Delayed local recurrence with progression of tumor morphology in HPV-related multiphenotypic sinonasal carcinoma

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Introduction

It is well known that human papillomavirus is implicated in about 25% of head and neck carcinomas, including those found in the sinonasal tract. HPV-associated malignancy is classically associated with non-keratinizing squamous cell carcinoma.

In 2013, Bishop et al described an HPV-associated malignancy that was morphologically similar to adenoid cystic carcinoma, designated “HPV-related carcinoma with adenoid-cystic like features”. In 2017, a larger case series expanded on this diagnosis, finding that the range of histological findings was actually much broader than originally thought.

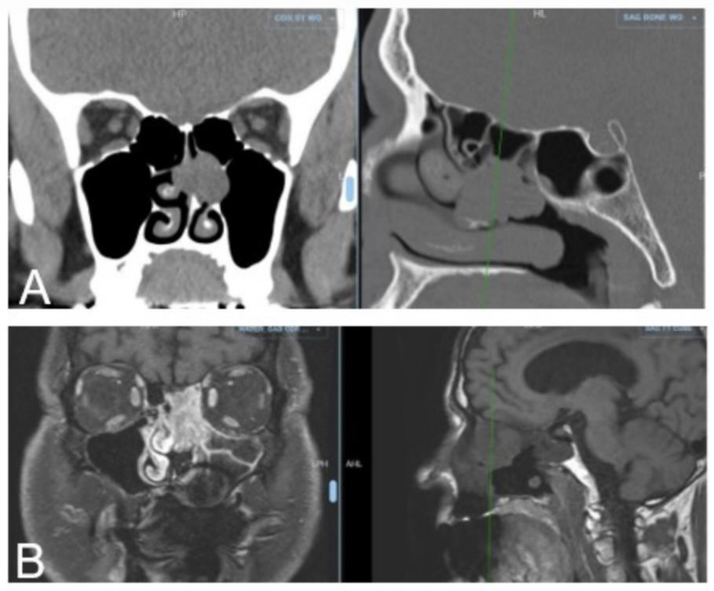
Now designated HPV-related multiphenotypic sinonasal carcinoma (HMSC), this malignancy of the sinonasal tract that is associated with human papillomavirus (HPV) but also has features of salivary gland carcinomas such as adenoid cystic carcinoma as well as squamous cell carcinoma-type features.

We present a case of a tumor that was originally diagnosed in 2017 as HPV-related carcinoma with adenoid cystic-like features, now known to be HPV-related multiphenotypic sinonasal carcinoma. We review the unusual histologic features and clinical course of the patient, who had a delayed local recurrence with different morphological features.

Illustrative Case

- A 60-year-old male with a history of basal cell carcinoma of the forehead, a 60-pack year smoking history and a long history of working in a paper mill presented to an outside hospital with epistaxis and congestion in 2017.
- He underwent endoscopic sinus surgery and resection of a nasal septal mass. Pathology was consistent with invasive poorly differentiated carcinoma with basaloid features and adenoid cystic-like features with HPV E6/E7 positivity. He was taken to the operating room at our institution for a repeat margin analysis and clearance with medial maxillectomy and sphenoid drill-out. A muti-disciplinary tumor board recommended against adjuvant therapy at that time.
- In July of 2025, he re-presented with 6 weeks of left nare drainage concerning for rhinorrhea and a recurrence of the left nasal septal mass. He underwent a combined bifrontal craniotomy and endoscopic endonasal approach with multi-layered reconstruction of the anterior skull base and negative margins were achieved both intracranially and intranasally.
- Final pathology was consistent with a grade 3 nonkeratinizing papillary squamous cell carcinoma. Post-operatively he underwent proton radiation therapy.
- On re-review of his 2017 pathology, his tumor is consistent with HPV-related multiphenotypic sinonasal carcinoma in the updated WHO classification. Immunoperoxidase studies were positive for Cam 5.2 and CD117, highlighting a focal ductal epithelial component, and in situ hybridization studies were positive for HPV.
- The pathology in 2025 was described as invasive poorly differentiated non-keratinizing papillary squamous cell carcinoma, staining positive for p63 and p40, a basal/myoepithelial cell marker, and cytokeratin AE/AE3, Cam5.2, KIT, and p16. The tumor also tested positive for HPV. On comparison to the 2017 pathology, the morphology of the two tumors is markedly different.

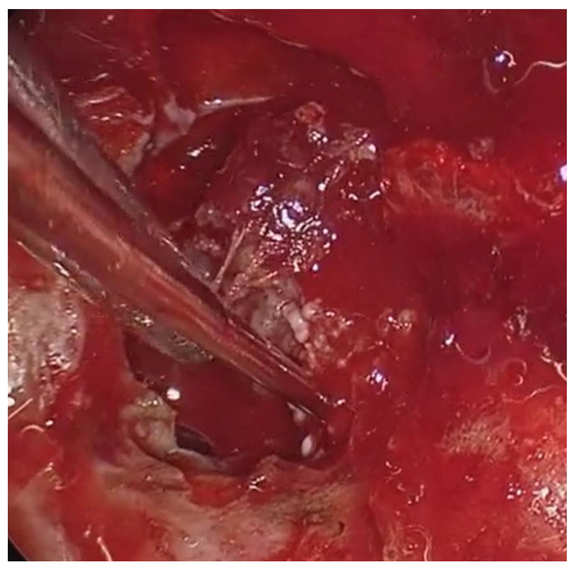
Imaging



Preoperative coronal and sagittal CT showing tumor of the nasal septum at time of original presentation in 2017 (A) and coronal and sagittal MRI showing recurrent tumor in 2025 (B)

Operative Management

- We performed a combined bifrontal craniotomy and endoscopic endonasal approach. The cribiform plate was positive for tumor and was resected. Negative margins were achieved. A multilayer closure with autologous fascia lata and a vascularized pericranium flap plus nasoseptal flap was performed for reconstruction



Intradural tumor being resected endonasally

Discussion

- HPV-related multiphenotypic sinonasal carcinoma is a newly defined and uncommon sinonasal malignancy with 124 cases reported in the literature
- 60% are diagnosed as T1 or T2 tumors with only 15% lymph node involvement. Distant mets reported in only 1 patient.
- About half of patients were managed with surgery alone, 22% with surgery plus adjuvant radiation, 17.8% with radiation and chemotherapy
- Locoregional occurrence occurred in 38.7% of cases with a collective 85.3% of patients alive after a mean follow-up period of 29 months
- The patient’s recurrence, found at 8 years after his initial resection, was found to be a morphologically different and more invasive squamous cell carcinoma requiring adjuvant proton beam therapy.

Conclusions

While HPV-related mutiphenotypic sinonasal carcinoma is considered a relatively indolent disease that does carry a risk of local recurrence, but overall a good prognosis, we report a case of local recurrence that revealed a morphologically different, more invasive tumor. This possibility is an important consideration in management of recurrence in these patients.

References

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