Clear Cell Carcinoma of the Tonsil with Myoepithelial Features

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INTRODUCTION

Clear cell carcinoma—not otherwise specified (CCC-NOS) of the salivary gland is named for the characteristic monomorphic cells with clear cytoplasm which make up the tumor. Many other salivary gland neoplasms can contain foci of clear cells, but when they predominate in the specimen, the differential diagnosis includes primary tumors, such as mucoepidermoid, myoepithelial, and clear cell tumors in addition to metastases, such as renal cell CA or balcony cell melanoma. Microscopic analysis, including histochemical stains and immunohistochemistry are used to make the diagnosis and distinguish this entity from its mimickers. The distinction however, may be difficult, and it has been proposed that there exists a continuum between epithelial and myoepithelial derived neoplasms.

PATHOLOGY

The specimen revealed a 3.5 x 2.6 x 2.2 cm well demarcated non-encapsulated minimally infiltrative tumor in the tonsillar fossa, abutting skeletal muscle and undermining the squamous mucosa. Focally, tumor approximated peripheral nerve, but definitive evidence of invasive growth or vascular/lymphatic involvement was not seen. Standard hematoxylin and eosin staining as well as histochemical staining and immunohistochemistry was performed. The tumor was monomorphic, devoid of ductal components and was characterized by cells with clear cytoplasm exhibiting solid, trabecular and cord-like growth. Nuclei were round, slightly eccentric, with small nucleoli. Mitotic activity or necrosis was not seen. By histochemical staining, no mucin was present but intracytoplasmic diastase-sensitive, PAS-positive material indicative of glycogen was present. Cells were diffusely reactive to wide spectrum keratin (WSK), CD34, and p63, while S100 protein, smooth muscle actin and vimentin were negative to equivocal. Carcinoembryonic antigen (CEA) and glial fibrillary acidic protein (GFAP) were negative.

DISCUSSION

Most cases of clear cell carcinoma originate in the oral cavity from minor salivary glands. They are typically low grade, and present as a painless mass with minor ulceration or oral discomfort. Although follow up is not uniform among case series, recurrence was estimated at from 11.5-19%, and distant metastases at 8.8-21%4,5,6. Death due to disease is rare but has been reported. The tonsil is a rare subsite with only 1 previous case found in the literature6.

The spectrum between epithelial and myoepithelial lineages has been important in defining clear cell carcinoma. In the normal salivary gland, myoepithelial derived cells represent the basal compartment of the ductule, which typically express markers such as smooth muscle cell actin, calponin, S100, and GFAP.6,8 This is in contrast to the luminal, or epithelial elements which lack these markers. These staining properties and microscopic ductal architecture define whether the tumor is purely epithelial such as clear cell carcinoma, or myoepithelial derived such as epithelial-myoeipithelial CA and clear cell myoepithelial CA.

P63 is a nuclear protein expressed in normal and malignant salivary gland myoepithelial and basal duct cells6. P63 staining of this tumor is highly unusual for clear cell carcinoma and may characterize this tumor as trending toward the myoepithelial lineage. However, a battery of immunostains is required for unequivocal tumor type designation, and definitive myoepithelial differentiation cannot be assumed in the absence of concomitant staining with other myoepithelial markers such as CD10, S100, GFAP and smooth muscle actin.

CONCLUSIONS

Clear cell carcinoma is a rare malignant neoplasm which has only recently been categorized. In the past, multiple names have been used to describe this entity, however this was standardized in 2007 as clear cell carcinoma—not otherwise specified. Management generally involves total resection with negative margins, and neck dissection or radiation is not typically performed. Recently it has been appreciated that locoregional recurrence is not uncommon and distant metastases may occur, and therefore close surveillance is necessary for proper management. In addition, the influence of microscopic features and markers such as p63 on clinical behavior has not been defined. With better understanding and standardized diagnosis of these rare neoplasms, we may be able to better predict tumor behavior and tailor the treatment accordingly.

REFERENCES