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Case report

Tracheal epithelial-myoepithelial carcinoma associated with sarcoid-like reaction: A case report

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A B S T R A C T

Epithelial-myoepithelial carcinomas are rare tumors that primarily originate in the salivary glands but have also been found in the tracheobronchial tree. We report the first case of epithelial-myoepithelial carcinoma associated with sarcoidosis. A 61 year old Hispanic man presented with altered mental status and hypercalcemia. Imaging revealed diffuse intra-thoracic and intra-abdominal lymphadenopathy. A diagnostic bronchoscopy was performed where an incidental tracheal nodule was discovered and biopsied. Pathology was consistent with epithelial-myoepithelial carcinoma. Lymph node biopsy demonstrated non-caseating granulomas consistent with sarcoidosis. Patient underwent tracheal resection of the primary tumor with primary tracheal reconstruction. Hypercalcemia subsequently normalized with clinical improvement. Repeat CT imaging demonstrated complete resolution of lymphadenopathy. Our findings are suggestive of a possible paraneoplastic sarcoid-like reaction to the epithelial-myoepithelial carcinoma with associated lymphadenopathy and symptomatic hypercalcemia.

Introduction

Epithelial-myoepithelial carcinomas (EMCs) are rare, encompassing <1% of all tumors. They are typically low-grade and primarily salivary gland in origin. However, they have also been reported to occur in the mucinous glands of the airway, sweat glands and breast [1,2]. Sarcoidosis is a multisystem disease of unclear etiology. Its diagnosis is based upon typical clinical and radiographic findings, exclusion of other diseases, and confirmation of non-caseating granulomas in tissue. Sarcoidosis has been reported to occur in conjunction with a variety of solid tumors. We describe a rare case of tracheal EMC and the first case associated with sarcoidosis and hypercalcemia.

Case presentation

A 61-year-old Hispanic man was brought for evaluation for weeks of altered mental status associated with weight loss and malaise. Initial laboratory evaluation was notable for hypercalcemia (14.0 mg/dL) prompting further evaluation. Parathyroid hormone was undetectable (<2.5 pg/dL) with a normal Vitamin D 1.25(OH)2 level (27.5 ng/mL), elevated angiotensin converting enzyme level (108 U/L) and a slightly elevated parathyroid hormone related protein (34 pg/mL). Imaging demonstrated intra-thoracic and intra-abdominal lymphadenopathy with moderate (F-18) 2-Fluoro-2-deoxy-D-glucose avidity. Normalization of mental status paralleled the normalization of hypercalcemia with saline, calcitonin and pamidronate.

Imaging findings prompted diagnostic bronchoscopy, which was unremarkable except for an incidental 0.7 cm tracheal nodule (Fig. 1). The nodule was sampled and pathology demonstrated a tumor composed of glands with a double layer of lining cells (Fig. 2). The inner layer was composed of eosinophilic cells, immunoreactive to cytokeratin-7. The outer layer was composed of clear cells, immunoreactive to smooth muscle actin and p63 (Fig. 3). The tumor was classified as an epithelial-myoepithelial carcinoma. Mediastinal lymph nodes were also sampled. Non-caseating granulomas were identified consistent with stage I sarcoidosis. There was no evidence of infection or other malignancy. Three-ring tracheal resection with primary tracheal reconstruction was performed with a normal calcium level at one-month follow up. Serial imaging demonstrated complete resolution of lymphadenopathy with no evidence of recurrence at 1 year.

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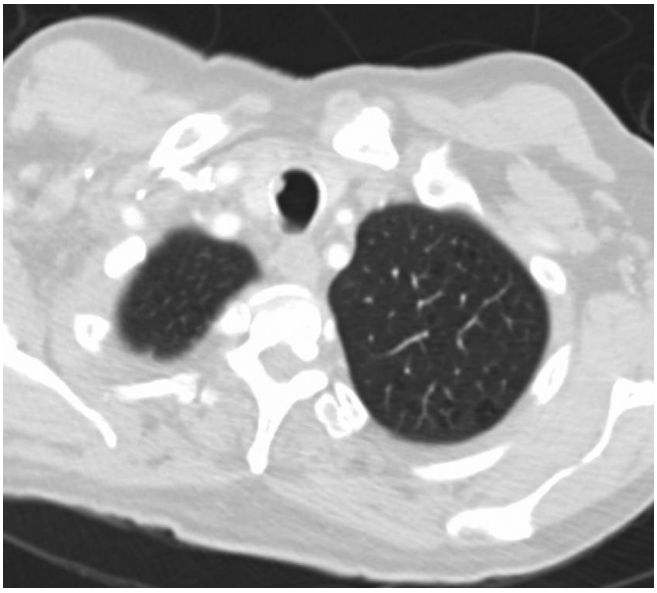

Fig. 1. Small tracheal lesion seen on computer tomography imaging of the chest.

Discussion

Epithelial-myoepithelial carcinomas are rare tumors. They are typically salivary gland in origin with only about 30 reported cases in the tracheobronchial tree [3–12]. The World Health Organization defines EMCs as a "malignant tumor composed of variable proportions of 2-cell types … represented by an inner layer of duct lining, epithelial-type cells, and an outer layer of clear myoepithelial-type cells" [13]. The inner epithelial layer generally stains positive for cytokeratin and the outer myoepithelial layer for smooth muscle actin and S-100 [7].

Horinouchi reported the first EMC case in 1993 [3]. Thirty-two additional EMC cases describe an age range between 34 and 81 with no gender propensity [3–12]. Presenting symptoms included dyspnea, cough and post-obstructive pneumonia. Only 3 cases in literature have reported EMC as occurring in the trachea [3,11,12]. In all other cases, the lesions were seen in the lobar bronchi with no propensity for either side.

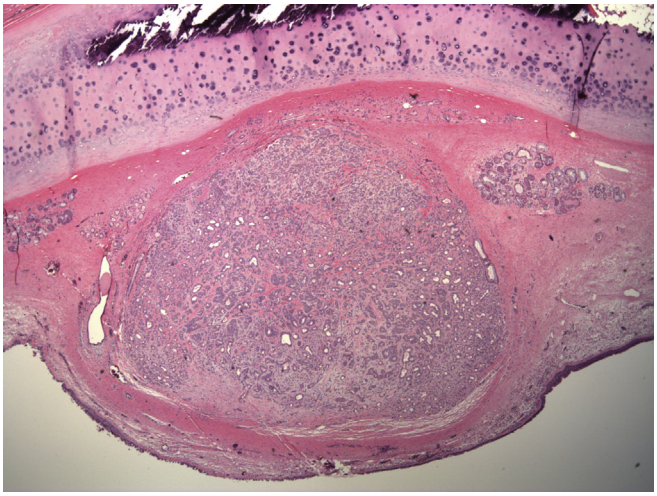

Fig. 2. Epithelial-myoepithelial lesion seen on pathology (H + E stain, 2× magnification).

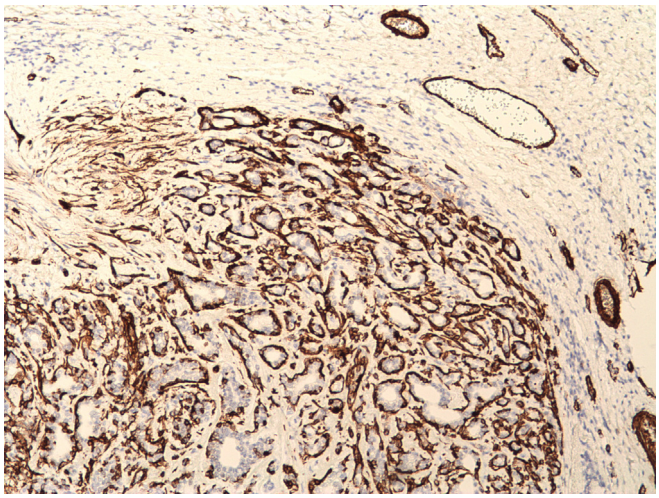

Fig. 3. High resolution view with smooth muscle actin staining (10× magnification).

EMCs are considered a low-grade tumor given the lack of significant cellular atypia, mitosis, necrosis, or surrounding invasion. However, there are three reported cases of aggressive behavior. Doganay reported a case with local invasion into the pulmonary parenchyma and Nishihara described a metastatic skull lesion [4,9]. In the third case, Muslimani described local recurrence and contralateral pulmonary parenchymal metastasis attributed to the piecemeal removal of the primary tumor by bronchoscopy [6]. There has not been any report of mortality attributed to EMC. A surgical approach is advocated for the management of EMCs, given its unclear malignant potential.

Although the EMC and sarcoidosis with associated hypercalcemia may have been coincidental in our case, the fact that both lymphadenopathy and hypercalcemia resolved after resection of the primary tumor suggests a more intimate relationship. Non-caseating granulomas resembling sarcoidosis has been observed in association with an underlying malignancy as early as 1911 by Wolbach [14]. Many such cases lack findings suggestive of systemic manifestations of sarcoidosis and have been termed "sarcoid-like reaction" [15]. While this type of reaction has been typically associated with lymphoproliferative disorders such as lymphoma and leukemia, an increasing number of case reports also demonstrate a correlation with solid tumors [16,17]. These solid tumors have included lung, breast, testicular and others (Table 1) [16–19]. Since

Table 1
Solid tumors associated with sarcoid-like reaction.

Breast cancer
Cervical carcinoma
Cholangiocarcinoma
Colon adenocarcinoma
Gastric adenocarcinoma
Hepatocellular carcinoma
Kaposi's sarcoma
Lung adenocarcinoma
Lung small cell carcinoma
Melanoma
Ovarian adenocarcinoma
Pancreatic cancer
Renal cell carcinoma
Squamous carcinoma of skin
Testicular germ cell tumor
Thyroid carcinoma
Uterine cancer

sarcoid-like reaction most often involves regional lymph nodes, an induced T-cell host response to antigenic tumor factors has been a proposed mechanism [20].

Conclusions

To our knowledge, this is the first report of an association between epithelial-myoepithelial carcinoma and sarcoidosis. The complete resolution of lymphadenopathy and hypercalcemia with local resection suggests a paraneoplastic sarcoid-like reaction. The potential for recurrence and metastatic disease is low based on limited available literature. Surgical resection is considered to be the current standard of care.

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"Tracheal epithelial myoepithelial carcinoma ex pleomorphic adenoma incidentally discovered during evaluation of diffuse lymphadenopathy in a patient presenting with hypercalcemia."

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