CHOROIDAL METASTASIS FROM LUNG ADENOCARCINOMA

Diagnosis of choroidal malignancy should prompt a workup for systemic disease in patients with no known history of cancer.

BY WEILIN SONG, MD; JULIE K. KWON, MD; BASIL K. WILLIAMS JR, MD; AND JAYANTH SRIDHAR, MD

Choroidal metastasis is the most common intraocular malignancy and the first sign of systemic malignancy in up to a third of patients with cancer.[1,2] The two most common primary tumor sites are breast and lung, which are found in 40% to 53% and 20% to 29% of cases, respectively.[1] The choroid's rich vascular supply makes it the most common site of uveal metastases.[3] Due to the predominance of metastases involving the post-equatorial region and its frequent association with subretinal fluid, patients typically present with blurred vision and, less commonly, flashes, floaters, and ocular pain.[3-5] However, 9% to 11% of patients are asymptomatic at presentation, and lesions may be found on routine ocular examination.[3]

The diagnosis of ocular metastasis is based on clinical examination and ocular imaging and, in patients without a known history of cancer, can prompt expedited evaluation and treatment of the primary cancer. While choroidal metastases frequently occur in the later stages of disseminated disease and are generally considered a poor prognostic sign, recent advances in systemic therapies have significantly improved survival rates.[1]

Here, we present a case of choroidal metastasis from lung adenocarcinoma, with improvement of visual function and near complete resolution of the metastatic lesion and subretinal fluid after initiation of systemic chemotherapy and immunotherapy.

OCULAR MANIFESTATION AS AN EARLY SIGN

A 59-year-old woman presented for evaluation of acute onset blurry vision and photopsia in her right eye. Her past medical history was significant for tobacco use (10 pack-years) and chronic obstructive pulmonary disease. Of note, she was also undergoing workup of a lung mass and multiple pulmonary nodules, which were detected incidentally on imaging for persistent pain after trauma to the right chest. She had recently undergone bronchoscopy and biopsy, with nondiagnostic pathology showing rare, atypical cells.

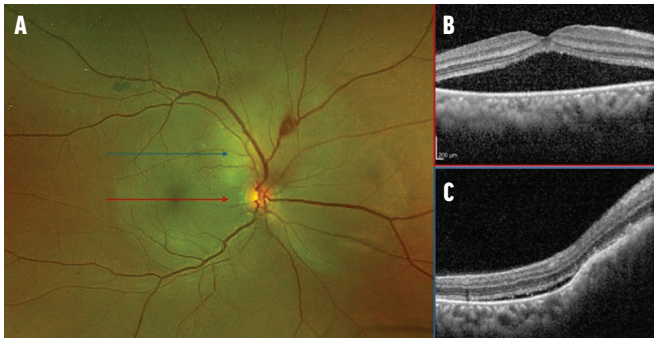

Figure 1. Color fundus photography illustrated a choroidal mass superior to the optic nerve with associated subretinal fluid extending to the macula and nasally to the nerve, a superonasal flame hemorrhage, and a superotemporal pigmented choroidal lesion along the superior arcades (A). OCT through the central macula showed subfoveal subretinal fluid (B). OCT through the superior macula showed a large choroidal mass with an irregular surface and shallow subretinal fluid (C).

On initial ophthalmic examination, her VA was 20/200 OD and 20/25 OS. The anterior segment was unremarkable bilaterally. Dilated fundus examination of her right eye was notable for a choroidal mass superior to the nerve with associated macula-involving subretinal fluid and a flame hemorrhage lesion (Figure 1A and B); her left eye was unremarkable. The choroidal mass had moderate echo-density on B-scan ultrasound and an irregular

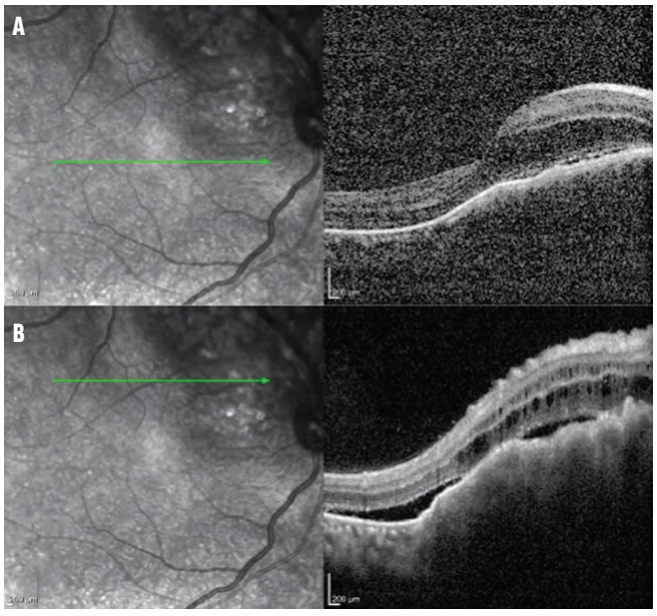

Figure 2. OCT through the central macula showed subfoveal extension of the choroidal mass and shallow subretinal fluid (A). OCT through the superior macula showed increased surface irregularity and intraretinal and subretinal fluid (B).

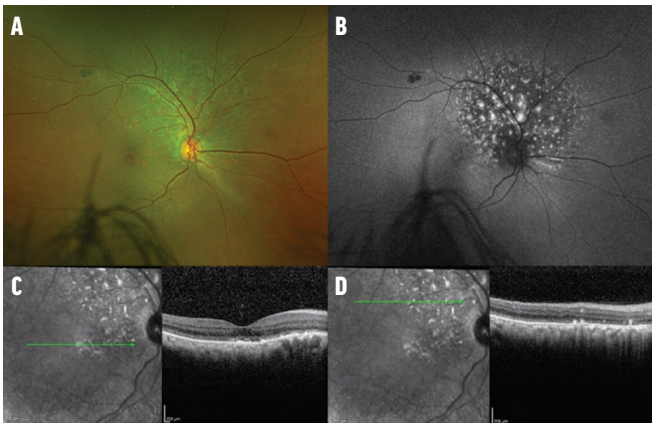

Figure 3. Fundus photography showed regression of the choroidal mass and resolution of the subretinal fluid and flame hemorrhage after treatment (A). FAF showed hyperautofluorescent and hypoautofluorescent regions corresponding to the prior choroidal mass (B). OCT through the central macula showed regression of the choroidal mass and resolution of the subretinal fluid (C). OCT through the superior macula similarly showed regression of the choroidal mass, resolution of the subretinal and intraretinal fluid, and hyperintense areas of lipofuscin primarily in the outer retina corresponding to the hyperautofluorescent regions on FAF (D).

surface on OCT (Figure 1C).

Based on a strong suspicion for metastatic disease, the patient received MRI of the brain and orbits, which did not show any other lesions. On follow-up 6 weeks later, the patient was pending repeat lung biopsy with interventional radiology. The subretinal fluid had improved, but there appeared to be progression of the choroidal mass toward the fovea, along with increased peripapillary intraretinal fluid (Figure 2).

The patient was diagnosed with stage IV metastatic non-small cell lung cancer (NSCLC), with fine-needle aspiration sample of a supraclavicular lymph node consistent with lung adenocarcinoma. She was initiated on systemic chemotherapy with carboplatin and pemetrexed, and immunotherapy with pembrolizumab was added during the fourth cycle. Maintenance therapy with pemetrexed and pembrolizumab was initiated on the seventh cycle.

Three months after initiating therapy, the patient's VA had improved to 20/50 OD, the subretinal fluid had resolved, and the choroidal metastasis had significantly regressed (Figure 3). On OCT and fundus autofluorescence (FAF), there was ellipsoid zone attenuation and multiple small hyperreflective areas consistent with lipofuscin in the prior area of choroidal metastasis. The patient's oncologist also noted improvement of systemic disease burden on subsequent CT imaging.

IS IT METASTASIS, OR SOMETHING ELSE?

As demonstrated in this patient, choroidal metastases generally appear as creamy white or pale-yellow masses that are flat or plateau-shaped, although color and morphology can vary depending on the primary tumor site.[1,2] The most common associated feature is subretinal fluid, which is present in up to 73% of cases and is usually perilesional.[2,3] The differential diagnosis of choroidal metastases includes choroidal melanoma, hemangioma, granuloma, osteoma, and sclerochoroidal calcification.[5]

Certain imaging features can help differentiate choroidal metastases from other intraocular masses. On ultrasonography, choroidal metastases are generally flat or slightly dome-shaped and are characterized by a medium to high nonhomogeneous reflectivity. In contrast, choroidal melanomas have low-to-medium reflectivity and grow in a nodular configuration, sometimes leading to rupture of the Bruch membrane and appearing in a classic mushroom shape. On OCT, the most prominent feature of choroidal metastases is an irregular or lumpy anterior surface, as was seen in this case, as opposed to a smooth mound or dome of a nevus or melanoma.[6,7] Hyperreflective areas of lipofuscin have been previously described in the literature and are thought to be the shed outer segments of photoreceptors.[7,8]

MANAGEMENT

While most patients have known or suspected systemic cancer at the time of choroidal metastasis detection, those without a history of cancer should undergo prompt, thorough investigation for systemic malignancy. In cases of an unidentified primary source, fine-needle aspiration biopsy can assist in providing cytological information to help differentiate between metastasis versus primary lesion.[9,10]

WHILE CHOROIDAL METASTASES FREQUENTLY OCCUR IN THE LATE STAGES OF KNOWN DISSEMINATED DISEASE, UP TO A THIRD OF PATIENTS HAVE NO KNOWN HISTORY OF CANCER AT THE TIME OF CHOROIDAL METASTASIS DIAGNOSIS.

The treatment approach depends on multiple considerations, including the patient's life expectancy, presence of other metastases, and location and number of choroidal tumors. Systemic chemotherapy, immunotherapy, targeted therapy, or hormone therapy are preferred initial options for patients who can begin treatment quickly, especially for those with bilateral, multifocal choroidal metastases or systemic metastases.

In patients with metastatic NSCLC, platinum-based chemotherapy is the standard first-line treatment. The addition of immunotherapy with pembrolizumab may provide additional therapeutic effect by restoring the antitumor immunity mediated by T cells and is associated with significantly longer progression-free and overall survival with fewer adverse effects.[11]

There have been two reported cases of choroidal metastases from NSCLC treated with pembrolizumab and cytotoxic chemotherapy leading to regression, although one noted recurrence after the patient was continued on pembrolizumab alone as maintenance therapy.[11,12]

Focal therapy is advised in choroidal tumors that are causing visual loss if there is a delay in or minimal response to systemic therapy or if the primary tumor cannot be identified. This includes whole eye radiotherapy for bilateral or multifocal metastases and plaque radiotherapy, transpupillary radiotherapy, or photodynamic therapy for solitary metastasis.[5]

KEEP YOUR SKILLS SHARP

While choroidal metastases frequently occur in the late stages of known disseminated disease, up to a third of patients have no known history of cancer at the time of choroidal metastasis diagnosis.[1,2] Therefore, ophthalmologists should be familiar with the diagnostic features and workup to allow for prompt diagnosis and treatment of the primary cancer. ■

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WEILIN SONG, MD
- Ophthalmology Resident, Jules Stein Eye Institute, University of California Los Angeles, Los Angeles
- wsong@mednet.ucla.edu
- Financial disclosure: None

JULIE K. KWON, MD
- Retinal Staff Physician, Olive View-UCLA Medical Center, University of California Los Angeles, Los Angeles
- julie.you@gmail.com
- Financial disclosure: None

BASIL K. WILLIAMS JR, MD
- Associate Professor of Clinical Ophthalmology, Bascom Palmer Eye Institute, Miami
- basilkwilliams@miami.edu
- Financial disclosure: Consultant (Abbvie, Castle Biosciences, EyePoint, Genentech/Roche, Regeneron)

JAYANTH SRIDHAR, MD
- Chief of Ophthalmology, Olive View-UCLA Medical Center, University of California Los Angeles, Los Angeles
- jsridhar119@gmail.com
- Financial disclosure: Consultant (Apellis, Eyepoint, Genentech/Roche, Regeneron)