• Letter to the Editor •

Lung adenocarcinoma with initial binocular symptoms

Xiao-Lan Zhao[1], Yan-Qing Jiang[2], Zhen Yang[1], Chao-Qun Liu[1], Xiao-Li Yang[1]

[1]Department of Ophthalmology, Affiliated Hospital of North Sichuan Medical College, Nanchong 637000, Sichuan Province, China
[2]Department of Ophthalmology, North Sichuan Medical College, Nanchong 637000, Sichuan Province, China
Correspondence to: Xiao-Li Yang and Chao-Qun Liu. Department of Ophthalmology, Affiliated Hospital of North Sichuan Medical College, Nanchong 637000, Sichuan Province, China. 1574439563@qq.com; 312256738@qq.com
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Dear Editor,

Lung adenocarcinoma with choroidal metastasis is a common form of cancer, with breast cancer accounting for 40%-53% and lung cancer accounting for 20%-29% of primary cases with choroidal metastases[1]. This type of metastatic cancer typically affects people aged 40-70y, and is more prevalent in women than men[1]. Ocular symptoms, including vision loss, can be an early indication of the disease, as many tumors are asymptomatic in their early stages. Studies have shown that 40.3% of cases involve the macular region, which explains why ocular symptoms are often the first manifestation of the disease[2]. When choroidal metastasis is suspected in patients without a history of cancer, a combination of diagnostic tools should be used to identify the primary source of the tumor. Choroidal tumors can serve as an indication of future lung cancer diagnosis in some patients with lung cancer[1]. In this report, we present a case of bilateral lung adenocarcinoma where ocular symptoms were the first indication of the disease.

Case Report On October 5, 2022, a 57-year-old woman visited our ophthalmic clinic with complaints of painless vision loss in both eyes. Upon examination, her visual acuity was 20/50 in both eyes, and her intraocular pressure was normal. Anterior segment evaluation and ocular motility were normal in both eyes. Dilated fundus examination revealed multiple yellow-white lesions occupying the posterior pole in both eyes (Figure 1A and 1B). Optical coherence tomography (OCT) examination of both eyes revealed the presence of subretinal fluid (Figure 1C and 1D). Fluorescein angiography (FA) showed hyperfluorescence in the late venous phase, with dye staining in both eyes (Figure 2A and 2B). Ultrasonography showed solid lesions in the choroid of both eyes and secondary retinal detachment in both eyes (Figure 2C and 2D).

The initial diagnosis for the patient was bilateral choroidal occupations, but the nature of these was yet to be determined. In order to identify the primary tumor site, the patient underwent a series of diagnostic tests, including an orbital magnetic resonance imaging (MRI), breast ultrasound, chest and abdomen ultrasound, and tumor marker examination. The MRI scan of both orbits showed abnormal signals in the medial and lateral posterior wall of the right eye and localized thickening of the lateral posterior wall of the left eye towards the bulbous bulge, with moderate signal in T1W1 and moderate signal in T2W1 (Figure 2E and 2F). The computed tomography (CT) scan of the chest and abdomen revealed a dorsal segmental strip shadow in the lower lobe of the left lung and multiple nodules of unequal size in the liver (Figure 2G and 2H). A liver puncture biopsy confirmed the presence of adenocarcinoma of the lung (Figure 3), and elevated carcinoembryonic antigen was identified among the tumor markers. Single-photon emission computed tomography examination indicated multiple bone metastases throughout the patient's body.

The revised diagnosis for the patient was as follows: 1) bilateral choroidal metastasis; 2) lung adenocarcinoma with multiple metastases throughout the body (TP53+, EGFR, 21pL858R+). Subsequently, the patient received targeted therapy (anlotinib, bevacizumab) combined with radiotherapy for bone metastases at the Radiotherapy Department. The patient was re-evaluated in the Ophthalmology Department on November 20, 2022, and the relevant examinations revealed improved visual acuity, significantly reduced subretinal fluid, a flatter retina compared to the time of admission, and a smaller choroidal tumor volume than before (Figure 1A1, 1B1, 1C1 and 1D1). Unfortunately, the patient passed away due to bone cancer metastasis one month later during follow-up. The study was approved by the Medical Ethics Committee of the Affiliated Hospital of Sichuan North Medical College for ethical review. And signed an informed consent instrument with the patient.

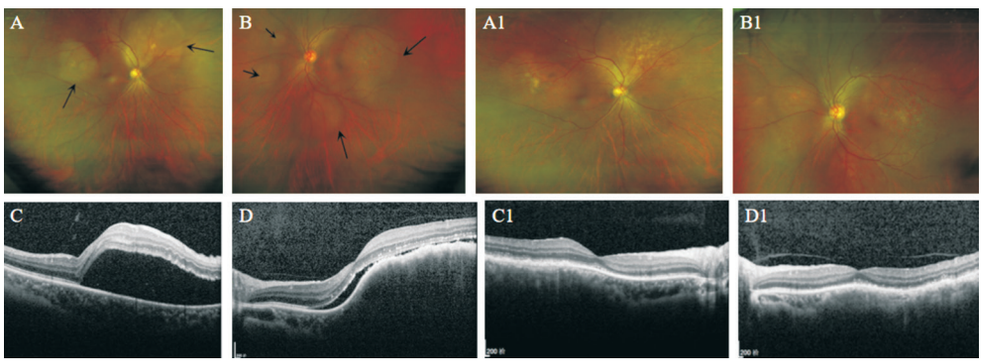

Figure 1 OCT and fundus photograph Initial consultation on October 5, 2022, with fundus photograph of both eyes showing multiple yellow-white occupied lesions (A and B). OCT examination of both eyes showing subretinal fluid (C and D). Re-examination in the Department of Ophthalmology on November 20, 2022, showed improved visual acuity, significantly reduced subretinal fluid (C1 and D1). A flatter retina than at the time of admission, and smaller choroidal tumor volume than before (A1 and B1). OCT: Optical coherence tomography.

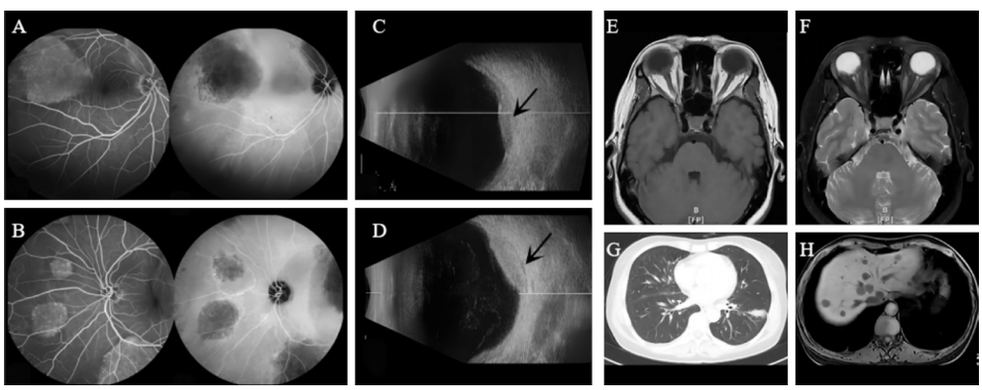

Figure 2 FA, ultrasonography, orbital MRI and CT of the chest and abdomen A, B: FA displaying hyperfluorescence in the late venous phase with dye staining in both eyes. C, D: Ultrasonography demonstrating multiple solid occupations. E, F: Orbital MRI showing abnormal signals in the medial and lateral posterior wall of the right eye and localized thickening of the lateral posterior wall of the left eye toward the bulbous bulge. Moderate signal in T1W1 and moderate signal in T2W1. G, H: CT of the chest and abdomen suggests a dorsal segmental strip shadow in the lower lobe of the left lung and multiple nodules of unequal size in the liver. FA: Fluorescein angiography; MRI: Magnetic resonance imaging; CT: Computed tomography.

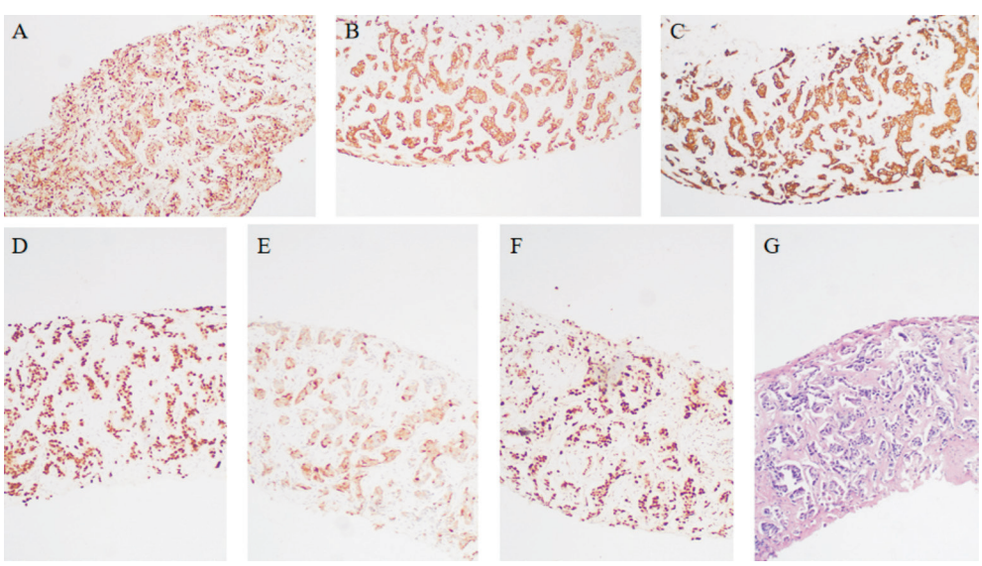

Figure 3 Liver puncture biopsy showing immunohistochemistry for thyroid transcription factor-1 (TTF-1), cytokeratin 7 and 19 (CK7, CK19), neoaspartate protease A (Napsin A), P53 (+, mutant), and Glypican3 were all positive, suggesting lung adenocarcinoma.

DISCUSSION

The incidence of intraocular metastatic cancer is estimated to be around 8%-10%, with approximately 88% of ocular metastases occurring in the choroid. This may be due to the

rich vascularity of the choroid[3]. Mitamura *et al*[2]. found that radiotherapy led to regression of choroidal tumors but decreased central choroidal blood flow and central choroidal thickness. It suggests that choroidal tumors may disseminate *via* oxygen-rich blood pathways[4-5]. Choroidal metastases are most commonly caused by breast and lung cancer, and the majority of cases are unilateral and unifocal[3]. The diagnosis of choroidal metastases can be made using a combination of fundus examination, ultrasound, fluorescence angiography, OCT, MRI, and biopsy (if necessary). Biopsy is rarely performed due to the risk of tumor dissemination. It is important to differentiate choroidal metastasis from choroidal melanoma, retinal pigment tumor, choroidal osteoma, choroidal hemangioma, choroidal neovascularization, posterior scleritis, *etc*.

Radiation therapy is considered the basis for ophthalmic malignancies[6]. For choroidal metastasis patients, treatment options include external radiation therapy, brachytherapy, gamma knife radiosurgery (GKR), and proton beam therapy (PBT). Local radiation therapy or intravitreal injection of anti-vascular endothelial growth factor (VEGF) drugs can have significant effects on the eye[1]. Targeted therapy is preferred for patients with sensitive gene mutations or those who are not suitable for ocular radiotherapy. Patients without drug-sensitive gene mutations or those with lesions near the optic disc require systemic chemotherapy. Palliative local therapy may be considered when intraocular metastases become resistant to systemic therapy. The goal of local therapy is to relieve ocular symptoms, maintain vision, and avoid or reduce the possibility of ophthalmic removal. Systemic treatment appears to be more rapidly effective on metastases located in highly vascularized areas, probably due to a greater supply of antiblastic drug with the blood flow. In the case presented, already at the 1-month check-up, a significant reduction in the choroidal neoplastic mass and reabsorption of the subretinal fluid was achieved[7-10]. Studies suggest that combined local treatment may have better outcomes than systemic treatment alone, but more research is needed to determine its safety and efficacy.

In this case, the patient was first diagnosed due to ocular symptoms, and the primary tumor was subsequently identified through detailed medical history and relevant examinations. However, multiple metastases had already occurred throughout the body, and the prognosis was poor. Although the ocular symptoms were relieved after systemic chemotherapy and targeted therapy, the patient ultimately succumbed to bone metastasis.

This case highlights the importance of early detection, timely diagnosis, and prompt treatment of intraocular metastasis. Notably, although topical treatment was not administered alone, ocular symptoms were significantly improved with systemic therapy. As such, it remains to be studied whether topical treatment is superior to systemic treatment in the management of intraocular metastasis. In this case study, the patients' ocular symptoms all improved after treatment.

Clinicians should maintain a high index of suspicion for choroidal metastasis in patients with exudative retinal detachment, and expediently investigate for underlying primary lesions. Prompt and appropriate management, including systemic therapy, may lead to symptom relief and improved patient outcomes.

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