

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

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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 atypical histologic features and p16 positivity are present. Tumor location often shapes diagnostic expectations, favoring more prevalent malignancies. This case highlights the diagnostic challenges of mucosal melanoma and its widespread metastatic potential.

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.

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 a history of malignancy. 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. 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. 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. This case highlights the importance of comprehensive immunohistochemical analysis in accurately diagnosing mucosal melanoma and underscores its potential for significant local invasion as well as widespread metastases.