JAMA Ophthalmology Clinical Challenge

Immunotherapy for a Choroidal Pigmented Lesion

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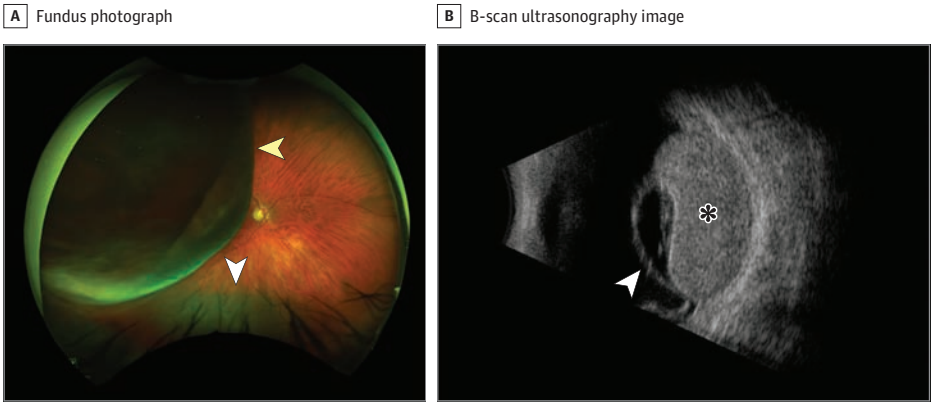

Figure 1. A, Fundus photography showing a partially pigmented choroidal lesion located superotemporally (yellow arrowhead), extending to the macula with associated exudative retinal detachment inferiorly (white arrowhead). B, B-scan ultrasound image of the lesion showing an acoustically solid lesion with prominent intralesional vascularity with an irregular internal structure (asterisk), measuring 26 × 21 × 8.1 mm, with subretinal fluid that overlies the lesion and extends inferiorly (arrowhead) on B-scan.

A 51-year-old male with a complaint of a 4-week history of redness and swelling of the right temporal bulbar conjunctiva was referred for evaluation of a choroidal lesion in the right eye. He had a history of *BRAF* V600 E mutation-positive, superficial spreading-type cutaneous melanoma (CM) on the chest with metastasis to a sentinel lymph node 3 years ago. He was treated at the time of diagnosis with excision of the primary tumor with clear margins and axillary lymph node dissection. He also had a papillary thyroid carcinoma 1 year earlier treated with thyroidectomy and radioactive iodine-131. He had a follow-up visit with his oncologist 2 days before his presentation to our ocular oncology clinic and he did not have any systemic findings suggestive of recurrence of his previous malignancies.

The best-corrected visual acuity after a new refraction was 20/30 in the right eye and 20/20 in the left eye. Anterior segment examination of the right eye revealed temporal conjunctival hyperemia with dilated episcleral vessels. Fundus examination of the right eye revealed a partially pigmented choroidal lesion, measuring 26 × 21 × 8.1 mm, superotemporally extending to the macula associated with exudative retinal detachment inferiorly (**Figure 1**A). Ultrasonography showed an acoustically solid lesion with prominent intralesional vascularity with irregular internal structure on B-scan and mid to low internal reflectivity on A-scan (Figure 1B).

WHAT WOULD YOU DO NEXT?

A. Plaque radiotherapy

B. Enucleation

C. Fine-needle aspiration biopsy

D. Observation

CME Quiz at jamacmelookup.com

Diagnosis

Solitary choroidal metastasis secondary to primary cutaneous melanoma of the chest

What to Do Next

C. Fine-needle aspiration biopsy

Discussion

Solitary choroidal metastasis from CM is rare with only a few case reports in the literature.[1-4] It can be challenging to differentiate solitary choroidal metastases of CM from primary choroidal melanoma through clinical examination and imaging studies. Due to recent advances in immunotherapy and targeted therapies, it is important to differentiate the 2 tumors as treatment options might differ accordingly. Though cutaneous and choroidal melanomas have similar embryonic origin and histological features, their epidemiological and cytogenetic characteristics differ.[5]

Genetic testing can assist in distinguishing CM from primary uveal melanoma since they have genetically distinct initiating mutations with different genetic mutational profiles. CMs most commonly have activating mutations in BRAF kinase. In contrast, uveal melanomas typically lack BRAF mutations and are characterized by mutations in GNAQ, GNA11, BAP1, EIF1AX, and SF3B1.[5] In our case, the cytopathology came out to be consistent with melanoma with tumor cells positive for SOX10 and Melan A and negative for TTF1 and PAX8 as assessed by immunohistochemical staining. An allele-specific polymerase chain reaction assay revealed the tumor was positive for *BRAF* c.1799T>A V600E mutation, which was the key to the diagnosis of metastatic CM.

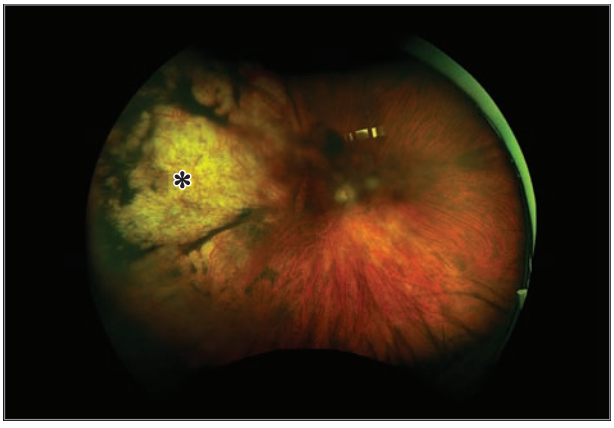

Figure 2. Fundus photography at the last visit after completion of immunotherapy showing regressed choroidal metastatic lesion (asterisk) and resolved exudative retinal detachment.

Three days after the choroidal fine-needle aspiration biopsy (FNAB) procedure, the patient noticed a new dark-colored skin nodule on his right neck. FNAB of this lesion also proved to be melanoma. He also had a whole-body workup and had no further systemic metastases.

He was diagnosed with choroidal and cutaneous metastasis from CM of the chest. Two agents of immunotherapy, nivolumab and ipilimumab, were started. At examination after 3 months of immunotherapy, the metastatic choroidal lesion had regressed to a flat scar, measuring 26 × 21 × flat mm, and the exudative retinal detachment was resolved. After 10 cycles of treatment, he discontinued immunotherapy due to adverse effects. His metastatic cutaneous lesion on the right neck completely resolved, too. Choroidal metastasis from CM is reported to be treated with radiation, enucleation, chemotherapy, and most recently with immunotherapy and targeted therapies.[1-5] Rieth et al[3] reported a case with systemic metastasis from CM who received immunotherapy after external beam radiotherapy with BRAF/MEK inhibitors. Choroidal metastasis regressed within 1 month. CMs are shown to be responsive to immunotherapy, especially combined nivolumab and ipilimumab therapy, with a 58% response rate and 52% at 5-year survival rate.[6] To the best of our knowledge, our case is the first report that shows the effectiveness of immunotherapy-alone treatment in the eye, showing an eye-preserving option for choroidal metastasis from CM.

In this case, based on the previous history of multiple systemic cancers without any known systemic metastasis and clinical and imaging findings of choroidal lesion, FNAB (option C) will be the first step to confirm the diagnosis and plan management. After the correct diagnosis, the management options of plaque radiotherapy (option A), enucleation (option B), or observation while receiving systemic therapy if it is metastasis (option D) could be considered. After the metastasis was diagnosed, immunotherapy was started as a globe-preserving treatment due to the detection of another metastatic site in the neck and to avoid the possible ocular adverse effects of plaque radiotherapy. The patient was followed up closely, and external beam radiotherapy or enucleation was reserved as a second line if immunotherapy fails. Plaque brachytherapy was deferred as the lesion exceeded the size limits.[7] This case shows an eye-preserving outcome for choroidal metastasis from CM associated with immunotherapy alone in the eye.

Patient Outcome

At last examination 2 years later, the patient's best-corrected visual acuity was 20/50 in the right eye. The anterior segment examination was unremarkable except cataract formation in the right eye. In fundus examination, the right metastatic choroidal lesion remained regressed as chorioretinal scar tissue, measuring 21 × 20 × flat mm (**Figure 2**). There was no other systemic metastasis.

ARTICLE INFORMATION

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Published Online: May 30, 2024. doi:10.1001/jamaophthalmol.2024.1518

Conflict of Interest Disclosures: Dr Demirci reported being on the advisory board for Castle Bioscience. No other disclosures were reported.

Funding/Support: This study in part was supported by Richard N. and Marilyn K. Witham Professorship. Dr Sezenoz is funded by the Scientific and Technological Research Council of Turkey (TUBITAK).

Role of the Funder/Sponsor: The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Additional Contributions: We thank the patient for granting permission to publish this information.

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