Metastatic melanoma to the orbit with dedifferentiation

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Introduction

Melanoma can metastasize through hematogenous, lymphatic, and perineural routes, with metastatic cutaneous melanoma representing 3-20% of metastases to the orbit and 1.4% of space-occupying lesions of the orbit in general[1-9].
Common histologic markers for melanoma include S100, HMB-45, Melan-A, MITF and SOX-10.
Dedifferentiation refers to the process where a carcinoma loses histopathologic features of its tissue of origin[10] .It leads to difficulty in accurate diagnosis because if a dedifferentiated section is all that is sampled, the above mentioned immunohistologic markers that aid in diagnosis, are lost.
We present the first documented case of metastatic melanoma to the orbit with perineural spread and dedifferentiation demonstrated on radiology and histopathology.

Case Description

A 64-year-old Caucasian male presented to the emergency department with restricted extraocular movement (EOM), decreased vision, and pain of the right eye (OD). The left eye (OS) was unaffected.

Past oncologic history:
- Poorly differentiated parotid gland carcinoma
- Melanoma of the lip and neck
- Poorly differentiated carcinoma involving left mandible and Meckel's cave.

Physical exam (Figure1A):
- Right sub-brow mass superolateral to supraorbital notch
- Proptosis
- Significant right upper eyelid edema with ptosis

Computerized Tomography (CT) scan:
- Intraorbital mass (OD) measured 2.2 x 1.7 x 1.8 cm.
- Preseptal mass upper eyelid (OD) measured 1.4 x 0.9 x 1.3 cm

The patient presented to the ophthalmology clinic 21 days later
- Best-corrected visual acuity (BCVA): 20/50 OD, 20/20 OS.
- EOM <30 degrees in all fields of gaze
- Hertel exophthalmometry revealed 16 mm of proptosis (Figure 1A).
- Slit-lamp exam: Exposure keratopathy and macular folds OD.

Magnetic Resonance imaging (MRI):
- Enlargement of both masses relative to initial imaging.
- Intraorbital mass (OD) measured 2.6 x 3.2 x 3.5 cm (Figure 1B).
- Pre-septal mass (OD) measured 1.2 x 3.5 x 1.2 cm (Figure 1C).
- Perineural spread along the supraorbital nerve (Figure 1D).

Intervention

Intraoperatively, two distinct sub-brow masses were found to be connected by a bridge of malignant tissue with projections interlocking with the surrounding soft tissue; the masses were firm, black, and poorly vascularized (Figure 2A). Dissection around the medial sub-brow mass revealed it was connected to the supraorbital neuromuscular bundle and the intraorbital tumor, which appeared tan/yellow, avascular, and lobulated (Figure 2B); complete excision was deemed unsafe due to the extent of soft tissue invasion and risk of optic nerve injury, so the intraorbital mass was debulked until proptosis improved and the pressure to retropulsion was nearly symmetric

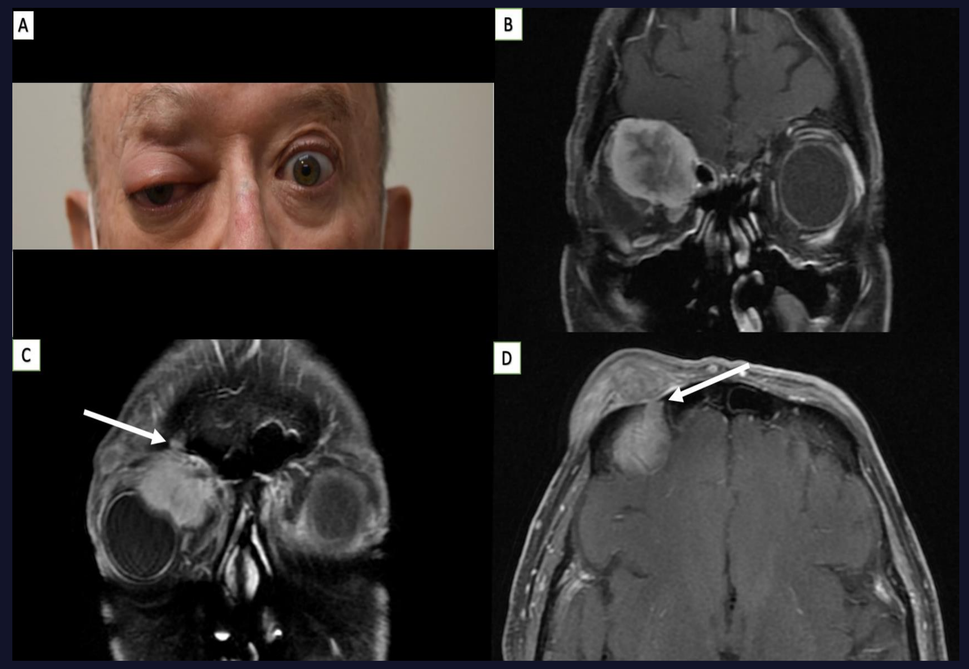

Figure 1: A) Clinical appearance of the patient B) Coronal T1 FS postcontrast image demonstrating approximately 3.5 cm heterogeneously enhancing right intraorbital mass. C) Coronal T1 FS postcontrast image demonstrates abnormal enhancement with the right supraorbital foramen (arrow), consistent with perineural spread of tumor along the supraorbital nerve. D) Axial T1 FS postcontrast image at the level of the supraorbital foramen demonstrating abnormal enhancement consistent with perineural spread of tumor (arrow). The Tumor has additionally spread into the superficial supraorbital soft tissues via this route.

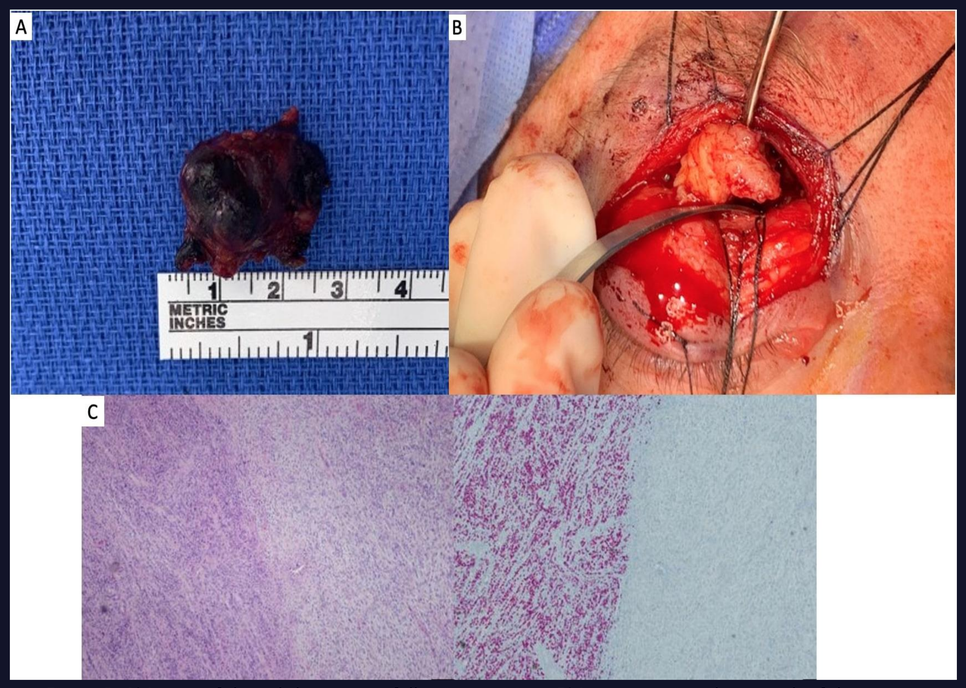

Figure 2: A) Image of the sub-brow mass following excision. B) Intraoperative photograph of the intraorbital mass being debulked through upper eyelid anterior orbitotomy. C) H&E staining (left) and SOX10 immunohistochemical staining (right) of the intraorbital mass demonstrating dedifferentiation.

Timeline

Post-operative day 1:
- Visual acuity (20/25 OD), proptosis, and EOM markedly improved
- Histology of both sub-brow and intraorbital masses:
  - Distinct areas of loss of SOX-10 and Melan-A, consistent with melanoma with dedifferentiation (Figure 2C)
  - Areas with loss of SOX 10 expressed more spindled morphology with larger, vascular nuclei and prominent nucleoli
  - Areas with SOX 10 expression showed hyperchromatic nuclei without conspicuous nucleoli and a more nested architecture

Post-operative day 12:
- Patient developed vertigo, worsening proptosis, decreased vision, nausea and confusion
- CT scan revealed 3.4 x 3 x 2.5 cm mass demonstrating recurrence of intraorbital tumor
- Surgical management deferred, and care transitioned to radiation and medical oncologist
- Local radiotherapy performed followed by monoclonal antibody therapy using pembrolizumab (Keytruda)

Post-operative month 2:
- Patient had no light perception OD
- Complete paralysis of right levator palpbrae secondary to radiotherapy
- Hertel exopthalmometry demonstrated 1mm of proptosis.

Despite an initial positive response to immunotherapy, the patient died at postoperative month 6 due to his systemic metastases.

Conclusion

We present the first case of metastatic melanoma to the orbit with perineural spread and dedifferentiation demonstrated on radiology and histopathology. The adaptability of malignant melanocytes to the local microenvironment imparts diagnostic and therapeutic challenges. With the incidence of Melanoma doubling in the past forty years, we advocate for a thorough review of a patient's personal and family oncologic history[11]. We also encourage a full dermatologic exam if there is a history of melanoma, and MRI as the primary imaging modality if there is concern for perineural spread.

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