation, such as keratin pearl and keratohyaline granule formation is not noted. In contrast to the reported cases, most of the infiltrating inflammatory cells in the stroma are lymphocytes and plasma cells and eosinophils occupy negligible proportion (Fig. 4). The tumor cells are immunoreactive for cytokeratin (AE1/AE3 cocktail) and CEA but thyroglobulin, chromogranin and calcitonin are not expressed in the tumor cells by immunohistochemistry. The remaining normal thyroid parenchyma is

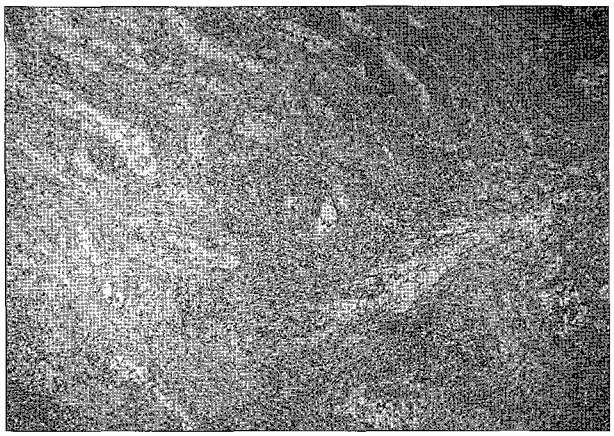

Fig. 2. A photography showing prominent sclerosis of the stroma and the tumor cells forming cords, small islands, and pseudoangiomatous clefts (H & E ×40).

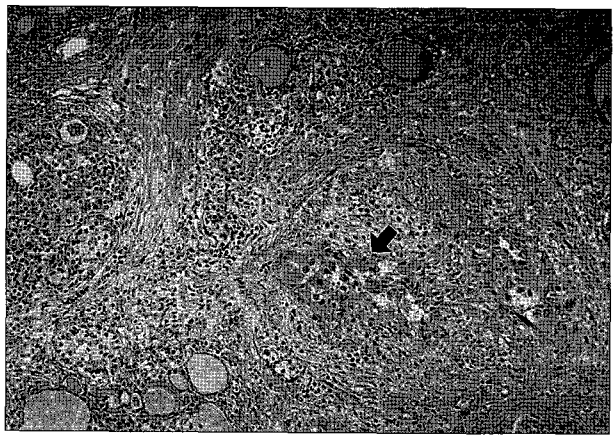

Fig. 3. A photography showing focal squamoid differentiation of the tumor(arrow) (H & E ×100).

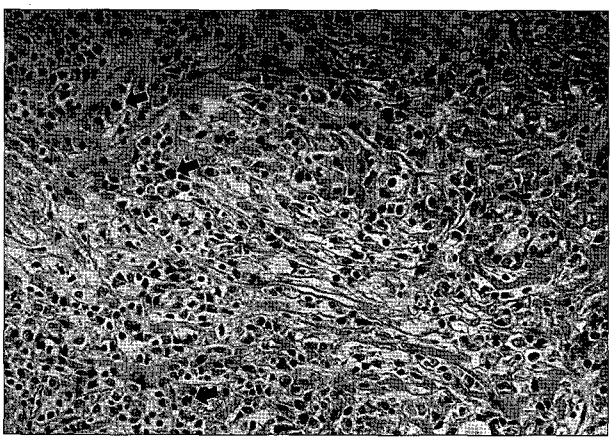

Fig. 4. A magnification view showing a few eosinophils(arrows) (H & E ×200).

densely infiltrated by small lymphocytes forming germinal centers in some areas but oxyphilic thyrocytes are not observed. The subsequent right lobectomy specimen showed a 0.5×0.5×0.5cm-sized ill-defined, solid, firm nodular mass in the parenchyma and it shows the same histologic findings as those of right-sided tumor. The dissected central lymph node measures 0.4cm in its greatest dimension and tumor metastasis focally extending to the perinodal fat is present.

Discussion

SMECE is a relatively recently established entity by Chan et al in 1991[1]. Although the nosologic term of "mucoepidermoid carcinoma" was used for this type of rare thyroid tumor, the tumor cells in SMECE do not exactly share the cytomorphologic features with a salivary type mucoepidermoid carcinoma (MEC). Most of the tumor cells in SMECE are round to polygonal cells with clear or pale eosinophilic cytoplasm of an uncertain lineage and definite squamous and mucous differentiation of the tumor cells have been reported to be only focally present. Tumor cells having cytomorphologic features of so called "intermediate cell" of salivary type MEC were not described to be present. Moreover, the origin of the tumor cells is definitely different and myoepithelial cells are not involved in the tumorigenesis of SMECE. Actually SMECE shares many histologic features with mucoepidermoid carcinoma of the thyroid gland and there is an opinion that they are two morphologic variations of the same entity. In contrast to SMEC, MEC of the thyroid gland were reported to exhibit more confluent growth pattern, more obvious mucinous differentiation, less prominent sclerotic stroma and no tissue eosinophilia. In contrast to MEC which commonly associated with lymphocytic thyroiditis, nearly all reported cases of SMECE is associated with Hashimoto's thyroiditis. In our case, histologic findings of scattered arrangement of tumor cells without forming a confluent mass, minimal mucinous differentiatefion revealed only by histochemical stains, and prominent sclerotic stroma heavily infiltrated by lymphocytes and plasma cells reach the diagnosis of SMECE. However, our case shows a few morphologic variations from the classic description of SMECE due to it shows negligible eosinophilic infiltration and we could not observe definite evidence of squamous differentiation even after extensive sampling. In addition, the remaining thyroid tissue shows histologic findings of lymphocytic thyroiditis not Hashimoto's thyroiditis and our case is also associated with a calcified follicular adenoma in the center of the tumor. Other histologic differential diagnosis of SMECE includes diffuse sclerosing variant of papillary carcinoma, undifferentiated carcinoma, and metastatic carcinoma, but they could be easily exclude once acquainted with the characteristic histologic findings SMECE.

The origin of SMECE is unclear as neither squamous nor mucin-secreting cells are present in the normal thyroid. Various postulates regarding the origin of SMECE have been made but no definitive conclusion has been made. Chan et al[1] proposed that SMECE porbably arose through malignant transformation of the metaplastic follicular epithelium based on the observation of gradual merging of the tumour cords and islands with the benign appearing metaplastic cell nests. Other suggestion was SMECE originates in the benign squamous nests that are often found in Hashimoto's thyroiditis, based on its constant association and close intermingling with Hashimoto's thyroiditis[2]. However the reported case of SMECE arising in the absence of background of Hashimoto's thyroiditis and squamous me-

taplasia does not support this idea. As in MEC, SMECE could possibly be originated from solid cell nests of the thyroid. Although our case revealed follicular adenoma in the center of SMECE, we think it just represents a coincidental finding without any pathogenetic relationship.

The clinical features of SMECE reflect that this is a disease affecting primarily middle-aged women with background Hashimoto's thyroiditis. However only a minority of the patients presented with known Hashimoto's thyroiditis, and most are euthyroid[1-3]. The chief complaints are painless, hard nodules in the thyroid and hoarseness, and pressure symptoms, such as dyspnea and dysphagia, are occasionally associated. SMECE was once known to have a relatively indolent course with excellent prognosis. According to the study conducted by Chan et al.[1], 5 of the 8 patients who had undergone surgery were free of disease for 6 months to 5.5 years after the initial diagnosis. One of the patients who had a recurrence of the tumor 16 months after the operation was also successfully treated by radiotherapy and remained well during the 3 year follow up. But several recent papers reported an aggressive behavior manifested by metastatic dissemination[2-5]. Out of the 5 reported cases with aggressive clinical courses, 1 patient died after a surgery, 1 patient demonstrated worsening of pulmonary metastasis despite of an intensive care. The remaining patients who had recurrences showed no evidence of tumor after having undergone either post-op radiotherapy or chemotherapy. Sites of metastasis varied from regional sites including perioesophageal and peritracheal tissues to distant sites such as the lung, liver, peritoneum, bone and epidural tissue. Although there was no mention about the proper treatment modalities for SMECE in the literlatures, aggressive treatment, curative resection and postoperative chemoratiation therapy, would be necessary concerning the cases with aggressive behavior.

The case described in this report is a still under-recognized very rare tumor of the thyroid, SMECE, which shows some morphologic variation from the classic reported cases in the points that there was focal squamoid differentiation of the tumor cells without definite evidence of squamous cellular component, such as keratin pearl and keratohyaline granule formation, and most of the infiltrating inflammatory cells in the stroma are lymphocytes and plasma cells and eosinophils occupy negligible proportion. To our knowledge, our case, which showed rapid growing tumor recurrence only two months after surgery, has more aggressive behavior than all the cases of SMECE reported.

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