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HPV-Related Multiphenotypic Sinonasal Carcinoma

Lester D. R. Thompson, MD[1]

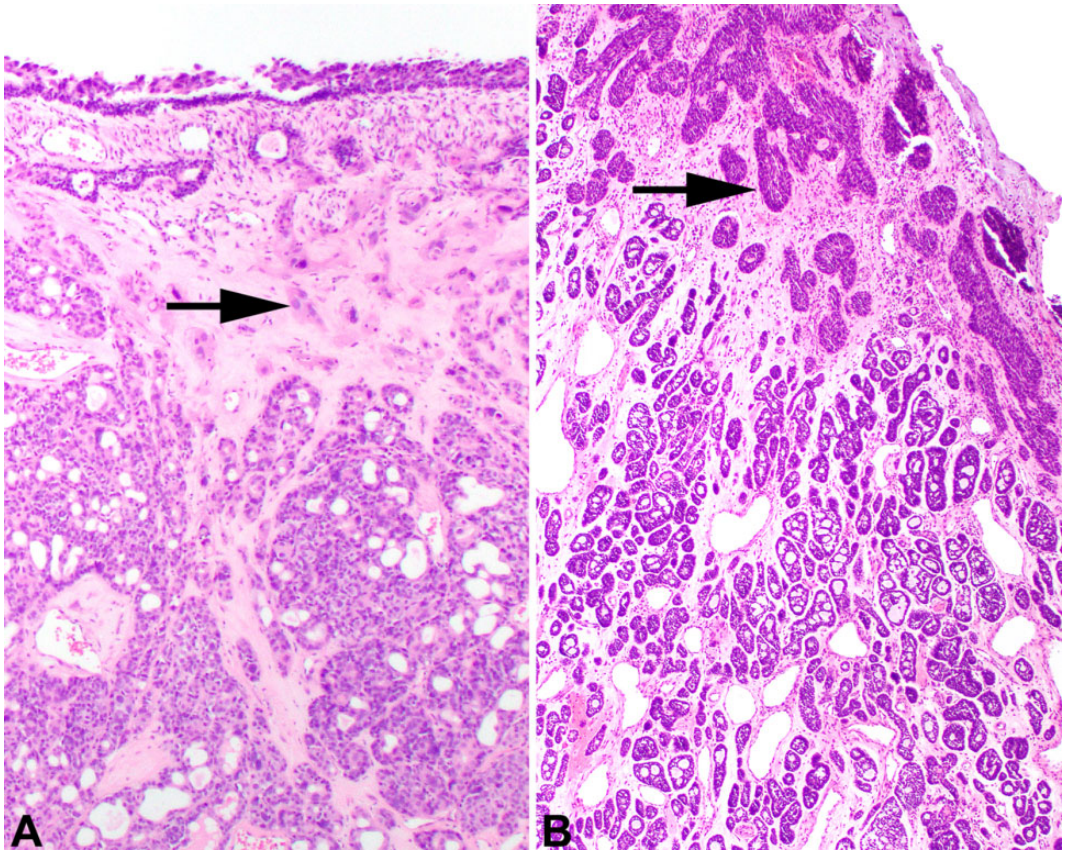

Figure 1. A, Surface squamous dysplasia is seen, with extension into the basaloid proliferation (black arrow). B, The surface squamous differentiation is noted as a more solid proliferation (black arrow), while the cribriform adenoid cystic-like pattern is well developed in the rest of the tumor.

Human papillomavirus (HPV)-related multiphenotypic sinonasal carcinoma (originally called HPV-related carcinoma with adenoid cystic-like features) is a recently recognized variant of sinonasal carcinoma showing histologic features of surface dysplasia and salivary gland carcinoma (adenoid cystic carcinoma specifically) and showing a strong association with HPV, especially HPV 33. Women are affected slightly more often than men, with a mean age at presentation in the sixth decade, frequently with high T-stage disease. Tumors involve the nasal cavity and paranasal sinuses, often with extension into adjacent structures. Even though the tumors are often large and destructive sinonasal tract tumors, they tend to exhibit a relatively indolent behavior, although local recurrence is frequent, but distant metastasis and death from disease are very uncommon. As such, this tumor should be distinguished from histologic mimics as there is a better prognosis.

Histologically, the tumors show a variety of different patterns of growth, including surface squamous dysplasia, often severe (Figure 1), and solid to basaloid and cribriform nests of epithelial

[1] Department of Pathology, Southern California Permanente Medical Group, Woodland Hills Medical Center, Woodland Hills, CA, USA

Corresponding Author:
Lester D. R. Thompson, MD, Department of Pathology, Southern California Permanente Medical Group, Woodland Hills Medical Center, Woodland Hills, CA, USA.
Email: entjournal@phillyent.com

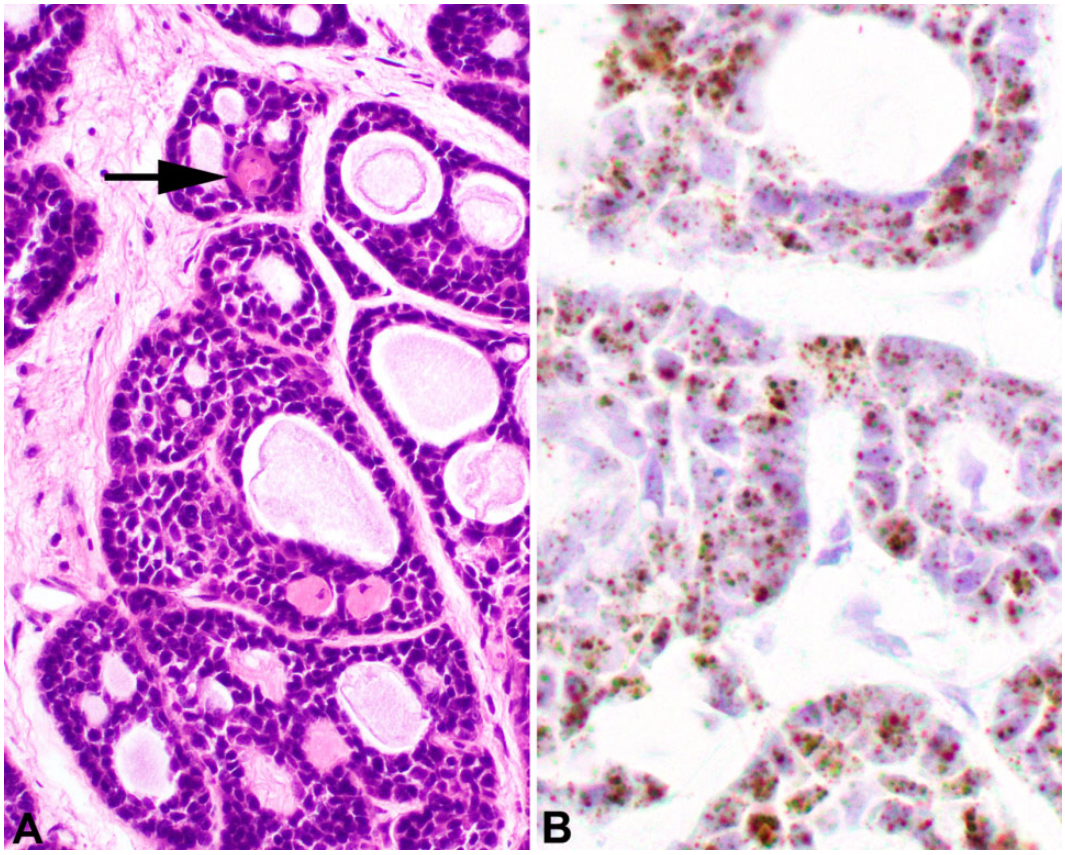

Figure 2. A, A very well-developed basaloid adenoid cystic-like pattern is seen in this tumor, including a small duct (black arrow). B, All of the neoplastic cell nuclei demonstrate a punctate localization with high-risk human papillomavirus (HPV) by RNA in situ hybridization.

and myoepithelial cells. These latter groups have an appearance that is similar to adenoid cystic carcinoma, although the ducts tend to be inconspicuous (Figure 2). Thus, the tumors are biphasic with eosinophilic ductal cells scattered within the predominant background of basaloid cells. The basaloid cells have a high nuclear-to-cytoplasmic ratio and hyperchromatic nuclei. Myoepithelial features are represented with cytoplasmic clearing, plasmacytoid appearance, and tumor cell spindling. Isolated bizarre, pleomorphic cells may be seen. There is often a high mitotic rate and areas of necrosis. Bone invasion is common, but perineural invasion is seen in about 10% of cases, while lymphovascular invasion is not readily apparent. The tumor, in isolated cases, may include squamous cell carcinoma, sarcomatoid transformation, and even some cartilaginous differentiation. One of the diagnostic features of this tumor is the presence of HPV, which can be detected with p16 as a surrogate marker, while RNA in situ hybridization for HPV demonstrates HPV, most commonly serovar HPV 33. Importantly, there is no *MYB*, *MYBL1*, or *NFIB* gene fusions, which are characteristics for adenoid cystic carcinoma. The neoplastic cells display reactivity with pancytokeratin, with biphasic staining of the basal/myoepithelial cells with p40, p63, calponin, and smooth muscle actin, while the luminal cells show a stronger reactivity with keratin. CD117 and S100 protein are positive, but often in a mixed pattern. Due to remarkable difference in long-term outcome and management, the tumor must be separated from sinonasal undifferentiated carcinoma, squamous cell carcinoma, adenoid cystic carcinoma, NUT carcinoma, and *SMARCB1*-deficient sinonasal carcinoma among others.

Declaration of Conflicting Interests

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Suggested Reading

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