• Letter to the Editor •

The application of ultra-wide-field fundus autofluorescence in early metastatic choroidal tumor screening

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Dear Editor,

I am Dr. Ke Yao, from Eye Center, the Second Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou, China. I write to present three cases with metastatic choroidal tumor using an ultra-wide-field scanning laser ophthalmoscope.

Metastatic choroidal tumor is the most common intraocular malignancy and accounts for approximately 1%-8% of patients with systemic malignancy[1-3]. It presents as the first sign of a systemic malignant tumor in up to a third of patients with cancer. Most choroidal metastases locate posterior to the equator of the retina and some in the peripheral retina. The tumor appears as a flat, undetectable lesion at the early stage, and the patient may be asymptomatic. As the tumor grows, it becomes an elevated and visible choroidal mass and may result in serous retinal detachment and optic disc edema. Thus, an accurate and prompt diagnostic method should be used in early choroidal metastasis screening to avoid misdiagnosis and missed diagnosis.

The main methods o f detecting choroidal tumor include ophthalmoscopic examination, ultrasonography (US), optical tomography coherence (OCT), fundus fluorescein angiography (FFA), and indocyanine green angiography (ICGA)[4]. However, due to poor health conditions or allergic reactions, it is usually difficult to perform FFA or ICGA in patients with systemic malignancy. Fundus autofluorescence (FAF) captures lipofuscin autofluorescence in retinal pigment epithelium (RPE) cells and provides a noninvasive image detection technique for such patients[5-6]. An ultra-wide-field scanning laser ophthalmoscope offers green wavelength imaging for recording FAF, providing a good tool for detecting peripheral, slight, and early lesions of metastatic choroidal tumor.

Case 1 A 61-year-old woman had complained of decreased vision in her left eye for one month. She had been diagnosed with breast cancer and undergone mastectomy four years earlier. Her best corrected visual acuity (BCVA) was 0.8 in the right eye and 0.1 in the left. The ultra-wide-field retinal image showed a yellowish, irregular, flat mass in the posterior pole of the retina, with an obscure boundary in the left eye and no visible lesion in the right (Figure 1). The ocular B-ultrasound found an irregular flat mass with a medium-to-high reflectivity beneath the posterior pole of the retina in the left eye and no obvious positive sign in the right. FAF found a mixture of hyper- and hypofluorescent dots in the central and inferior midperiphery retina of the left eye. An oval lesion with a mixture of hyper- and hypofluorescence was observed in the inferotemporal retina of the right eye. OCT showed a dome-shaped elevation with a slight subretinal fluid corresponding to the lesion in the left eye and a slight elevation in the right eye. The patient was transferred to a tumor hospital for further treatment.

Case 2 A 35-year-old woman had complained of blurred vision in her right eye for 10d. She had suffered from systemic lupus erythematosus for nine months. Since then, she had taken steroids on doctor's orders. Her BCVA was 1.0 in both eyes. Three lesions were found by the ultra-wide-field retinal image: one pale yellow lesion with white dots in the temporal part of the macula, one in the superonasal quadrant, and one in the inferonasal quadrant of the retina (Figure 2). FAF showed the macular lesion was a hyperfluorescent plaque with central hypofluorescent dots, and the other two were hyperfluorescent in the right eye. A hyperfluorescent lesion was also found in the superonasal quadrant of the left eye. The patient had no previous history of diagnosed tumor. OCT revealed a dome-shaped elevation of the choroidal tumor and subretinal fluid with hyper-reflective foci in the right eye. However, OCT failed to detect the lesion in the left eye because it was too

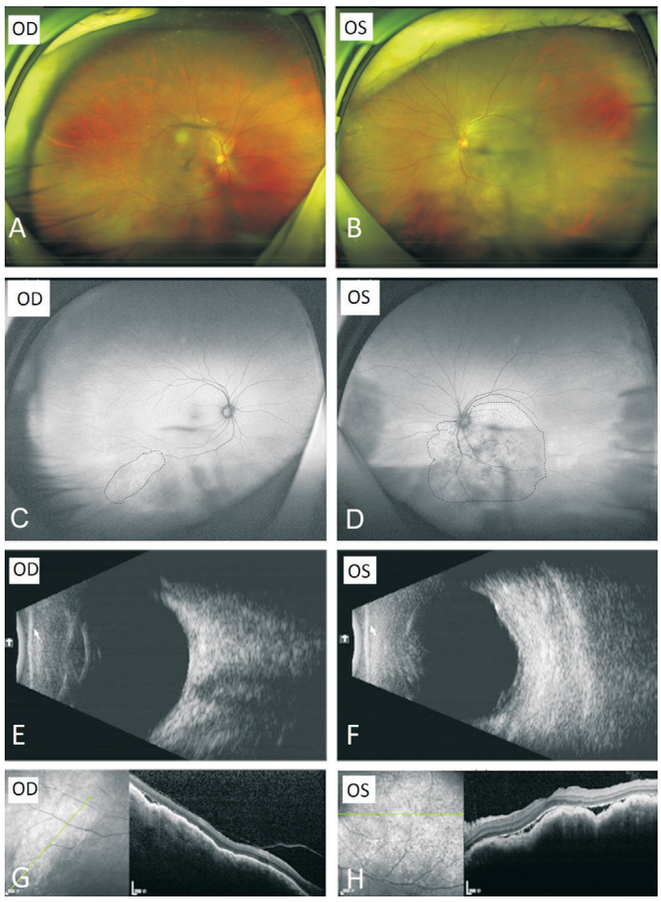

Figure 1 Ophthalmic findings in Case 1 A, B: An ultra-wide-field fundus photograph showed no visible lesions in the right eye (A) and a yellowish, irregular, flat mass with obscure boundary in the posterior pole of the retina in the left eye (B). C, D: FAF found an oval lesion with a mixture of hyper- and hypofluorescence in the inferotemporal retina of the right eye (C) and a mixture of hyper- and hypofluorescent dots in the central and inferior midperiphery retina of the left eye (D). E: B-ultrasound results of the right eye. F: B-ultrasound results of the left eye revealed an irregular flat mass with a medium-to-high reflectivity. G, H: OCT showed a slight elevation of the lesion in the right eye (G) and a dome-shaped elevation with slight subretinal fluid corresponding to the lesion in the left eye (H).

peripheral. Because of these findings, a metastatic choroidal tumor was suspected, and a systemic examination found non-small-cell lung cancer with metastasis to the lymph nodes.

Case 3 A 71-year-old woman was referred for decreased vision with metamorphopsia in her right eye for one month. She had had pulmonary nodules for one year. Her BCVA was 0.2 in the right eye and 1.0 in the left. Two lesions were found in the right eye: one dome-shaped choroidal mass in the posterior pole and one in the inferior retina (Figure 3). The posterior lesion was found to be isoechoic by B-ultrasound. One lesion was also found in the nasal retina of the left eye. The ultra-wide-field FAF showed that the lesions in the right eye were interphase masses with hyper- and hypofluorescence and that the lesion in the left eye was a hyperfluorescent

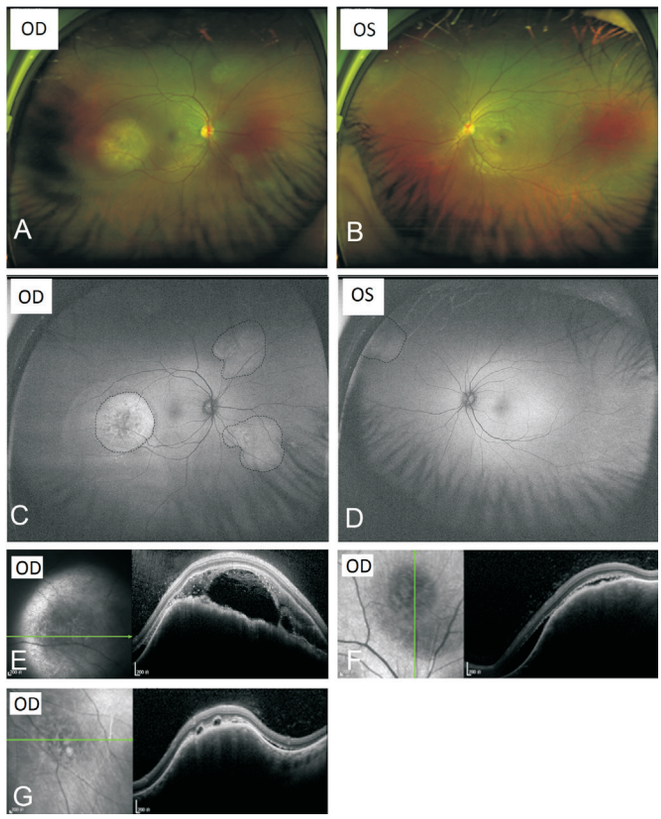

Figure 2 Ophthalmic findings in Case 2 A, B: An ultra-wide-field image found three lesions in the right eye (A) and an obscure lesion in the left eye (B). C: FAF showed the macular lesion was a hyperfluorescent plaque with central hypofluorescent dots, and the other two were hyperfluorescent in the right eye. D: FAF found a hyperfluorescent lesion in the superonasal quadrant of the left eye. E-G: OCT revealed a dome-shaped elevation with subretinal fluid in correspondence to the three lesions in the right eye.

patch. FFA showed hypofluorescence in the early phase and hyperfluorescence with pinpoints and leakage areas on the masses in the late phase. Because of these findings, metastatic choroidal tumor was suspected, and a systemic examination was performed. A pulmonary biopsy confirmed lung adenocarcinoma, and the patient underwent pneumonectomy and chemotherapy.

DISCUSSION

The clinical diagnosis tools for choroidal metastasis have improved over decades, including fundoscopy, US, FFA, ICGA and OCT. FFA and ICGA, particularly ultra-wide-field angiography, play an important role in the differential diagnosis of choroidal tumor. Case 1 and Case 2 patients had positive reaction to sodium fluorescein skin test and therefore could not receive FFA examination. OCT provides useful information for tumor morphology and has the advantage in detecting small choroidal lesions before they are clinical visible[4]. The OCT characteristics of choroidal metastasis include irregular anterior surface of lesion, subretinal fluid and choriocapillaris compression[4].

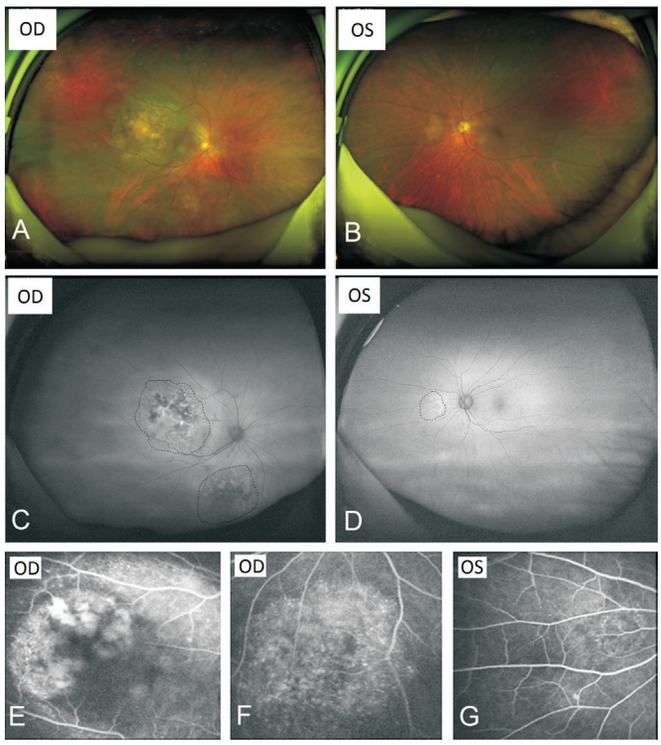

Figure 3 Ophthalmic findings in Case 3 A: An ultra-wide-field image of the right eye showed one dome-shaped choroidal mass in the posterior pole and one in the inferior retina. B: An ultra-wide-field image of the left eye found a lesion in the nasal retina. C, D: Ultra-wide-field FAF revealed that the lesions in the right eye were interphase masses with hyper- and hypofluorescence (C) and that the lesion in the left eye was a hyperfluorescent patch (D). E-G: FFA showed hyperfluorescent in the late phase, with pinpoints and leakage areas on the lesions.

FAF imaging is a rapid, noninvasive technique that can evaluate photoreceptor and RPE cells function[7-8]. It can be used to detect lipofuscin and other fluorophores. Reduced FAF indicates a dysfunction of photoreceptors or RPE cells, whereas increased FAF implies the abnormal accumulation of fluorophores. In normal eye, it shows a diffuse background autofluorescence; normal macula appears a decreased autofluorescene with the intensity being the least at the fovea due to the blockage by luteal pigments such as lutein and zeaxanthin; the optic disc appears dark owing to the absence of autofluorescent material while the retinal vessels show dark due to the absorption of light by the pigments of the blood[9]. It was found that the abnormal accumulation of lipofuscin could be secondary to damaged lysosomal activity with incomplete degeneration[7-8]. In these cases, the flat, early lesions showed uniformly hyperfluorescent in the FAF pattern, and the larger, dome-shaped ones showed hyperfluorescent interphased with hypofluorescence. A possible explanation is that lipofuscin accumulation in the early stage leads to hyperfluorescence and, after a period of time, the dysfunctional photoreceptor or RPE cells cause the decreased autofluorescence. The results were consistent with previous reports[5-7].

The Optos Tx200 ultra-wide-field imaging device can capture up to 200 degrees of retina (approximately 82% of the retinal area) in one image[10]. Patients with peripheral lesion usually have no complaints regarding visual function until the lesions grow and invade the macular area. Also, the lesion in the peripheral retina is easily overlooked with a normal color fundus pattern and can not be readily scanned or focused upon by OCT. The contrast between lesions and normal retina in the FAF pattern is obviously enhanced in comparison to a color photograph pattern. For the patients in Cases 1 and 2, it was easy to find lesions in the symptomatic eyes, but the fellow eyes also had suspected lesions, which could not be readily found in a normal color photograph pattern. The superonasal lesion in the left eye of Case 2 can't be detected by OCT because it was too peripheral. In this circumstance, ultra-wide-field FAF imaging pattern can provide an excellent way to capture lesions in the peripheral retina at a very early stage.

In patients with a known history of primary tumor, it is necessary to detect the fundus to exclude choroidal metastasis. The keys to the prognosis are early detection and early treatment. In patients with multiple suspect choroidal lesions but no previous history of tumor, it is important to conduct a systemic examination, especially of the lung and breast. We can first screen by the FAF pattern of ultra-wide-field imaging and subsequently verify the presumed lesion by OCT.

In conclusion, ultra-wide-field FAF is a valuable noninvasive tool for the early diagnosis for metastatic choroidal tumor, especially for occult and peripheral lesions, and is effective in early choroidal metastasis screening.

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