Malignant Melanoma Presenting As Nasal Obstruction

Robert W. Martin III, M.D., Charles R. Potter, M.D., W. Gerald Klingler, M.D., and Kenneth H. Neldner, M.D.

***Abstract*: Mucosal melanomas arising in the nasal cavity are rare tumors comprising less than 1 percent of all melanomas. Often, the common clinical symptom is nasal obstruction. Grossly, they may or may not be pigmented and frequently attain large sizes. Histologic diagnosis of these tumors may be difficult, requiring immunohistochemical or electron microscopic confirmation. Aggressive surgical management is the treatment of choice in clinical stage I disease. Subsequent surveillance for recurrence is mandatory. Markers such as 5-S-cysteinyldopa may prove useful in staging, prognosticating, and postoperative surveillance for early recurrence, but their exact role has yet to be delineated. Ultimate prognosis is poor. (J Am Board Fam Pract 1990; 2:283-7.)**

Melanoma of the nasal mucosa represents less than 1 percent of all melanomas.[1,2] Even though most patients are diagnosed with clinical stage I disease, the disease is usually fatal. Because primary care physicians evaluate and treat many disorders that have nasal obstruction, awareness that melanoma is a possible cause is important, especially in those patients who do not respond to medical management. The histologic diagnosis may be difficult and often delayed because of anatomic considerations and complacency about relatively benign presenting symptoms. Aggressive surgical treatment with or without postoperative radiation is the treatment of choice despite the dismal prognosis. We report our experience with a case of nasal mucosal melanoma.

Case Report

A 66-year-old white man gave a 3-week history of nasal congestion and obstructive symptoms despite the fact that his lesion must have been present much longer. There was no history of epistaxis. There was no family history of melanoma or dysplastic nevus syndrome, although one brother died of a brain tumor (pathology unknown).

Physical examination showed a mass in the left nasal fossa, visible with use of a nasal speculum. It did not decongest, was firm to palpation, and bled readily on contact. There was a 2-cm mass in the left parotid gland anterior to the left lobule, and fluid was aspirated from it. There were no suspicious cervical nodes. Complete skin examination showed a 2-mm blue nevus on the left midback and a 12 × 7 mm actinic keratosis on the left tip of the nose (both proved by biopsy). The remainder of the examination was normal.

Biopsy of the left nasal fossa lesion showed a probably malignant melanoma on light microscopy (Figure 1) and hematoxylin and eosin (H & E) stain. The diagnosis was confirmed by a strongly positive reaction for S-100 protein on immunohistochemical staining and by identification of melanosomes and premelanosomes within the tumor cells on electron microscopy (Figure 2).

Complete blood count and blood chemistry, urinalysis, and HIV antibody count were within normal limits. Nasal culture yielded *Staphylococcus epidermidis*.

A computerized tomography (CT) scan of the sinuses showed a soft tissue mass that filled most of the nasal cavity but did not appear to have infiltrated the lateral nasal wall into the left maxillary antrum. The mass filled the entire inferior aspect of the left nasal airway and obliterated the inferior turbinate. CT scans of the chest, liver, and spleen were normal as were sinus and chest radiographs. Total body bone scan showed increased accumulation in the 8th rib, 5th lumbar vertebra, right acromioclavicular joint space,

From the Department of Dermatology, Texas Tech University Health Sciences Center, Lubbock, TX, and Departments of Otolaryngology and Dermatology, Springfield Clinic, Springfield, IL.

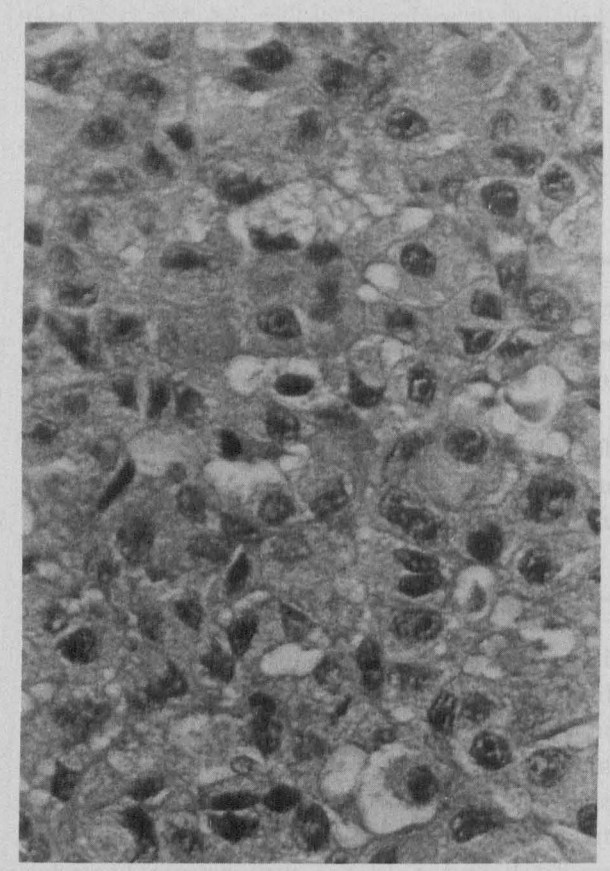

Figure 1. Light micrographs at 400 times magnification. Histology displays sheets of tumor cells under a normal-appearing squamous epithelium. The tumor cells have large hyperchromatic nuclei containing prominent central nucleoli. Some of the nuclei are eccentrically located within the cells. Subsequent S-100 was positive.

and the medial compartment of the right knee, but detailed bone radiographs of these areas failed to confirm metastatic disease.

The patient underwent left lateral rhinotomy with left medial maxillectomy and total parotidectomy with facial nerve preservation (Figure 3). Pathologic evaluation of the surgical specimens showed melanoma in the maxillary bone, the posterior margin of the inferior turbinate, and metastasis to one lymph node in the anterior parotid gland. The 2-cm left parotid gland mass was a Warthin tumor.

Ten months postoperatively, a recurrence in the anterior inferior maxillary sinus was discovered during endoscopic examination. A left sternocleidomastoid lymph node was also palpable. CT scan of the lungs showed metastasis to the upper lobe of the left lung. The patient underwent palliative laser destruction of the lesions using a microscopically controlled CO_2 laser through the left nostril, reflected off manipulated mirrors within the nasal fossa. Beginning 6 weeks postoperatively, the patient was given Echinomycin™ (a clinical trial chemotherapeutic agent) at 1200-mg dose IV at weekly intervals for four doses. The medication was subsequently discontinued because of tumor progression. Four weeks later, alpha interferon and interleukin-2 therapies were initiated. To date, the patient has received two courses of this regimen at intervals of 2 weeks.

Discussion

Head and neck melanomas constitute 15 to 20 percent of all melanomas,[3-5] with nasal mucosa and sinus melanomas comprising 3 percent of this total.[1,2] Since the first nasal melanoma was reported by Lücke in 1869,[5] approximately 300 other cases have been reported.[2]

Mucosal melanoma of the nasal passages is predominantly a disease of older whites[6-8] (age range

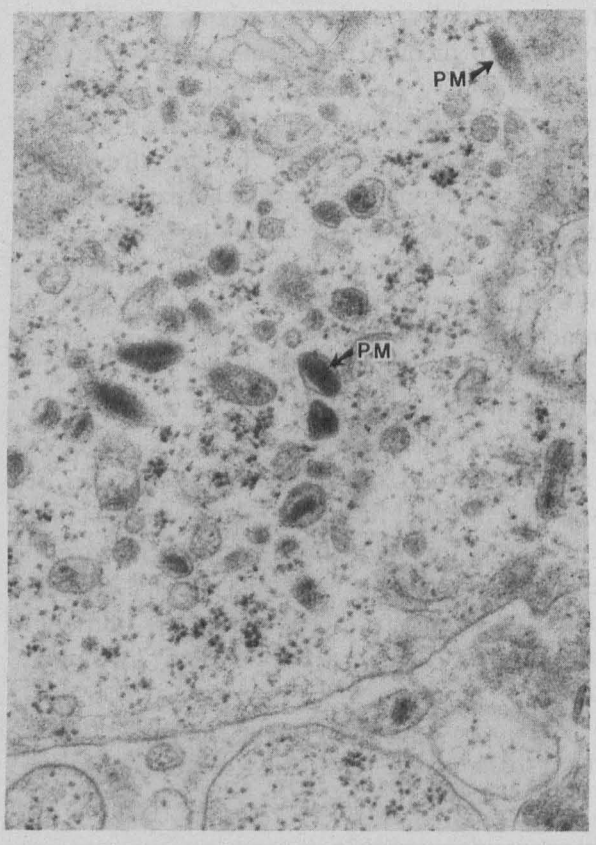

Figure 2. Electron microscopy showed the presence of melanosomes and premelanosomes confirming the diagnosis of malignant melanoma.

40 to 70 years[9]), although a 16-year-old patient has been reported.[10] In general, a slight preponderance of men is observed.[7,8,11,12] Data regarding racial or ethnic patterns are conflicting.[3] The etiology of mucosal melanomas is unknown.[9] Ultraviolet light exposure cannot be considered etiologic because of the location of occurrence.[3] Melanosis or mucosal nevi (a rare occurrence in whites) may be precursor lesions, although such lesions are rarely recognized.[11,13]

Presenting symptoms include epistaxis, obstruction, discharge, epiphora, facial pain, and swelling.[2] Some patients have a history of nasal polyps,[6,14] which may contribute to their ignoring recurrent obstructive symptoms.[10]

The lesions vary from flat to raised, fleshy to black, and have a firm consistency.[9,15] Approximately 50 percent of nasal melanomas have no obvious pigmentation.[15]

More than 75 percent of the lesions originate in the nasal cavity,[2,8] most frequently involving the septum, followed by the inferior and middle turbinates.[6,8,10,12,16] Sites of predilection correspond to the distribution of melanocytes within the mucosa.[13,17] Although most patients are first seen with clinical stage I disease,[2,8] the tumor has a high metastatic and recurrence rate. This may be due in part to its tendency to compress local structures as it grows radially.[17]

Histologic misdiagnosis may occur unless clinical suspicion is high and a diligent search for melanocytes is undertaken. The absence of readily identifiable melanin by light microscopy in one third of the cases[15] and the tumor's tendency to be more pleomorphic than cutaneous melanomas[17] may contribute to misdiagnosis. Immunohistochemical demonstration of S-100[18] or HMB-45 proteins are useful markers for malignant melanomas, especially the amelanotic type. Electron microscopy is useful in establishing the presence of premelanosomes and melanosomes.[9]

While cutaneous melanomas are classified into four basic clinicopathologic entities (i.e., superficial spreading, acral, nodular, and lentigo maligna melanomas), no analogous classification exists for nasal mucosal tumors. Determining a Clark's level for a mucosal lesion is not possible because of a lack of reproducible landmarks within the mucosa and submucosa of the upper respiratory tract.[3,7,19] However, in a fashion analogous to Breslow, who correlated depth of cutaneous melanoma with clinical outcome,[20] Trapp has suggested that any mucosal lesion with greater than 0.7-mm invasion carries a dismal 3-year prognosis.[2]

Figure 3. Melanoma removed at surgery.

Recently, plasma 5-S-cysteinyldopa has been used to distinguish cutaneous primary melanomas without lymph node involvement and to monitor tumor regression or progression after therapy.[21] The marker's correlation with tumor mass rather than thickness[21] may improve classification of mucosal melanomas and have prognostic value.

Treatment usually advocated is aggressive surgical resection of the tumor locally (in the absence of regional or distant metastases).[2,4,6-9,11,12,15-17,22,23] Prophylactic lymph node dissection, while controversial, is generally not recommended because of the low rate of subsequent regional nodal recurrence (19 percent in one series[17]) in the absence of local or distant metastasis at the time of surgery.[8,17]

While melanoma is generally considered to be poorly responsive to radiotherapy,[6-8,11,16,24] it has been used in some cases. Harwood has suggested that the melanoma cell may not be radio-resistant but may have a large capacity to repair sublethal radiation damage.[25] This has led to the use of a large dose-per-fraction regimen to provide tumorcidal doses.[25-28] Despite reported examples of "cure" subsequent to radiation therapy,[29,30] most authors consider radiation therapy an adjunct to surgery.[10,17,31]

Chemotherapy is usually reserved for treatment failure or metastatic disease because there is no existing agent with uniformly high activity against mucosal melanoma. Other modalities,

such as electrodesiccation,[11] cryotherapy (in selected cases),[32] and stimulation of the immune system using bacille Calmette-Guérin (BCG) vaccine,[33] have shown inconsistent results and are not used.

The reported 5-year survival rate for head and neck mucosal melanomas varies from 1 to 38 percent,[2,6-8,11,12,15-17,34,35] even though most patients present with clinical stage I disease[2,8] (Freedman reported the best results with an overall survival rate of 46.2 percent at 3 years and 30.9 percent at 5 years[6]). The poor prognosis suggests that this tumor's biologic behavior may be more aggressive than its cutaneous counterpart,[36] probably because of its mucosal and its anatomic location. Further, the host-tumor immunologic balance is crucial to the natural history of the disease.[10]

Because these tumors may remain undetected for extended periods of time, they are often large when diagnosed; however, age, sex, duration of symptoms, size, and pigmentation do not appear to correlate with survival.[10] The constant risk of fatal metastases is present no matter how long after treatment the patient survives.[9,10,34]

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