A 79-year-old African American woman presented with a 3-week history of right-sided epistaxis, purulent rhinorrhea, and facial swelling. The patient also complained of a red bulging right eye with tearing. Her past medical history was significant for bilateral breast carcinomas treated with bilateral mastectomies (1986 and 1993) and adjuvant chemotherapy and radiotherapy. In addition, she had hypertension, obesity, diabetes mellitus, and asthma. She had smoked 2 packs per day (80 pack-years), but she had quit approximately 20 years earlier. An obvious nasal mass was noted upon examination. Magnetic resonance imaging of the sinuses demonstrated a large mass (indicated by asterisk in Figure 1) involving the right maxillary sinus and into the nasal cavity. The tumor extended to the right orbit and to the temporal and pterygoid fossae. The inframedial aspect of the right orbit and the greater wing of the sphenoid were also involved. A radionuclear study of the whole body failed to reveal any other tumor. No skin lesions were identified. The mass was biopsied and submitted for pathologic examination. Histologic examination showed polypoid fragments of respiratory mucosa with a submucosal tumor composed of a dense cellular infiltrate (Figure 2, hematoxylin-eosin, original magnification $\times 100$). The tumor extended focally to the mucosa. Prominent areas of necrosis were present, with the viable tumor forming an angiocentric pattern (Figure 3, hematoxylin-eosin, original magnification $\times 100$). The cells were relatively small and had a moderate amount of cytoplasm. The nuclei were round and had inconspicuous nucleoli. The mitotic rate was high, with an average of 2 per high-power field (Figure 4, hematoxylin-eosin, original magnification $\times 400$). The immunohistochemical results were critical for the diagnosis. Subsequently, the patient underwent a maxillectomy with orbital exenteration. The tumor measured 3.5 cm in greatest dimension and focally extended to the outer aspect of the eye; however, the uveal tract (choroid and ciliary body) was not involved, and there was no tumor mass inside the globe. The skin overlying the maxilla was also not involved.

What is your diagnosis?
Sinonasal “Mucosal Melanoma”

Immunohistochemically, the tumor was strongly positive for S100 and HMB-45 but negative for epithelial (pankeratin AE1/AE3) and lymphocytic/natural killer (CD3, CD4, CD8, and CD56) markers. A diagnosis of mucosal melanoma was rendered.

Most mucosal melanomas are anorectal or are found on the female genitalia. Mucosal melanomas of the head and neck are much less common, representing only 0.4% to 1.8% of all melanomas. In the head and neck region, nasal and oral cavities are the most commonly affected sites. Most of the tumors occur in the seventh decade of life.

There are geographic/racial differences in the incidence of head and neck mucosal melanomas. The proportion of oral melanomas to all melanomas in Japanese people is as high as 7.5%. In Ugandan Africans, oral and nasal primary melanomas form 10% of all melanomas.

These tumors originate from the melanocytes present in the mucous membranes; however, the risk factors for cutaneous melanomas (eg, sun exposure) do not apply for mucosal tumors. Microscopically, sinonasal mucosal melanomas may show an angiocentric pattern due to extensive necrosis and preservation of the tumor cells around blood vessels. Immunohistochemically, these tumors also stain positive for S100 and HMB-45. The differential diagnosis includes metastatic cutaneous melanoma, poorly differentiated carcinoma, and angiocentric T-cell/natural killer cell lymphoma. Because cutaneous melanoma metastasizes to mucosa in 2% to 9.3% of cases, metastatic lesions should always be excluded.

The absence of a cutaneous primary and the presence of mucosal involvement make a metastasis unlikely. Ocular melanomas usually arise from the uveal tract and initially form an intra-ocular mass. Immunohistochemical stains for epithelial and lymphoid/natural killer markers will rule out a poorly differentiated carcinoma and an angiocentric nasal/sphenoid T-cell/natural killer cell lymphoma, respectively. The prognosis of the sinonasal melanomas is extremely poor, with a 5-year survival of 6.5% to 34% and with more than 50% of patients dying within 3 years. The tumor thickness, depth of invasion, and nodal involvement are important prognostic factors. The site of the tumor is also important. It appears that the melanomas of the oral cavity have a higher frequency of lymph node metastases than do the sinonasal primaries. These lesions are most commonly treated with wide local resection. Surgery combined with radiotherapy is sometimes used. The addition of chemotherapy has no impact on survival.

References