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Evolution in Sinonasal Mucosal Melanoma Management

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Abstract

Sinonasal mucosal melanoma is a rare and aggressive cancer with poor prognosis. Surgical resection with clear margins, when possible, remains the treatment of choice. Radiation therapy is generally used in the adjuvant setting with improved rates of local control following complete resection. Traditional chemotherapeutic agents do not improve the rates of locoregional control or survival. Immunotherapy has been used with some responders but with overall relatively poor outcomes. These outcomes highlight the need for new agents and more prospective trials in this space. We provide a unique case report of a patient with an advanced sinonasal mucosal melanoma and an overview of the recent literature pertaining to the management of this disease.

Keywords

- melanoma
- sinonasal mucosal melanoma
- immunotherapy
- management
- review

Introduction

Sinonasal mucosal melanomas are rare with most presenting with locally advanced disease.[1,2] Traditionally, management relied on radical resection followed by radiation therapy. Regardless of local treatment, outcomes are historically poor secondary to high rates of distant metastasis.[3,4] With emergence of immune checkpoint inhibition (ICI) and a focus on quality of life, management of this disease has evolved.

Case Review

A 79-year-old male presented with left nasal obstruction, epistaxis, and proptosis. A magnetic resonance imaging demonstrated a multicompartmental sinonasal mass that measured $6.8 \times 4.9 \times 3.8$ cm with invasion of the inferior rectus muscle and orbital apex (►**Fig. 1A**, **B**). Biopsy demonstrated mucosal melanoma. Following progression after radiation therapy (30 Gy) and PD-1 blockade (nivolumab), the patient then received combined programmed cell death protein 1 (PD-1) blockade with cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) inhibition (ipilimumab). The patient had a complete response after only one dose (►**Fig. 1C**, **D**). The patient developed treatment-related toxicities including diabetes, hypothyroidism, and autoimmune ocular disease, and unfortunately died 18 months after treatment due to a pulmonary embolus.

Literature Review

Head and neck mucosal melanoma carries a 5-year overall survival (OS) of 20%.[5] Radical resection of sinonasal malignant melanoma (SNMM) with clear margins can entail severe cosmetic and functional impairments.[6] In a large retrospective study, positive margins were noted in 22% of patients demonstrating some of the biological challenges of this disease.[5] Open craniofacial resection is no longer recommended due to poor outcomes and associated morbidity.[7] Endoscopic resection has been shown to have lower morbidity, better quality of life, and comparable survival outcomes to open surgery.[3,8,9] Adjuvant radiation therapy has been shown to improve local control but does not seem to improve survival.[10,11]

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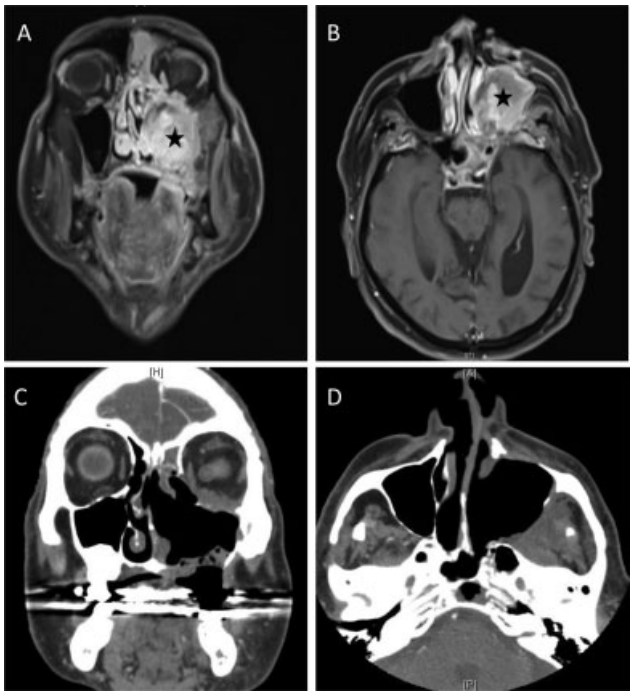

Fig. 1 Pretreatment coronal (**A**) and axial (**B**) magnetic resonance imaging scans of left sinonasal malignant melanoma. Posttreatment images represent complete response of the tumor to combination immune checkpoint inhibition on coronal (**C**) and axial (**D**) computed tomographic scans.

In contrast to cutaneous melanoma, SNMM is notable for a lack of BRAF mutations (0–3%) and a high incidence of c-KIT (4–53%) and NRAS (14–48%) mutations.[12,13] Studies of the tyrosine kinase inhibitor imatinib mesylate in select cases demonstrated an overall response (OR) of 16 to 29%.[14,15] For SNMM with NRAS mutations, mitogen-activated protein kinase inhibitors have been trialed with modest responses and questionable clinical benefit.[16,17] With a lower response rate than cutaneous melanoma, ipilimumab and pembrolizumab monotherapy for mucosal melanomas was shown to have an OR of 6.7 and 23%, respectively.[18,19] In another study comparing combination PD-1 and CTLA-4 inhibition versus monotherapy in mucosal melanoma, OR was found to be 37% (3% complete response) compared with 23% (nivolumab) and 8% (ipilimumab).[20] However, grade 3 and 4 adverse events were significantly higher in the combination group (40 vs. 8%).

In a single-institution retrospective study assessing outcomes over time with integration of endoscopic surgery, advances in radiation, and immunotherapy, there have been no changes in overall survival.[4] Modern management relies on ICI, but the appropriate timing of integration is unclear. Future studies are needed to analyze the impact of new agents and protocols on survival outcomes and quality of life.

Conflict of Interest
None.

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