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Case study

Malignant perivascular epithelioid cell tumor of the oropharynx with strong TFE3 expression mimicking alveolar soft part sarcoma: a case report and review of the literature ☆

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Summary Perivascular epithelioid cell tumors (PEComas) in the head and neck region are rare, with 26 cases described in literature. These distinct mesenchymal tumors normally express both myoid and melanocytic markers. We here report an interesting and challenging case of malignant PEComa that showed transcription factor E3 (TFE3) protein expression and rearrangement, paucity of muscle and melanocytic marker expression, and morphologically mimicked alveolar soft part sarcoma. Awareness of this morphologic pitfall and recognition of *TFE3* gene–rearranged PEComa, as a distinct subtype of PEComa, is essential to avoid misdiagnosis.

1. Introduction

Perivascular epithelioid cell tumors (PEComas) are a distinct set of mesenchymal tumors that are characterized by coexpression of myoid and melanocytic markers [1]. The PEComa family comprises a wide variety of tumors that include angiomyolipoma, clear cell "sugar" tumor of the lung, lymphangiomyomatosis, and other uncommon clear cell tumors arising at various visceral, bone, and soft tissue sites [1]. PEComas in the head and neck region are rare, with 26 cases (excluding angiomyolipoma) described in the English literature. In the head and neck region, nasal cavity followed by orbit is the most common location for PEComas [2-11]. Pharynx is an extremely rare site for PEComas because only one case has been reported arising in the hypopharynx [12].

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Generally, PEComas are considered benign tumors; however, rarely tumors with malignant potential have been described at various sites [13]. We here report an intriguing case of a distinct subtype of malignant PEComa, which involved the oropharynx and morphologically mimicked alveolar soft part sarcoma (ASPS). In addition, the tumor cells showed strong transcription factor E3 (TFE3) protein expression and gene rearrangement with paucity of myoid and melanocytic marker expression. We also review previously reported cases of PEComas in the head and neck region.

2. Case report

2.1. Case history and radiologic findings

A 28-year-old woman presented with 1.5-week history of sore throat, hemoptysis, and dysphagia. A computed tomographic (CT) imaging study of the neck revealed a 7.2 × 5.1 × 2.9-cm oropharyngeal mass with curvilinear calcifications, and with extension into the retropharyngeal/parapharyngeal space (Fig. 1). Positron-emission tomography study revealed a maximum standardized uptake value of 5.1 in the mass. No lymphadenopathy or involvement of any other site was noted. Because the mass was causing airway compression, the patient underwent emergent intubation and biopsy of the mass, followed by tracheostomy.

2.2. Microscopic findings

Microscopic examination of the oropharyngeal biopsies showed overlying benign sinonasal mucosa with focal ulceration and dystrophic calcifications. Within the submucosa, there was proliferation of tumor cells arranged in nested and focally diffuse pattern (Fig. 2A). The tumor cells were associated with a delicate vascular stroma and scattered thin fibrotic bands with interspersed lymphocytes and plasma cells. There were few focal areas reminiscent of tumor cells arranged around thin vessels; however, distinct perivascular proliferation of tumor cells around thick blood vessels was not identified. The tumor cells were epithelioid, oval to polygonal, with eosinophilic granular and clear cytoplasm, centrally placed round to oval vesicular nuclei with occasional prominent nucleoli (Fig. 2B). Rare binucleated and multinucleated giant cells were noted. Occasional mitotic figures (up to 6/10 high-power fields) including few atypical forms (Fig. 2B) and areas of confluent coagulative necrosis were identified (Fig. 2A). No lymphovascular or perineural invasion was noted. The morphologic differential diagnosis included ASPS, granular cell tumor, melanoma, clear cell sarcoma (melanoma of the soft parts), poorly differentiated carcinoma, PEComa, paraganglioma, rhabdomyoma adult type, germ cell tumor, or metastasis from a renal or hepatic primary.

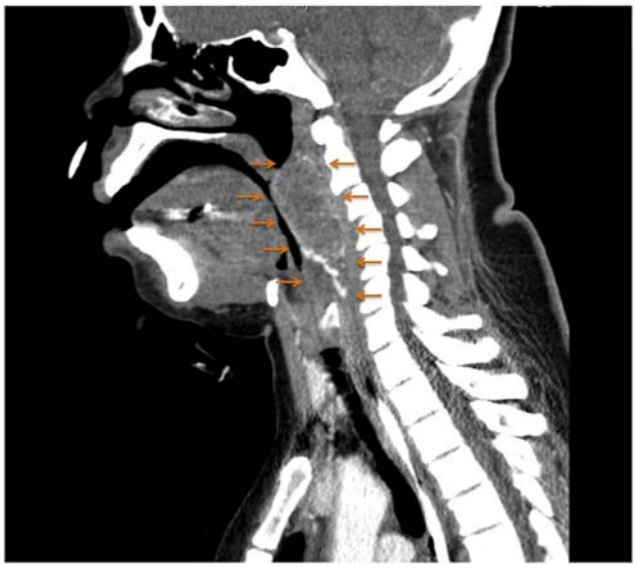

Fig. 1 Computed tomographic sagittal image shows a 7.2-cm oropharyngeal mass (arrows) with curvilinear calcifications with focal extension into the retropharyngeal/parapharyngeal space.

Immunohistochemical (IHC) stains were performed and showed tumor cells positive for vimentin, HMB-45 (focal) (Fig. 2D), pan-melanoma cocktail (focal), smooth muscle actin (SMA; patchy) (Fig. 2C), TFE3 (strong and diffuse) (Fig. 2E), and desmin (few scattered cells), and were negative for various cytokeratins (pan-cytokeratin AE1/AE3, CAM5.2, CK7, CK20, and epithelial membrane antigen), synaptophysin, chromogranin, S100, Melan-A, MITFD5, SOX-10, myogenin, MyoD1, calponin, inhibin, OCT-4, SALL-4, PAX-8, and HepPar-1. Most tumor cells showed cytoplasmic glycogen (periodic acid–Schiff [PAS] positive–diastase sensitive) with occasional cells showing PAS-positive, diastase-resistant granules (Fig. 2F). Ki67 labeling index in the tumor cells was 20% to 25%. Based on the above IHC results, the differential diagnosis included malignant PEComa or ASPS.

2.3. Fluorescence in situ hybridization and molecular findings

Fluorescence in situ hybridization analysis performed on formalin-fixed, paraffin-embedded tissue was positive for *TFE3* gene rearrangement in 65.5% (131/200) of nuclei examined. However, no *TFE3/ASPSCR-1* rearrangement [(X;17) translocation] was identified. Molecular studies using RNA from formalin-fixed, paraffin-embedded tissue sections by nanofluidics-based qualitative real-time polymerase chain reaction did not detect any of the 36 fusion transcripts tested including *PAX3/FOXO1*, *ASPSCR1/TFE3*, *EWSR1/ATF1*, *EWSR1/CREB1*, *LMNA/NTRK1*, and *BCOR/CCNB3*.

2.4. Follow-up

Based on morphologic features and ancillary study results, a diagnosis of malignant PEComa was rendered. No personal