Unmasking Melanoma at Autopsy:
A Case of Misdiagnosed Nasal Malignancy with Widespread Metastases

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Background

Melanoma is a highly aggressive malignancy with a broad histopathologic spectrum, often mimicking other neoplasms. Mucosal melanomas are rare, frequently amelanotic, and may exhibit variable immunohistochemical staining, complicating diagnosis. In the nasal cavity, where squamous cell carcinoma (SCC) is far more common, melanomas may be misclassified, especially when:

- Histologic features are atypical
- p16 positivity is present
- Tumor location favors other malignancies.

This case highlights the diagnostic challenges of mucosal melanoma and its potential for widespread metastases.

Case Presentation

An 81-year-old woman with a history of nasal cavity SCC, diagnosed in October 2023, declined treatment. Five months later, she presented with acute hypoxia and pulmonary emboli, and imaging was concerning for metastases. Examination revealed an extensive tumor protruding from her right nostril, extending posteriorly around the palate into the oropharynx, with invasion through the nasal septum into the left nasal cavity. Despite anticoagulation, she deteriorated rapidly and passed away.

Autopsy revealed extensive metastases involving the epicardium of the cardiac apex, mesentery, thyroid, peripancreatic space, brain, and lungs, with multiple well circumscribed, pigmented nodules in several locations.

Histologic examination of the pigmented lesions revealed pleomorphic epithelioid cells with prominent nucleoli and intracytoplasmic melanin deposits. Immunohistochemistry demonstrated strong positivity for melan-A and HMB-45, with weak S100 expression, confirming the diagnosis of metastatic melanoma. The cardiac lesion also stained strongly for p16, mirroring the original nasal cavity biopsy, which had previously been diagnosed as SCC based on morphology and p16 positivity. However, retrospective analysis of the nasal biopsy with additional melanocytic markers confirmed the primary diagnosis as nasal mucosal melanoma.

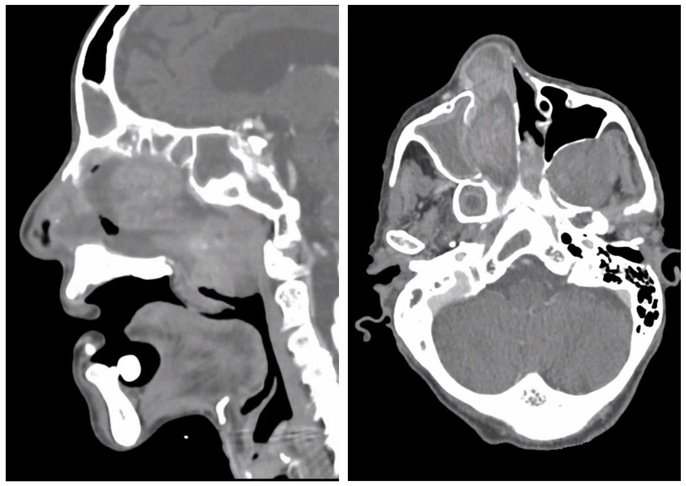


Figure 1. CT Maxillofacial with Contrast taken upon hospital admission, demonstrating a10+ cm heterogenous enhancing mass within right nasopharynx with extension anteriorly and posteriorly. Imaging shows a mass effect on the soft palate with obliteration of the posterior nasopharyngeal space. The mass extends to involve the right palatine tonsils and posterior nasopharynx. There is total opacification of the right maxillary and bilateral sphenoid sinuses as well as the right mastoid air cell complex (A) Sagittal. (B) Axial.

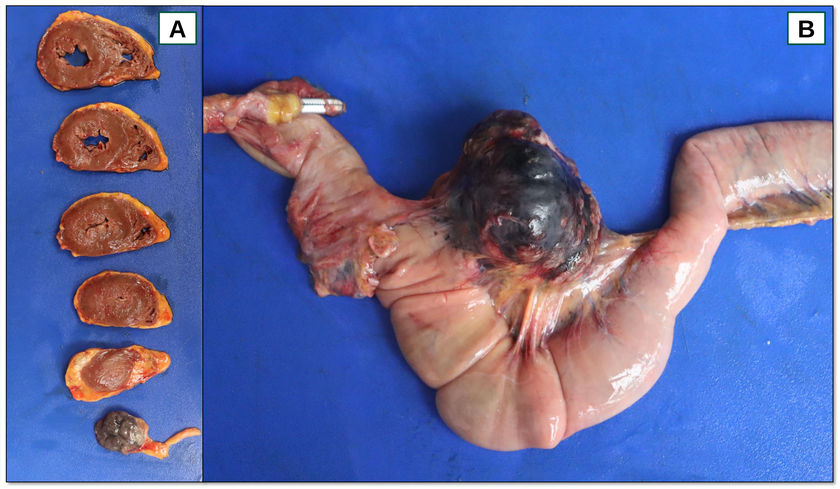


Figure 2. Gross pathology at autopsy revealed multiple black, circumscribed, nodular lesions. Notable sites included the cardiac apex (A) the mesentery (B), with additional lesions in the peripancreatic space, the left thyroid lobe, and the right cerebral caudate.

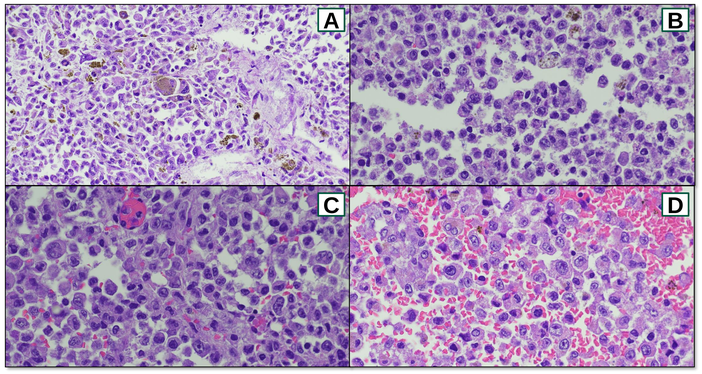
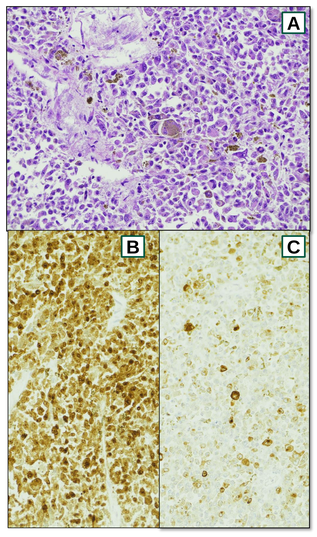


Figure 3. Composite histopathology images from representative lesions. Sections were obtained from the cardiac apex (A), mesenteric nodule (B), pancreas (C), and thyroid (D) for microscopic examination. **Figure 4.** Histologic and immunohistochemical analysis of the cardiac apex lesion. H&E staining is shown in (A), with immunohistochemical staining for p16 (B) and Melan-A (C).



Discussion

Unusual Locations

This case illustrates the aggressive, widely metastatic potential of mucosal melanoma with dissemination to multiple visceral and central nervous system sites, including the epicardium of the cardiac apex, which is a less commonly reported site of melanoma metastasis. Awareness of melanoma's potential to metastasize to unusual locations, such as the heart and mesentery, is also crucial in postmortem evaluations of patients with malignancy.

Atypical Invasion

While these melanomas have a known propensity for early metastatic spread, they are most often confined to the primary site, with the nasal cavity being the most common location in the head and neck. In contrast, this patient's tumor exhibited aggressive local invasion more characteristic of SCC, contributing to the initial misdiagnosis.

Morphologic Deception

The misclassification of the primary lesion as SCC highlights the need for the histopathologic consideration of melanoma in poorly differentiated tumors, particularly in the nasal cavity where SCC is more common. Given melanoma's ability to mimic SCC both morphologically and immunohistochemically, melanoma ought to be considered, and at least one melanocytic stain such as SOX10, S100, Melan-A, or HMB-45, should be included alongside traditional SCC markers to avoid misdiagnosis.

Confounding Markers

The expression of p16, while typically associated with HPV-related SCC, can also less frequently be seen in melanomas, making reliance on p16 staining alone insufficient for definitive diagnosis. Additionally, weak S100 staining in some melanomas, particularly mucosal and desmoplastic subtypes, can further complicate diagnosis.

Comprehensive immunohistochemical analysis is essential for accurately diagnosing mucosal melanoma, which can exhibit aggressive local invasion as well as widespread and unique metastases.