Sclerosing mucoepidermoid carcinoma with eosinophilia of the thyroid: A cytological dilemma

ABSTRACT
Sclerosing mucoepidermoid carcinoma with eosinophilia (SMECE) of the thyroid is a rare primary thyroid tumor arising in a background of Hashimoto’s/lymphocytic thyroiditis and has been recently introduced in the World Health Organization (WHO) classification of thyroid tumors. It is characterized by extensive sclerosis, squamous and glandular differentiation, and inflammatory infiltrate rich in eosinophil. Here, we are discussing the cytological features of this rare case in a 35-year-old female presented with thyroid swelling and lymph-node enlargement.

Key words: Eosinophilia; sclerosing mucoepidermoid carcinoma; thyroid

Introduction
Sclerosing mucoepidermoid carcinoma with eosinophilia (SMECE) of the thyroid is a recently recognized primary malignant neoplasm of the thyroid gland associated with Hashimoto’s thyroiditis/lymphocytic thyroiditis.[1] Till now, cases have been reported in the literature that are diagnosed histologically.[2-4] And only very few studies have described its cytological features.[5,6]

Fine needle aspiration (FNA) from SMECE often show nonspecific features and most often the diagnosis of a poorly differentiated or undifferentiated carcinoma is rendered in most of the cases; but careful examination of cytological features and the background may sometimes be helpful in diagnosis. Here, we describe the cytological features of this rare case along with its differential diagnosis.

Case Report
A 35-year-old female presented with thyroid swelling for 3 years and ipsilateral lymph-node swelling of 6-month duration. Her physical examination revealed right-sided thyroid swelling of 4 cm × 4 cm size and lymph-node of size 1.5 cm × 1.5 cm. Her thyroid profile revealed mild hypothyroidism, while routine blood examination and serum calcitonin levels were within normal limits. FNA was performed with a 22-gauge needle from both thyroid as well from lymph node and on aspiration from both sites blood mixed material was obtained. The prepared smears were stained with hematoxylin and eosin and with pap stain. Smears from both sites revealed an almost similar picture. The richly cellular smears showed predominantly round to oval cells lying singly as well as in loosely cohesive clusters. These cells had rounded hyperchromatic nuclei

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with an occasional prominent nucleus and a moderate amount of eosinophilic cytoplasm. A few cell clusters showed squamoid differentiation in the form of pyknotic to densely compact nucleus and deeply orangophilic cytoplasm [Figure 1a]. At a few paces, the cells formed ill-defined epithelial pearl-like structures and only very occasionally the cells showed intranuclear cytoplasmic inclusion (INCI) [Figure 1b]. Background population comprised predominantly of lymphocytes and a significant number of eosinophils (1-2 cells/hpf) [Figure 1c]. The important negative findings were the lack of mucus-secreting cells and intermediate cells. There was no background colloid or mucin. So, depending on the abovementioned cytological features, we made the diagnosis of a primary thyroid malignancy with squamous differentiation with a differential of poorly differentiated carcinoma, mucoepidermoid carcinoma with eosinophilia, and a metastasis from a different site.

The patient underwent radical thyroidectomy. On histology, the diagnosis of SMECE was confirmed. The nontumorous thyroid parenchyma showed changes consistent with lymphocytic thyroiditis. Histological diagnosis was further confirmed immunohistochemically as the tumor was positive for thyroid transcription factor-1 (TTF-1) and cytokeratin and negative for thyroglobulin and calcitonin [Figure 2].

Discussion

SMECE is a rare slow-growing neoplasm of thyroid described in adults between 35 years and 70 years of age with a female predominance (female to male ratio — 17:1). Though a few studies have described its histological features, only occasional reports have described the cytological features in which it has been described as a tumor with “deceptively bland morphology” or as carcinoma with cytoplasmic eosinophilia. Cytologically, SMECE should be differentiated from benign conditions showing squamous metaplasia as well as from primary thyroid neoplasm that can show foci of squamous differentiation such as papillary carcinoma, medullary carcinoma, conventional mucoepidermoid carcinoma, and primary or metastatic squamous cell carcinoma.

Papillary thyroid carcinoma can be differentiated from SMECE by its characteristic nuclear features such as nuclear clearing, nuclear grooves, and INCI. Although, INCI is present in very occasional cells but the diagnostic nuclear character was absent in the cells, rather the nucleus was hyperchromatic in

![Image](image1.jpg)

Figure 1: (a) Smear reveals round to oval cells with hyperchromatic nuclei with a cell cluster showing deep cytoplasmic eosinophilia and dense compact chromatin (H and E, ×40) (b) Tumor cells are forming epithelial pearl-like structure and a cell showing INCI (thin arrow) (H and E, ×200) (c) Background population consists of lymphocytes and eosinophils (arrow) (H and E, ×200)

![Image](image2.jpg)

Figure 2: (a) Histology showed island of squamoid cells embedded in a sclerotic stroma and dense eosinophilic cell infiltrate (H and E, ×100) (b) Normal thyroid parenchyma showed lymphocytic thyroiditis (H and E, ×200) (c) Calcitonin negative (calcitonin, ×200) (d) TTF-1 positivity (TTF-1, ×200) (e) Thyroglobulin negative (thyroglobulin, ×200) (f) Cytokeratin positive (cytokeratin, ×200)
the cells. Medullary carcinoma have a characteristic nuclear chromatin pattern, i.e., a salt-and-pepper pattern and usually lacks background population of lymphocytes and is usually associated with raised calcitonin levels.[9]

Primary squamous cell carcinoma is extremely rare and is classified as anaplastic carcinoma while this neoplasm usually has more nuclear atypia and pleomorphism and is frequently associated with necrosis that lacks a background population of lymphocytes and eosinophils.[9]

Most of the time straightforward cytological diagnosis of SMECE is not an easy task and on cytology there is often a dilemma about the diagnosis. Likewise, we put forth the differential of a poorly differentiated carcinoma with squamous differentiation and have kept the differential of SMECE owing to the absence of characteristic nuclear features of papillary and medullary carcinoma, the presence of hyperchromatic nuclei, and the background population of eosinophils and lymphocytes that suggest background thyroiditis.

Histologically, SMECE is characterized by small nest and cords of tumor cells separated by fibrocollagenous sclerotic stroma and dense eosinophil cell infiltrate. Tumor cells display prominent squamous differentiation characterized by intercellular bridge and keratin pearl formation. Focal areas may show glandular differentiation and small mucinous cyst formation. Immunohistochemically, SMECE is negative for thyroglobulin and calcitonin and positive for TTF-1 and cytokeratin.[10]

The histogenesis of SMECE is unclear. Its constant association with Hashimoto's thyroiditis/lymphocytic thyroiditis has suggested that SMECE originates from the metaplastic squamous nest found in Hashimoto's thyroiditis/lymphocytic thyroiditis.[1,2,6] Many authors additionally suggested the origin from ultimobranchial body or solid cell nest.[4] A few have suggested follicular origin.[11] While others suggested origin from C cell, parathyroid, ectopic salivary gland, and thyroglossal duct.[11]

Though the definitive cytological diagnosis of this rare neoplasm is very difficult and often has cytologically nonspecific features but whenever a thyroid tumor exhibits squamous features with the absence of characteristic nuclear features of papillary and medullary thyroid carcinoma one must keep the differential of SMECE.

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Conflicts of interest
There are no conflicts of interest.

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