Sclerosing Mucoepidermoid Carcinoma of The Thyroid Gland

Tiroid Glandının Sklerozan Tip Mukoepidermoid Karsinoması

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Abstract
An extremely rare case of sclerosing mucoepidermoid carcinoma (SMECE) of the thyroid in a 22-year-old woman is reported. The patient initially presented with a thyroid nodule. Fine needle aspiration cytology of the nodule showed features of a malignant tumor that was different from the usual types of thyroid carcinoma. Total thyroidectomy and right cervical lymph node dissection were performed, and pathology confirmed SMECE. The patient remains asymptomatic and no further recurrence or metastasis has been noted in the postoperative course of five years. She is the youngest patient with SMECE in literature. In this report, we briefly present the clinical and biologic course of this patient's neoplasm and also review the associated literature. *Turk Jem 2008; 12: 39-41*
Key words: Thyroid neoplasm, mucoepidermoid carcinoma, sclerosis, and eosinophilia

Özet
Oldukça nadir görülen ve yirmi iki yaşındaki kadın hastada tespit edilen tiroid glandında sklerozan tip mucoepidermoid karsinoma olgusu (SMECE) sunuldu. Hasta tiroidde nodül nedeniyle başvurdu. İnce iğne aspirasyon sitolojisi malign tumor özellikleri taşımakla birlikte genellikle görülen tiroid karsinomlarından farklıydı. Total tiroidektomi ve sağ servikal lenf nodu disseksiyonu uygulandı. Patoloji Sklerozan tip mukoepidermoid karsinoma (SMECE) ile uyumluydu. Hasta halen asemptomatik olup postoperatif 5 yılda rekürrens veya metastaz izlenmedi. Bu olgu sunumunda neoplazmın klinik ve biyolojik davranışı anlatılmış ve literatür gözden geçirilmiştir. *Turk Jem 2008; 12:39-41*
Anahtar kelimeler: Tiroid kanseri, mukoepidermoid karsinoma, sklerozis ve eozinofili

Introduction

Mucoepidermoid Carcinoma (MEC) most commonly occurs in the salivary gland (1), but has also been reported in other locations, including the respiratory tract, esophagus, breast, subglottic region, pancreas and thyroid gland (2-7). It has been described as a low-grade indolent tumor that rarely metastasizes and recurs locally without morbidity (8). In 1977 Rhatgian et al (9), first reported a MEC of the thyroid gland in a 20-year-old woman. Two types of tumors have been defined histopathologically, under this title: 1) Mucoepidermoid Carcinoma (MEC) and 2) Sclerosing Mucoepidermoid Carcinoma with Eosinophilia (SMECE) (10).

Primary MEC is a rare tumor of the thyroid with indolent biologic potential. It is associated with epithelial thyroid cancers (11). MECs have been described as foci of squamous change with mucin production and lacking in immunoreactivity for thyroglobulin (10). The origin of MECs is unknown, but it has been suggested that these tumors originate from solid cell nests, which in turn are thought to be of ultimobranchial body derivation (12-13). MECs show both squamous and glandular differentiation in the background of a noninflamed gland (10). The clinical features of the reported cases and the presence of ground glass nuclei and psammoma bodies in some of these tumors suggest that they may represent papillary carcinomas with an extreme degree of squamous and mucinous metaplasia (14).

A distinctive variant of this tumor is represented by the SMECE, which is characterized by extensive sclerosis, squamous and glandular differentiation, a concomitant inflammatory infiltrate rich in eosinophils, and a background of lymphocytic thyroiditis (10). Microscopically, strands and nests of squamous tumor cells with mild to moderate pleomorphism are seen infiltrating a dense fibrohyaline stroma. Foci of definite squamous differentiation and mucin secretion are often present. There is a constant and often striking infiltration by mature eosinophils. The tumor

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cells are immunoreactive for keratin but not for thyroglobulin (14). In this report, we present a patient with this unusual malignancy, describe the cytologic, histologic and immunohistochemical findings and also review the associated literature.

Case Report

A 22-year-old woman was admitted for evaluation of a thyroid nodule that had just been noticed by the patient. There was no history of previous irradiation to the neck or chest, nor was there familial disease of the thyroid, other endocrine disorders, or autoimmune disease. In physical examination, a 2.0x1.5 cm, firm nodular enlargement of the right lobe of the thyroid was determined. The patient was clinically euthyroid. The thyroglobulin antibody and microsomal antibody tests were negative. Serum thyroglobulin and calcitonin levels, blood counts and biochemical tests, including serum calcium and phosphorous levels, were within normal limits. The thyroid scintigraphy showed a cold area in the right lobe. Fine needle aspiration cytology of the nodule showed features of a malignant tumor that was different from the differentiated thyroid carcinomas but could not be classified. An excision of the right lobe of the thyroid was performed. Frozen sections made from the nodule and right cervical lymph nodes were interpreted as 'malignant tumor' and 'metastatic lymph nodes', respectively. Because of these findings, a total thyroidectomy was performed and the cervical lymph nodes adjacent to the right lobe were also removed. After the pathologic examinations, the final diagnosis was SMECE with a background of lymphocytic thyroiditis and lymph node metastasis. The patient remains asymptomatic and clinically euthyroid with L-thyroxin replacement therapy, and no further recurrence or metastasis has been noted in the postoperative course of five years.

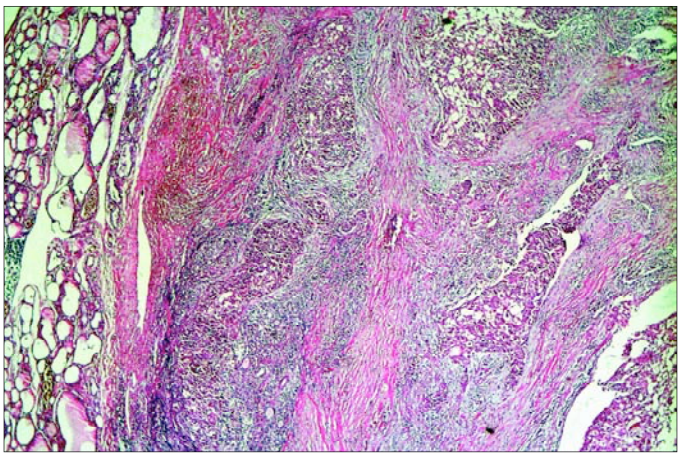

Figure 1. Tumor consisting of solid sheets and islands within surrounding compressed thyroid tissue. Neoplastic cells are surrounded by dense connective tissue. H&E x 40.

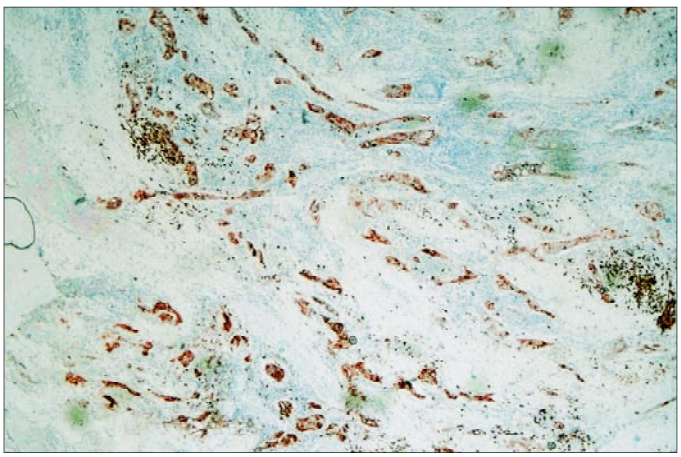

Figure 2. Diffuse and strong CEA positivity in the tumor. Peroxidase- antiperoxidase, CEA x 200.

Pathologic Findings

Macroscopic Findings

The resected thyroid gland weighed 20 g and the capsular surface was smooth. The right lobe measured 4.0x4.0x1.0 cm and the left lobe measured 4.0x3.0x1.0 cm. On sectioning, the right lobe revealed an ill-defined, yellow-white firm nodule measuring 2.1x2.0x1.5 cm. The left lobe contained a grayish irregular area of 0.3 cm. Multiple perithyroideal and right cervical lymph nodes were white and firm.

Microscopic Findings

Histologically, the non-neoplastic portion of the thyroid showed typical features of Hashimoto's thyroiditis. The stroma was infiltrated by lymphocytes and plasma cells. Lymphoid follicles with prominent germinal centers were present. No eosinophils were identified in these particular areas. There was an infiltrative tumor within the surrounding compressed thyroid tissue (Figure 1). The tumor was composed of solid cords, islands, and sheets of tumor cells with hyperchromatic nuclei and polygonal, moderate to abundant cytoplasm. These were supported by fibrous stroma showing focal hyalinization. Prominent anaplasia was not found. Small duct-like structures and microcytic changes were also observed. Mucus was observed in the lumens of these structures and spills into the adjacent stroma were occasionally seen. Intracytoplasmic mucus was also found in the cytoplasm of cells singly and distributed throughout the tumor areas. Keratin pearl formation and individual cell keratinization were not observed. Histochemically, mucicarmen staining confirmed the presence of intracellular and intercellular mucus. PAS Alcian blue pH 2.5 stain showed that the mucus had neutral and alcinophilic acidic components. Vascular invasion was not seen. Metastatic carcinoma was identified in 2 of 3 perithyroideal lymph nodes. Metastasis was absent in 16 right cervical lymph nodes.

Immunohistochemical Findings

The tumor cells were diffuse and strongly positive for carcinoembryogenic antigen (CEA) (Figure 2) and low molecular weight cytokeratin (LMWK). High molecular weight cytokeratin (HMWK) was found to show a prominent but focal staining in tumor cells. However, they were negative for thyroglobulin, calcitonin and chromogranin.

Discussion

Chan et al. first described SMECE, in 1991 (15). They reported 8 cases of low-grade carcinoma arising in women with Hashimoto thyroiditis. Histologically, these tumors were composed of cords and nests of cells. The characteristics of these ill-defined tumors included dense sclerotic stroma, heavy

eosinophilic infiltration, small nests or strands of squamous cells with occasional mucous cells, the invasion and obliteration of medium-sized vessels by the tumor, and the background of Hashimoto thyroiditis in the uninvolved thyroid tissue. The tumor often showed perithyroideal extension into the adipose tissue and skeletal muscle, and in some cases it extended more widely into the larynx, trachea, and/or esophagus. The tumor cells were immunoreactive for keratin and CEA but negative for thyroglobulin and calcitonin (15). The differential diagnosis of SMECE includes fibrosing Hashimoto's thyroiditis, primary or metastatic squamous cell carcinoma, and papillary carcinoma with squamous metaplasia (11,15-18). Since its initial description, 15 additional case reports of SMECE in the thyroid gland have been presented (10,16-24). The tumor most commonly occurs in women (15). The SMECE can behave in a slowly growing manner, and even in the case of extension outside the thyroid, it exhibits a prolonged survival (10). Although the initial description by Chan et al (15) characterized SMECE as a low-grade carcinoma, aggressive behavior with extrathyroidal extension and distant metastasis have been noted in more recent cases (16-18). Sim et al. (1997) reported two cases, one presented with local invasion and another with pulmonary and humeral metastases (16). Geisinger et al. (1999) reported two cases with pulmonary and vertebral metastases (17). Bondenson et al. (1996) reported a patient presenting with recurrent laryngeal nerve invasion as well as pulmonary metastases (18).

In this report we presented the clinical and pathologic findings of a case of SMECE of the thyroid in a 22-year-old woman. She is the youngest patient with SMECE in literature. The tumor in our patient behaved in a clinically aggressive manner with multiple lymph node metastases at the time of initial diagnosis. Total thyroidectomy and right modified neck dissection was performed. The operation was followed by evaluation of the patient every 6 months with ultrasonography and/or computerized tomography. No further recurrence or metastasis has been noted in the postoperative course of five years.

In summary, SMECE is a rare neoplasm of the thyroid gland that proved capable of aggressive behavior manifested by distant metastasis. It most commonly occurs in women with Hashimoto's thyroiditis. There are still too few cases documented and with inadequate follow-up periods to state the definitive clinical course of SMECE. More cases are needed for clarification. The therapy is a total thyroidectomy until more is known about these tumors' potential for local aggressiveness as well as metastatic spread.

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