



# Malignant Sinonasal Mucosal Melanoma

## A Case Report and Review of the Literature

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### Abstract

Sinonasal mucosal melanoma represents an aggressive and rare neoplasm that presents similarly to other common ENT complaints of nasal obstruction and epistaxis but overall portends a poor prognosis. Roughly 0.5% of malignant melanoma arises in nasal cavity and is much more aggressive than its cutaneous counterpart. This submission provides an overview of malignant mucosal melanoma in the sinonasal cavity, preferred diagnostic methods and modern treatment. Additionally, we report a case of malignant melanoma of the sinonasal cavity in an 88-year-old male who presented with nasal obstruction, epistaxis, proptosis, and maxillary sinus tenderness. CT and MRI imaging along with immunohistochemical staining of S100 and HMB 45 confirmed the diagnosis. The overall rarity of this presentation necessitates a comprehensive examination of the current methods to diagnose and treat this condition.

### Introduction

- Nearly 1/2 of all mucosal melanomas (MMs) arise in the head and neck region making otolaryngologists history and clinical exam vital in diagnosing this disease entity.
- Overall, the mucosal form of melanoma represents < 1% of all melanomas and behaves more aggressively than its cutaneous counterpart.
- MM is a destructive neoplasm that exhibits unique features relative to other paranasal sinus and head and neck malignancies, as well as features entirely distinct from cutaneous melanoma.
- Approximately 2/3 of these lesions arise in the nasal cavity and paranasal sinuses, 1/4 are found in the oral cavity, and the remainder occur sporadically in other mucosal sites of the head and neck.
- The four stages of disease for MM are represented by III, IVA, IVB, and IVC. The AJCC System omits both T1 and T2 categories, that is justified by the very poor prognosis for even small superficial lesions.
- At this time, key genetic mutations such as BRAF and KIT are rarely seen in MM, thus making systemic treatment with targeted agents problematic and not universally indicated or utilized.

### Case Presentation

- 88-year old male presented in office with left sided epistaxis.
- The patient had been experiencing epistaxis for several months from the left nostril intermittently that generally resolved with conservative management. He denied any history of nasal packing/cautery or family/personal history of bleeding disorders.
- PMH: Hypertension, Heart Failure, Atrial Fibrillation (not on anticoagulation), BPH, Ambulatory dysfunction.
- PSH: Right hip replacement, Ventral hernia repair.
- Social History: Denies EtOH, Tobacco, illicit drug use. Former carpenter.
- Medications: furosemide, lisinopril, melatonin, metoprolol, multivitamin, ocular lubricant, pantoprazole, tamsulosin, venlafaxine, acetaminophen, albuterol-ipratropium, aspirin, budesonide, cholecalciferol, donepezil, ferrous sulfate, fluticasone nasal.
- Family History: no head and neck cancer in his family.
- Physical exam:
  - Tenderness to palpation overlying the left maxillary sinus.
  - Subtle proptosis of the left eye without ophthalmoplegia.
  - Clots and mild oozing from the left nasal cavity, soft tissue.
  - Neck supple without masses or lymphadenopathy.
  - Nasopharyngoscopy:
    - Large soft tissue mass in the left nasal cavity.
- Procedure: Attempted bedside debridement of clots from the left nasal cavity, however, the area was exquisitely tender. Attempts were terminated and the debrided clots/tissue.
- Nasal endoscopy with biopsy
  - Pathology: +S-100, +HMB-45
- Imaging:



Figure 1: CT Maxillofacial without contrast

Confluent expansile sinonasal cavity soft tissue mass with involvement of left maxillary, ethmoidal, and frontal sinuses as described above. Differential includes chronic sinonasal polyposis, inverting papilloma, however malignancy is also difficult to exclude.

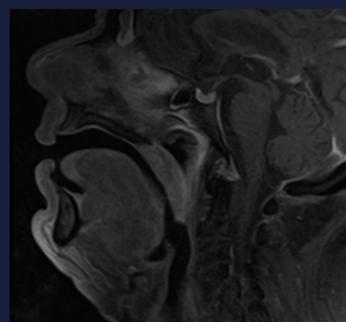


Figure 2: MRI Face/Neck/Orbit with and without contrast

Expansile left sinonasal soft tissue mass with heterogeneous enhancement, centered in the middle and upper meatuses as described. There is mass effect and displacement of the left cribriform plate and medial wall of the left orbit, without other findings to suggest intracranial or orbital invasion. The differential includes benign etiologies such as chronic obstructive sinonasal polyposis, and inverting papilloma. As the mass does bow the medial orbital wall, malignant differentials remain a consideration, such as squamous cell carcinoma or rhabdomyosarcoma.

Staging:  
Tumor – T3  
Node – N3  
Metastasis – M0  
Stage – III

### Discussion

- Melanocytes are cells whose primary function is to produce melanin, which is a pigment that has unique protective properties against UV radiation.
- Most melanomas are therefore cutaneous; however, melanoma can also arise from the mucosal surfaces of the eyes, reproductive mucosal surfaces, and anywhere of the respiratory tract, including the paranasal sinus and nasal cavity mucosa.
- By in large, mucosal tissues are generally not exposed to sunlight and so do not require UV protection. It is not entirely clear why melanocytes are found in the mucosal epithelium, but some sources suggest a possible immunologic function of these cells.
- When comparing the 5-year overall survival rate for CM is 80%, the rate for MM is only 25% and portends a much worse clinical course.
- When MM arises from the head and neck (MMHN), the 5-year overall survival rate is reported to be approximately 32% compared to other subsites.
- When comparing these forms of melanoma, locoregional nodal metastasis is far more frequent in MM (21%) compared to CM (9%) and carries a higher mortality than the N0 neck.
- The sinonasal cavity is the most common subsite of MMHN, nearly 70-80% arise in this area, representing roughly 4% of all sinonasal tumors.
- The median age of diagnosis in sinonasal MM is 60-69 years old; however, when present in the oral cavity, the typical age group is individuals less than 40 years old.
- The typical carcinogens responsible for other sinonasal malignancies are also implicated in MMHN. Tobacco, alcohol, formaldehyde, wood/textile dust, solvents have all been identified as risk factors for developing MMHN.
- In conjunction, both CT and MRI are useful in assessing overall extent of disease and allow accurate staging and surgical/therapeutic evaluation.
- PET-FDG may be helpful to screen for distant metastasis in patients with local advanced disease.
- As in the cutaneous counterpart, surgery remains the most important therapy for the best rate of cure, although it can be difficult to achieve negative margins secondary to the typical lentiginous spreading behavior of MM.
- Even with aggressive surgical resections, the local recurrence rates can be particularly high in ranges from 50%-90%.
- When localized to the sinonasal region, MM may require extensive craniofacial resection when there is involvement into the cribriform plate, orbital exenteration for orbit involvement, and radical nasal resection for diffuse mucosal disease.
- Endoscopic vs. open resections yield similar locoregional control, with an overall decreased morbidity with endoscopic approaches.
- Therapeutic neck dissection followed by radiation therapy has been shown to improve regional control in non-advanced MMHN.
- Few systemic treatments exist for advanced mucosal melanoma:
  - Dacarbazine and high-dose interleukin (IL)-2 in conjunction with MEK, PD-1, and CTLA-4 inhibitors
  - Vemurafenib, BRAF mutations (V600E)
  - Ipilimumab (IgG1 antibody)
  - Ongoing assessment of specific c-KIT, RAS-MAPK, MEK mutations as well as other molecular targets exist in the literature and are undergoing active clinical trials.

### Conclusions

Although the pathogenesis between mucosal and cutaneous melanoma shares a similar molecular course, patients diagnosed with MMHN have a poorer overall outcome than the cutaneous counterpart. Sinonasal MM represents <10% of sinonasal malignancies, with the majority arising in the nasal cavity. When compared to the nasal form of MM, sinus cavity MM has a much worse prognosis. Surgery remains the mainstay of treatment for these patients. While complete surgical excision of melanoma offers the only viable cure of this disease entity, the complex anatomy of the head and neck make these procedures high risk for surgical morbidity, while most patient still develop incurable metastatic disease. Endoscopic or a combined open and endoscopic approach can be used to minimize morbidity and maximize functional and aesthetic results without significantly compromising oncologic outcomes. Adjuvant radiotherapy conveys some locoregional control, without a significant effect on overall survival. Chemotherapy does not play a role for primary treatment of MMHN, but there is promising data to suggest the function of immunotherapy to confer survival benefit to patients with metastatic disease.

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