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Original Articles

Molecular Profiling of Salivary Oncocytic Mucoepidermoid Carcinomas Helps to Resolve Differential Diagnostic Dilemma With Low-grade Oncocytic Lesions

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Abstract

Oncocytic mucoepidermoid carcinoma (OMEC) is a rare but diagnostically challenging variant of mucoepidermoid carcinoma (MEC). OMEC is notable for differential diagnostic considerations that are raised as a result of overlap with other benign and low-grade oncocytic salivary gland tumors. Diffuse and strong immunoreactivity of p63 protein may be useful in distinguishing OMEC from its mimics. However, focal p63 staining can be present in benign oncytomas. Presence of mucin-containing cells, mucinous cystic formation, and foci of extravasated mucin are considered a hallmark of MEC. True mucocytes may be, however, very few and hardly discernable in OMECs. Recent evidence has shown that most MECs harbor gene fusions involving *MAML2*. A retrospective review of archived pathology files and the authors' own files was conducted to search for "low-grade/uncertain oncocytic tumor," "oncocytoma," and "oncocytic carcinoma" in the period from 1996 to 2019. The tumors with IHC positivity for p63 and/or p40, and S100 negativity, irrespective of mucicarmine staining, were tested by next-generation sequencing using fusion-detecting panels to detect *MAML2* gene rearrangements. Two index cases from consultation practice (A.S. and A.A.) of purely oncocytic low-grade neoplasms without discernible mucinous cells showed a *CRTC1-MAML2* fusion using next-generation sequencing, and were reclassified as OMEC. In total, 22 cases of oncocytic tumors, retrieved from the authors' files, and from the Salivary Gland Tumor Registry, harbored the *MAML2* gene rearrangements. Presence of mucocytes, the patterns of p63 and SOX10 immunopositivity, and mucicarmine staining were inconsistent findings. Distinguishing OMEC devoid of true mucinous cells from oncocytoma can be very challenging, but it is critical for proper clinical management. Diffuse and strong positivity for p63 and visualization of hidden mucocytes by mucicarmine staining may be misleading and

does not always suffice for correct diagnosis. Our experience suggests that ancillary studies for the detection of *MAML2* rearrangement may provide useful evidence in difficult cases.