CASE REPORT

Recurrent epistaxis leading to diagnosis of primary sinonasal melanoma

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SUMMARY

A 48-year-old man presented to urgent care with recurrent epistaxis over 6 months. Initially, nosebleeds were controlled with packing or cautery. Ultimately, he was referred to ear, nose and throat department and underwent nasal endoscopy which revealed polypoid tissue. A biopsy of the polyp showed non-specific inflammation with no evidence of malignancy. Follow-up maxillofacial CT revealed a large mass lesion in the right maxillary sinus, right nasal fossa, much of the ethmoids and right sphenoid, with destruction of adjacent bony structures. MRI revealed a mass in the right nasal cavity with extension into the ethmoid and anterior sphenoid sinus, anterior cranial fossa and medial orbits. Staging CT discovered metastatic disease in the adrenal glands and lymphadenopathy in the neck. The patient underwent endoscopic sinus surgery with debulking and tissue diagnosis of malignant melanoma. He completed radiation therapy to sinus and was subsequently enrolled in a clinical trial. Most recent imaging revealed complete metabolic response on positron emission tomography.

BACKGROUND

Epistaxis is a common complaint that brings patients to the primary care physician offices or emergency departments but recurrent epistaxis should lead to further investigation.

Although literature on cutaneous melanoma is abundant, reports on sinonasal malignant melanoma (SNMM) are rare. SNMM accounts for <5% of head and neck melanomas and <1% of systemic malignant melanomas.¹

Local recurrence is common, and outcomes are poor with an overall survival of 19.3 months and a 5-year survival rate of 34%.^{2,3}

CASE PRESENTATION

The patient's medical history is notable only for depression, type 2 diabetes and hypertension. His surgical history is notable for cholecystectomy. His family history consisted of: mother with diabetes mellitus (DM), coronary artery disease (CAD), hypertension (HTN) and stroke; father with DM, CAD and HTN; and maternal grandmother with lung cancer. The patient is a school teacher with remote 10-pack-year smoking history, no alcohol abuse and no drug use.

INVESTIGATIONS

A maxillofacial CT (figure 1) revealed a large mass lesion in the right maxillary sinus, right nasal fossa,

much of the ethmoids and right sphenoid, with destruction of all bone around it.

Brain MRI (figure 2) similarly revealed a mass in right nasal cavity with extension into ethmoid, anterior sphenoid sinus, anterior cranial fossa, medial orbits, right maxillary sinus with extension into soft tissues anteriorly, posteriorly to sinus and inferiorly to orbit.

Staging computer tomography angiography (CTA) of chest, CT abdomen pelvis and CT neck revealed bilateral adrenal masses suspicious for metastases.

Endoscopic sinus surgery for biopsy and debulking of mass was performed, with pathology positive for melanoma (figure 3) and negative for BRAF 600E/K and KIT mutations.

A biopsy of the adrenal gland was positive for distant metastasis.

DIFFERENTIAL DIAGNOSIS

- ▶ Hypertensive nasal bleed.
- ▶ Non-melanoma nasal neoplasms: squamous cell carcinoma, adenoid cystic carcinoma and inverted papilloma.
- ▶ Allergic or viral rhinitis.
- ▶ Acute sinusitis.
- ▶ Use of nasal steroids or other topical intranasal medications.
- ▶ Tonsillitis.
- ▶ Chronic excoriation.
- ▶ Chronic intranasal drug use.

Figure 1 CT head demonstrating sinonasal melanoma.

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Figure 2 MRI brain demonstrating sinonasal melanoma.

► Bleeding diathesis.

TREATMENT

The patient was treated at a tertiary university health centre, under the guidance of a multidisciplinary team consisting of experts in ear, nose and throat (ENT), radiation oncology and medical oncology.

The patient had presumed metastatic disease at time of evaluation by radiation/oncology. He was pending biopsy of adrenal masses at that time to confirm metastatic status. Given the patient's significant residual disease (minimal debulking surgery because of bleeding), stereotactic body radiotherapy to the right sinus region was recommended at a dose of 5–7 fractions for total dose of 20–35 Gy. The patient completed 28 Gy dose to the right sinus.

During this time, the patient's metastatic disease was confirmed, and he was enrolled in clinical trial NCT02186249 with ipilimumab 3 mg/kg intravenously every 3 weeks×4 doses and nivolumab 1 mg/kg intravenously every 3 weeks×4

(concurrent with ipilimumab), followed by nivolumab ipilimumab then 3 mg/kg every 2 weeks.⁴

OUTCOME AND FOLLOW-UP

His course was complicated by pustular psoriasis but continued on treatment with eventual complete metabolic response on positive emission tomography (PET). Treatment was stopped, and he was continued on surveillance.

Surveillance consisted of complete blood count, basic metabolic panel, maxillofacial CT and CT chest/abdomen/pelvis every 4 months, in addition to yearly brain MRI.

On most recent surveillance after 2.5 years since initial diagnosis, the patient is doing well with no evidence of new disease. The patient has gone back to work full time as a high school teacher. Serial imaging revealed an excellent partial response. He continued on the single agent nivolumab off protocol with continued excellent control of disease. The patient opted for stopping treatment due to side effects and continuing on surveillance.

DISCUSSION

SNMM is a rare oncological entity, which typically presents in an elderly population (in their seventh decade).⁵ Patients with SNMM can present with nasal obstruction, epistaxis or loss of smell.⁶ The average delay between onset of symptoms and diagnosis was 5.6 months.⁷ Our case describes a middle-aged man who presented multiple times to urgent care and to the emergency room (ER) with recurrent epistaxis. He was eventually found to have metastatic SNMM of the maxillary, sphenoid and ethmoid sinuses.

We suggest that primary care physicians and emergency department providers should maintain high index of suspicion for patients who present with recurrent epistaxis of unknown origin. These patients should be referred to ENT specialist, or imaging study of the sinuses should be obtained by primary care physicians, to avoid delay in diagnosis, as that can greatly alter the outcome of the disease. Mucosal melanoma of the head and neck is associated with poor outcomes despite technological developments in surgery, radiation therapy and advances in systemic strategies over a period of >60 years.⁸ The primary treatment modality for mucosal melanomas of the head and neck is complete surgical excision. A systematic analysis looking at postoperative radiation therapy found that

Figure 3 Sinonasal biopsy demonstrating malignant melanoma.

Learning points

- Epistaxis is a common complaint in primary care. Although usually benign, it is important to maintain nasal neoplasm as a differential diagnosis for recurrent epistaxis.
- Common presentation of sinonasal melanoma and other nasal neoplasms (squamous cell carcinoma, adenoid cystic carcinoma and inverted papilloma) is epistaxis.
- Treatment of recurrent epistaxis of unknown origin with packing/cautery should be followed by timely endoscopy with potential biopsy and then imaging.
- We suggest timely specialty referral (ear, nose and throat) or imaging of sinuses by primary care physicians for recurrent episodes of epistaxis.
- Earlier diagnosis of sinonasal melanoma greatly affects prognosis and options of treatment. Delay in imaging could postpone diagnosis and treatment and negatively affect an outcome of the disease.

it may improve locoregional control, but does not improve the overall survival rate.⁹ Another study found that receiving chemotherapy did not demonstrate an improved 5-year survival rate.¹⁰

Timely diagnosis and treatment might improve the outcome. Overall, <50% of patients are alive within 3 years of diagnosis. This prognosis may also improve with the advent of new biologic therapies. Our patient had a complete metabolic response on positron emission tomography to ipilimumab and nivolumab. He continues to do well without any evidence of new disease 2.5 years after his initial diagnosis.

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