Paranasal sinus melanoma masquerading as chronic sinusitis and nasal polyposis

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Abstract

Malignant melanoma of the nose and paranasal sinuses can be a devastating disease, typically presenting at an advanced stage, with a 5-year survival rate ranging between 20 and 30%. It is an uncommon process, often misdiagnosed both clinically and pathologically. We present the case of an 80-year-old man who had a 2-month history of progressively worsening left-sided epistaxis and nasal obstruction. Radiographic evidence indicated the presence of soft tissue in the left maxillary sinus and nasal cavity resembling massive nasal polyposis and chronic fungal sinusitis. Magnetic resonance imaging was not performed because the patient had a pacemaker. After endoscopic debridement of the soft-tissue mass, frozen-section analysis detected no evidence of tumor. The final pathologic diagnosis was malignant melanoma. Otolaryngologists should be familiar with the difficulties inherent in the diagnosis and management of sinonasal melanomas.

Introduction

Most malignant melanomas are found on the skin, and approximately 20% of skin melanomas are found in the head and neck region.1 Primary mucosal melanomas of the nasal cavity and paranasal sinuses are rare. First described by Lucke in 1869, melanoma of the nasal cavity and paranasal sinuses is estimated to account for less than 1% of all malignant melanomas and 2 to 8% of malignant neoplasms of the sinonasal tract.1

The diagnosis of paranasal sinus melanoma is fraught with difficulty, especially when a lesion lacks pigmentation, which occurs in more than one-third of cases.1 Signs and symptoms of paranasal sinus melanomas can be confused with those of nasal polyposis and chronic sinusitis. Intraoperative frozen-section diagnosis of melanoma is difficult to make, as special staining and immunochemistry are often required. We present a case of malignant melanoma that originated in the left maxillary sinus and masqueraded as chronic sinusitis and nasal polyposis.

Case report

An 80-year-old man was referred to our office with a 2-month history of intermittent left-sided epistaxis. His bleeding had been severe enough to require hospitalization for cauterization and transfusion. At presentation, the patient also complained of diminished olfaction, left-sided facial pressure, and nasal obstruction. He denied experiencing paresthesias, headaches, or visual changes. He had a history of cardiac disease, which had required the placement of a pacemaker. He did not smoke and drank alcohol only occasionally.

Physical examination revealed the presence of clotted blood in the left nasal cavity and obstruction with friable tissue in the left middle meatus. Computed tomography (CT) demonstrated a soft-tissue density in the left maxillary sinus, expansion of the medial wall of the maxilla, obstruction of the middle meatus, and opacification of the ethmoid sinus (figure 1). Because of the pacemaker, the patient could not undergo magnetic resonance imaging (MRI). He was admitted with a diagnosis of epistaxis with a left-sided nasal mass. The differential diagnosis included carcinoma, fungal sinusitis, papilloma, and chronic sinusitis with nasal polyposis. He was prepared for endoscopic biopsy and control of epistaxis.

In the operating room, the endoscopic examination detected clotted blood in the left nasal cavity; the blood was removed endoscopically. A middle-mental antrostomy revealed another large quantity of clotted blood in the maxillary antrum, which was also removed endoscopically. On gross inspection, the mucosa exhibited a marked amount of polypoid change, consistent with
chronic sinusitis. Frozen-section examination detected no evidence of tumor. An ethmoidectomy was also performed.

Three specimens were submitted. Grossly, the samples were dark red, yellow, and tan-brown soft-tissue masses. The largest measured 6 × 5 × 1.8 cm; the volume of the specimens totaled 64 cm$^3$. Microscopically, they demonstrated mostly blood clot, organized hemorrhage, and necrotic tissue. Malignant spindle-cell foci were noted in a few locations, many containing pigment consistent with melanin (figure 2). Immunohistochemically, the specimen showed negative staining for HMB-45 and melan-A and positive staining for S-100 protein, favoring a diagnosis of malignant melanoma.

At a follow-up visit 3 weeks after surgery, dry crusts in the maxillary and ethmoid regions were noted on endoscopic examination. Staging studies were obtained. Residual malignant melanoma was presumed to be present, and staging studies were ordered. Positron-emission tomography (PET) demonstrated no definitive evidence of tumor uptake, and CT of the chest and abdomen showed no evidence of distant metastases. Repeat CT of the sinuses showed moderate residual soft-tissue density within the left maxillary antrum.

Twelve days later, a repeat endoscopic examination in the operating room detected a granular mass involving the left maxillary antrostomy. Otherwise, no evidence of tumor or infection was seen. A gingival-buccal sulcus incision was made, and the maxillary antrum was entered via a Caldwell-Luc approach, revealing mucosal thickening with a granular change involving the medial wall of the maxilla. Frozen sections obtained from this area showed no evidence of tumor. The patient then underwent a medial maxillectomy.

On pathologic examination, no evidence of tumor was seen in any of the specimens; the medial maxilla exhibited chronic inflammation and necrosis but no evidence of tumor. S-100 protein staining was negative for occult foci of melanoma.

The patient completed a course of radiation therapy and was followed with serial examinations in the office. Two years following treatment, he continues to do well, with no signs of recurrence.

Discussion
While sinonasal malignant melanoma more often originates in the nasal cavity than the paranasal sinuses, in many ways this case is fairly representative of malignant melanomas originating in a paranasal sinus. The most common sinus involved is the maxillary sinus. Presenting symptoms often include epistaxis and nasal obstruction. Signs and symptoms indicative of later-stage disease include (1) diplopia or vision loss from orbital or optic nerve invasion, (2) epiphora from nasolacrimal duct obstruction, (3) facial swelling and malocclusion from bone destruction and invasion into the soft tissues of the mouth or face, (4) trismus from invasion of the pterygoid muscles, (5) development of a neck mass from local metastases, (6) hearing loss from serous otitis, and (7) facial numbness from invasion of the trigeminal nerve. Our case was unusual in that the patient presented at a relatively early stage, as most cases of sinus melanoma are diagnosed at a more advanced stage.

The differential diagnosis of a sinonasal mass includes benign neoplasms, intermediate neoplasms, and malignant neoplasms. Benign neoplasms include nasal polyps, osteomas and chondromas, schwannomas and neurofibromas, ossifying fibromas and cementomas, and odontogenic tumors. Neoplasms classified as intermediate include inverted papillomas, meningiomas, hemangiomas, and hemangiopericytomas. Squamous cell carcinoma is the most common malignant neoplasm, followed by adenoid cystic carcinoma and adenocarcinoma, as well as olfactory neuroblastoma, sarcoma, lymphoma, plasmacytoma, small-cell undifferentiated carcinoma, and melanoma.

The diagnostic workup for a sinonasal mass includes CT and MRI. Because of our patient’s pacemaker, we were not able to use MRI to visualize the mass before surgery but rather were obliged to use CT. MRI is generally viewed as superior to CT for the diagnosis of melanoma. On CT, melanomas and other paranasal sinus tumors can be difficult to distinguish from fluid or other soft-tissue masses. On MRI, it is much easier to distinguish fluid from soft tissue. Also, melanin’s paramagnetic properties cause melanomas to appear characteristically hyperintense on T1-weighted images.
imaging and hypointense on T2-weighted imaging. This pattern is specific to melanoma and only appears in tumors with abundant melanin pigment. In our case, MRI would have helped establish a diagnosis of a malignant neoplasm such as melanoma.

Sinus melanoma tumors are usually pigmented with abundant intracytoplasmic melanin, but diagnosis can be difficult since more than one-third of mucosal melanomas lack pigment entirely (amelanotic melanoma). Microscopically, the spindle-cell pattern in melanoma may be confused with that of sarcoma or spindle-cell carcinoma. Similarly, amelanotic spindle-cell melanoma is frequently confused with fibrosarcoma or malignant schwannoma, and epithelioid and pleomorphic patterns of melanoma may be mistaken for carcinoma. For these reasons, diagnosis is most reliably established by immunohistochemical techniques. S-100 protein is a sensitive but nonspecific melanoma marker, while HMB-45, a monoclonal antibody derived from melanoma extract, is more specific but may occasionally be detected in carcinoma cells. For cases in which staining for these two markers yields unclear results, a melanoma-specific marker known as melan-A is typically used. Melan-A has been shown to be highly specific in differentiating melanoma from other malignancies for which it may be confused on light microscopy, such as sarcomas, plasmacytomas, and carcinomas.

The frozen-section diagnosis of melanoma presents many more challenges. There are reports in the literature about the value of frozen-section analysis of sentinel lymph nodes in cutaneous melanomas, but there are none regarding melanomas in the paranasal sinuses. A study from the Netherlands published in 2000 found that frozen-section analysis (using hematoxylin and eosin [H&E] staining) of sentinel lymph nodes in patients with cutaneous melanoma had a 100% specificity but only a 38% sensitivity, leaving a high percentage of false negatives.

A larger study from New York published in 2002 showed that frozen-section analysis with H&E staining of sentinel lymph nodes in cutaneous melanomas had a specificity of 100% and a sensitivity of 59%. All confirmation of melanoma in both studies was done with immunohistochemical staining.

There is a more recent report on using rapid immunohistochemistry to stain intraoperatively for S-100, HMB-45, and a “melanoma cocktail” consisting of HMB-45, melan-A, and tyrosinase. Although this test added 20 to 25 minutes to the analysis, it resulted in higher sensitivities, ranging from 71 to 86%, while maintaining high specificity. However, because of its relative unavailability, rapid immunohistochemistry for melanoma is not widely performed.

In our case, not surprisingly, attempts at frozen-section analysis to rule out a malignancy were fruitless, as all frozen sections from the initial surgery were falsely negative for malignancy, not to mention melanoma. What makes frozen-section diagnosis even more difficult for paranasal sinus melanoma is the relative rarity of the disease—it is seldom high on the differential for a paranasal sinus mass. Also, in the face of bleeding, as was the case here, hemoglobin is converted to a brown pigment, hemosiderin, which is difficult to distinguish from melanin, even in optimal permanent sections. When spindle cells with pigment are seen, they are most commonly caused by fibroblasts and
hemosiderin, not melanoma. In fact, in our case most of the pigmented spindle cells were fibroblasts and hemosiderin; a smaller population of spindle cells was found to contain melanin after proper immunohistochemical stains.

There is no universally accepted staging system for paranasal sinus melanoma within the TNM staging system, largely because of the rarity of mucosal melanomas. Most clinicians use a simplified three-stage system: stage I for localized disease, stage II for lymph node metastases, and stage III for distant metastases. However, researchers at the Armed Forces Institute of Pathology published a proposed staging system for sinonasal tract and nasopharyngeal melanoma in 2003 in which T1 represents a primary tumor at a single anatomic site, T2 represents a primary tumor at two or more sites, N1 represents any lymph node metastasis, and M1 represents any distant metastasis. In our case, only one anatomic site was involved (the maxillary sinus), and PET and CT showed no evidence of lymph node or distant metastases, indicating a stage I neoplasm according to this system.2,8

It is generally agreed that the mainstay of treatment is surgical resection of the tumor with clear margins.2,9 Compared with squamous cell carcinoma, paranasal sinus melanoma metastasizes less frequently to cervical lymph nodes but more frequently to the lungs and the brain. Therefore, a neck dissection is not recommended for patients without clinical or radiologic evidence of cervical metastases. Accordingly, this was the treatment employed in our case.

On follow-up examination of our patient, the concern that the excision margins were not adequate to remove the entirety of the tumor was great enough that a second exploration was deemed necessary 1 month after the original surgery. Although no immunohistochemical evidence of residual tumor was found at that time, few would argue against the prudence of such a procedure when weighed against the dire consequences of possibly failing to remove residual tumor, especially in the case of a tumor with such aggressive metastatic potential.

While complete resection of the mucosal melanoma tumor is generally the goal in the absence of distant metastases, it should be noted that more than half of patients in whom local control is achieved after surgery ultimately develop distant metastases. This is largely because it is difficult to secure histologically disease-free margins in the affected anatomic areas. For this reason, some authors have investigated the use of radiation therapy after the resection of a mucosal melanoma, even though this tumor was traditionally believed to be radioresistant. While the evidence is currently under debate in the literature, many now believe this adjuvant therapy to be of benefit in preventing recurrence and ultimately prolonging survival.9

With regard to prognosis, the 5-year survival rate for sinonasal melanoma has been reported to range from 20 to 30%. A study by Patel et al at Memorial Sloan-Ket-tering Cancer Center in New York City revealed a 5-year disease-specific survival rate of 47% (n = 35). More importantly, four independent predictors of outcome were determined in this study: clinical stage at presentation, tumor thickness (±5 mm), the presence or absence of vascular invasion on histologic examination, and the presence or absence of distant metastasis. Because our patient had stage I disease, scant malignant cell foci of small thickness, no report of vascular invasion, and no current distant metastasis, he appears to have a relatively good prognosis compared with that of the average patient with sinonasal melanoma.

In conclusion, melanoma of the paranasal sinus can be a devastating disease. Therefore, otolaryngologists should maintain a high index of suspicion when evaluating unusual cases of chronic sinusitis or nasal polyposis—especially when they are associated with epistaxis or unilateral disease. However, even then, diagnosis can be exceedingly difficult. MRI is an extremely useful tool in the diagnosis of paranasal sinus melanoma, but when it is unavailable or contraindicated, the diagnosis becomes even more challenging.

About one-third of sinus melanomas are unpigmented, and the sensitivity of frozen-section analysis of melanomas is low, especially when bleeding causes false negatives. Appropriate immunohistochemical studies of all spindle-cell neoplasms should be performed to establish or exclude this diagnosis. We believe that the best therapy for paranasal sinus melanoma (in the absence of metastasis) is complete surgical excision followed by a course of radiation therapy.

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