Metastatic sclerosing mucoepidermoid carcinoma with eosinophilia (SMECE):
REPORT OF A PATIENT

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Disclosures

None
Sclerosing mucoepidermoid carcinoma with eosinophilia (SMECE) is a rare solid neoplasm. It most commonly affects the thyroid or salivary glands. Typically, it presents as a painless neck mass, usually 1-6 cm in diameter. It is usually low-grade and localized to the thyroid, parotid, or submandibular glands. Metastases may occur.
Background

- strong female predilection and is frequently associated with Hashimoto disease (chronic lymphocytic thyroiditis).
- classic histology; nests of squamoid tumor cells in a sclerotic or fibrohyaline stroma with eosinophilic infiltration, Mucinous epithelial cells and/or glandular
- strong positivity for cytokeratin, CD10, and beta-catenin.
- negative thryoglobulin, thyroid transcription factor-1 (TTF-1), and calcitonin staining.
- Rx usually surgical.
- radiotherapy and/or systemic chemotherapy- mets
Background

- The etiology of SMECE unknown
- Tumor-associated tissue eosinophilia represents a favorable prognostic factor and may explain the typically indolent nature of this malignancy
Relevance of case

- No standard of care!
A 71-year-old male with a history of hypertension and hypercholesterolemia underwent a screening ultrasound for asymptomatic carotid artery stenosis. A painless neck mass measuring approximately 3 to 4 centimeters in diameter was noted incidentally during the evaluation.

Upon further questioning, patient reported that he had experienced mild dysphagia during the preceding months.

A follow-up ultrasound of the head and neck was performed and revealed 3.85 x 5.49 x 3.7 cm and 1.79 x 3.35 x 1.33 cm masses on the right and left lobes of the thyroid, respectively. In addition, prominent cervical lymphadenopathy was noted on the right side.
Laboratory studies showed a slight elevation of thyroid stimulating hormone (4.67 mIU/L; reference range: 0.4 – 4.0 mIU/L), but normal thyroglobulin (21.2 ng/mL; reference range: 3 - 40 ng/mL). Calcitonin was significantly elevated (13.6 pg/mL; reference range: <10 pg/mL).
Case Presentation

- Fine-needle aspiration biopsy from the right thyroid mass and a right lymph node showed small clusters of cells which demonstrated marked nuclear enlargement, coarse chromatin, and prominent nucleoli.

- IHC showed rare cells positive for thyroid transcription factor-1 (TTF-1) but was negative for thyroglobulin, synaptophysin, chromogranin, and p63.

- Initial findings raised suspicion for localized medullary thyroid carcinoma. CT scan of the neck and chest showed findings consistent with metastatic disease.
Case Presentation

CT scan of the chest demonstrating ovoid nodules in the right upper (a) and lower (b) lobes of the lung measuring approximately 11 and 8 millimeters in diameter, respectively.
Subsequent biopsy showed a small component of well-differentiated papillary thyroid microcarcinoma in addition to a more extensive solid, squamoid proliferation.

Background fibrosclerotic stroma showed an eosinophil-rich lymphoplasmacytic infiltrate.

The squamoid area consisted of cells in small, glandular-appearing nests with intraluminal necrotic debris. IHC of the squamoid cells was positive for p63, PAX8, CK5/6, CK10, and CK19;

IHC Negative for thyroglobulin, calcitonin, Napsin A, synaptophysin, chromogranin, S100, Melan A, and HepPar1. The well-differentiated area of papillary thyroid carcinoma was positive for TTF-1.
Case presentation

- Provisional diagnosis of MEC or SMECE
- FISH testing: MAML2 gene rearrangement negative, favoring SMECE diagnosis.
- Next Generation sequencing revealed high PD-L1 positivity (tumor expression ≥50%).
- Right upper lobe lung biopsy cores showed metastatic SMECE within fibrous core biopsies as well.
Case Presentation

Intermediate magnification view of sclerosing mucoepidermoid carcinoma with eosinophilia (SMECE) shows a small component of well-differentiated papillary thyroid microcarcinoma in addition to a more extensive solid, squamoid proliferation. The background fibro-hyalinous stroma shows an eosinophil-rich lymphoplasmacytic infiltrate. The squamoid area consists of cells in small nests and sheets which have abundant eosinophilic cytoplasm with central, round nuclei, cleared chromatin and prominent nucleoli. Many of the nests have a glandular appearance with necrotic debris in the lumens.

[Hematoxylin and eosin; x10]
Case Presentation

Intermediate magnification view of sclerosing mucoepidermoid carcinoma with eosinophilia (SMECE), with Gland formation

[Hematoxylin and eosin; x10]
Case Presentation

High magnification view of sclerosing mucoepidermoid carcinoma with eosinophilia (SMECE), with adjacent small papillary cancer nuclear features

[Hematoxylin and eosin; x40]
Case Presentation

Intermediate magnification view of SMECE demonstrating negative thyroglobulin staining.

[Thyroglobulin immunohistochemistry; x10]
Case Presentation

High magnification view of SMECE demonstrating gland formation.

[Mucin immunohistochemistry; x40].
Case Presentation

- No standard of care for SMECE.
- Favorable response to radiotherapy was noted in several case reports.
- Pt was started on an 8-week course of intensity-modulated radiation therapy (IMRT) at a dose rate of 250 centigrays (cGy), with a final external beam dose of 5000 cGy.
- Marked PD-L1-positivity, hence was started on the checkpoint inhibitor atezolizumab; three infusions were performed over the course of six weeks.
### Table 1. Characteristics of patients with metastatic SMECE [1-5]

<table>
<thead>
<tr>
<th>C</th>
<th>Age (y)</th>
<th>Gender (G)</th>
<th>Hashimoto (H)</th>
<th>Site of Metastases (Mets)</th>
<th>Treatment (Tx)</th>
<th>Reference (Ref)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>36</td>
<td>F</td>
<td>+</td>
<td>Mediastinum</td>
<td>Radiation therapy</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>39</td>
<td>F</td>
<td>+</td>
<td>Liver and lungs</td>
<td>Radioactive iodine, radiation therapy, and carboplatin</td>
<td>3</td>
</tr>
<tr>
<td>3</td>
<td>39</td>
<td>F</td>
<td>-</td>
<td>Lungs</td>
<td>Cisplatin and etoposide, later followed by paclitaxel and doxorubicin</td>
<td>4</td>
</tr>
<tr>
<td>4</td>
<td>45</td>
<td>F</td>
<td>+</td>
<td>Lungs</td>
<td>Radiation therapy and metastatectomy</td>
<td>5</td>
</tr>
<tr>
<td>5</td>
<td>61</td>
<td>M</td>
<td>-</td>
<td>Thoracic spine, liver, and peritoneum</td>
<td>Systemic chemotherapy (type unknown)</td>
<td>4</td>
</tr>
<tr>
<td>6</td>
<td>70</td>
<td>F</td>
<td>+</td>
<td>Bone and lungs</td>
<td>Resection and methotrexate</td>
<td>2</td>
</tr>
<tr>
<td>7</td>
<td>71</td>
<td>F</td>
<td>U</td>
<td>Lungs</td>
<td>Radiation therapy</td>
<td>1</td>
</tr>
</tbody>
</table>

*Abbreviations: C = case; F = female; G = gender; H = Hashimoto disease present; Mets = site of metastases; NS = not stated; Ref = reference; Tx = treatment; U = unknown; y = years
Both therapies were well-tolerated. A repeat CT scan of the chest was obtained shortly after his last infusion and revealed significant regression of the previously-identified pulmonary metastases.

Repeat CT scan of the chest obtained three months after the initial CT scan demonstrates marked tumor regression. The nodule in the right upper lobe has decreased in size from approximately 11 to 8 millimeters in diameter (a); the nodule in the right lower lobe has decreased in size from approximately 8 to 4 millimeters in diameter (b).
SMECE Literature Review

- only 56 cases have been described in the medical literature as we know
  - 49 female
  - 7 male (including our patient)
- SMECE is almost always associated with Hashimoto disease.
  - our patient is only the third to present with SMECE arising in the absence of underlying Hashimoto disease.
- Mean age of presentation: ~55 years
may present with symptoms due to tumor extension.
- Hoarseness
- Dysphagia
- Dyspnea

Although SMECE is typically considered a low-grade malignancy, emerging evidence suggests metastatic SMECE is more common than previously recognized: up to 30%
<table>
<thead>
<tr>
<th>Thyroid gland</th>
<th>Salivary gland</th>
<th>Metastatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaplastic carcinoma</td>
<td>Acinic cell carcinoma</td>
<td>Nodular sclerosing Hodgkin disease</td>
</tr>
<tr>
<td>Follicular carcinoma</td>
<td>Adenoid cystic carcinoma</td>
<td></td>
</tr>
<tr>
<td>MEC</td>
<td>Clear cell carcinoma</td>
<td></td>
</tr>
<tr>
<td>Medullary carcinoma</td>
<td>Cystadenocarcinoma</td>
<td></td>
</tr>
<tr>
<td>Papillary carcinoma</td>
<td>Mucinous adenocarcinoma</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Oncocytoma</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pleomorphic adenoma</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PLGA</td>
<td></td>
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<tr>
<td></td>
<td>Salivary duct carcinoma</td>
<td></td>
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<td></td>
<td>Sebaceous腺癌</td>
<td></td>
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<tr>
<td></td>
<td>adenocarcinoma</td>
<td></td>
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<td></td>
<td>Warthin tumor</td>
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</tbody>
</table>

*Abbreviations: MEC = mucoepidermoid carcinoma; PLGA = polymorphous low-grade adenocarcinoma*
SMECE and MEC

Table 1. Clinical, genetic, histologic, and immunohistochemical features distinguishing MEC from SMECE [7,8]

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>MEC</th>
<th>SMECE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age:</td>
<td>49</td>
<td>55</td>
</tr>
<tr>
<td>2:1 female predilection</td>
<td></td>
<td>8:1 female predilection</td>
</tr>
<tr>
<td>Hashimoto thyroiditis present in approximately 40% of patients</td>
<td></td>
<td>Hashimoto thyroiditis present in nearly 100% of patients</td>
</tr>
<tr>
<td>Papillary thyroid cancer present in approximately 50% of patients</td>
<td></td>
<td>Papillary thyroid cancer uncommon</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Genetic features</th>
<th>MAML2 gene rearrangement-positive</th>
<th>MAML2 gene rearrangement-negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histologic features</td>
<td>Mildly fibrotic stroma</td>
<td>Extensive fibrosclerosis</td>
</tr>
<tr>
<td>Absent or rare eosinophils</td>
<td></td>
<td>Prominent eosinophils</td>
</tr>
<tr>
<td>Psammoma bodies may be present</td>
<td></td>
<td>No psammoma bodies</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Immunohistochemistry</th>
<th>Thyroglobulin-positive</th>
<th>Thyroglobulin-negative</th>
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<tbody>
<tr>
<td>TTF-1-positive</td>
<td></td>
<td>TTF-1-negative in over 50% of patients</td>
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<tr>
<td>CEA-negative in approximately 25% of patients</td>
<td></td>
<td>CEA-positive</td>
</tr>
</tbody>
</table>

*Abbreviations: CEA = carcinoembryonic antigen; MEC = mucoepidermoid carcinoma; SMECE = sclerosing mucoepidermoid carcinoma with eosinophilia; TTF-1 = thyroid transcription factor-1
Treatment

- Surgical

- Individuals presenting with locally-aggressive SMECE may also benefit from radiation therapy, particularly if extrathyroidal invasion involves the esophagus or trachea.

- There are no established guidelines for the treatment of metastatic SMECE.
  - Radioactive iodine, radiation therapy, and various chemotherapeutic agents have been used for the treatment of metastatic disease

- Screening for PD-L1, CTLA-4, and other biomarkers may be useful in treatment planning.
Conclusion

- SMECE is a rare solid neoplasm that most commonly affects the thyroid or salivary glands.

- Tumors are usually low-grade, but local invasion and/or distant metastases may occur in some individuals.

- Characteristic features include a fibrosclerotic stroma with nests of epidermoid and mucin-secreting cells and a prominent eosinophilic infiltrate.

- Our patient, a 71-year-old Caucasian male, was found to have SMECE of the thyroid gland with lung metastases and was treated with radiotherapy and atezolizumab (ongoing).

- In addition to radiotherapy and checkpoint inhibitors, radioactive iodine and chemotherapeutic agents may be effective in the management of metastatic SMECE.
References


Questions?