• Letter to the Editor •

Bilateral choroidal osteoma with unilateral polypoidal choroidal vasculopathy treated with conbercept

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Received: 2019-03-08 Accepted: 2020-02-12

DOI:10.18240/ijo.2020.06.23

Citation: Huang YM, Zhang L, Liang J, Yuan RD. Bilateral choroidal osteoma with unilateral polypoidal choroidal vasculopathy treated with conbercept. *Int J Ophthalmol* 2020;13(6):1009-1012

Dear Editor,

Chorodial osteoma (CO) is a rare choroidal tumor characterized by the presence of mature bone tissue predominantly in the juxtapapillary or macular region. CO mostly affects young healthy females in the second or third decades of life. It is unilateral in approximately 80% of cases[1], as patients have no obvious visual symptoms during the early stage of CO, and the growth of CO is slow. CO patients usually visit the eye clinic during the later stages of CO and have poor vision. Gradual decline in vision in CO patients is related to changes in retinal pigment epithelium (RPE) and photoreceptor atrophy. Choroidal neovascularization (CNV) and the resultant subretinal fluid and hemorrhage are the most frequent causes of sudden vision loss in CO[2]. We report a rare case of bilateral CO with unilateral polypoidal choroidal vasculopathy (PCV) in a middle-aged male.

CASE REPORT

A 51-year-old man was referred to the eye clinic due to sudden decline in his left eye vision. The best corrected visual acuity (BCVA) was 20/400 in the right eye and 20/200 in the left eye. The anterior segments in both eyes were unremarkable. Ophthalmoscopic examinations revealed extensive yellowish-white elevated choroidal lesions with well-defined, geographic borders located and adjusted to the optic disc in both eyes (Figure 1A, 1B). The choroidal lesion involved the macular of the right eye and was located adjacent to the macular of the left eye with submacular hemorrhage. B-scan of both eyes showed very high reflectivity on the surface with shadowing behind (Figure 1C, 1D). Optical coherence tomography (OCT) showed elevated fovea, irregular RPE, and neural retina in the right eye (Figure 1E). Submacular hemorrhage and hemorrhagic pigment epithelium detachment (PED) were observed in the left eye (Figure 1F). Fundus fluorescein angiography (FFA) revealed early patchy hyperfluorescence with late staining of the choroidal lesions (Figure 1G, 1H). In the left eye, an area of blocked fluorescence was observed in the macular area, which was suggestive of submacular hemorrhage without any leakage (Figure 1H). The patient had suffered a sudden decline in vision in the right eye twenty years ago, but had no medical record. His past medical and family histories were inconsequential. He was diagnosed with bilateral CO with suspected CNV in the left eye.

The patient underwent three intravitreal conbercept (Chengdu Kanghong Biotechnologies Co. Ltd., China) injections in the left eye. At 1-month follow up after the first injection, the BCVA of his left eye was elevated to 20/100, indicating an obvious resolution of submacular hemorrhage (Figure 2A, 2B). The mean central foveal thickness decreased from 552 to 106 μm and the hemorrhagic PED decreased (Figure 2D, 2E). FFA showed two dotted hyperfluorescence at the location of hemorrhagic PED (Figure 2H). Further indocyanine green angiography (ICGA) was performed. Characteristic dotted hyperfluorescence, branching vascular network, aneurysmal dilations, and polyps were observed in the left eye (Figure 2J-2L), which challenged our initial diagnosis of CNV associated with CO. The diagnosis should be bilateral CO with PCV in the left eye. The patient underwent two more conbercept injections. At 1-month follow up after the third injection, the BCVA of the left eye was 20/50, indicating an obvious resolution of subretinal hemorrhage on OCT (Figure 2F) and no leakage on FFA (Figure 2I). ICGA revealed partial regression of polyps and persistence of branching vascular networks (Figure 2M, 2N).

The patient's left eye remained stable for approximately 28mo in terms of vision after three consecutive treatments with conbercept. However, he subsequently complained of a sudden decline in vision. The visual acuity of the left eye was 20/200. Fundus photograph revealed expansion of the osteoma and changes in RPE. Additionally, deep retinal hemorrhage was observed

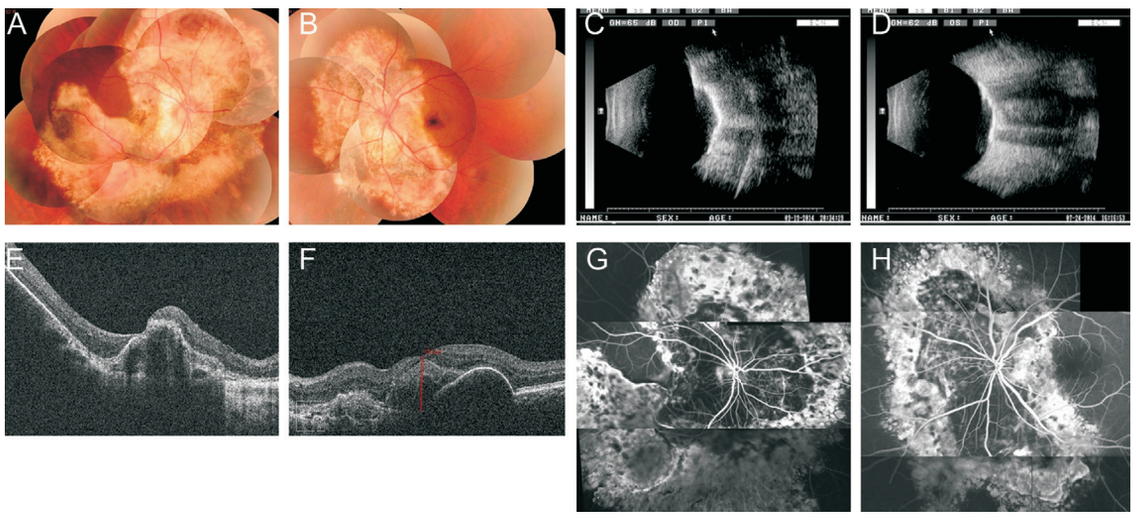

Figure 1 Color photos, B-scan, OCT and fluorescein angiography of both eyes at the first visit Color photos showing an orangish-yellow lesion in the macular area of the right eye (A) and submacular hemorrhage in the left eye (B). B-scan of both the right eye (C) and the left eye (D) showed very high reflectivity on the surface with shadowing behind. OCT showed elevated fovea in the right eye (E), and submacular hemorrhage and hemorrhagic PED in the left eye (F). Fluorescein angiography of the right (G) and left (H) eyes revealed early patchy hyperfluorescence with late staining of the choroidal lesions. Note the area of blocked fluorescence in the macular area suggestive of submacular hemorrhage without any leakage in the left eye (H).

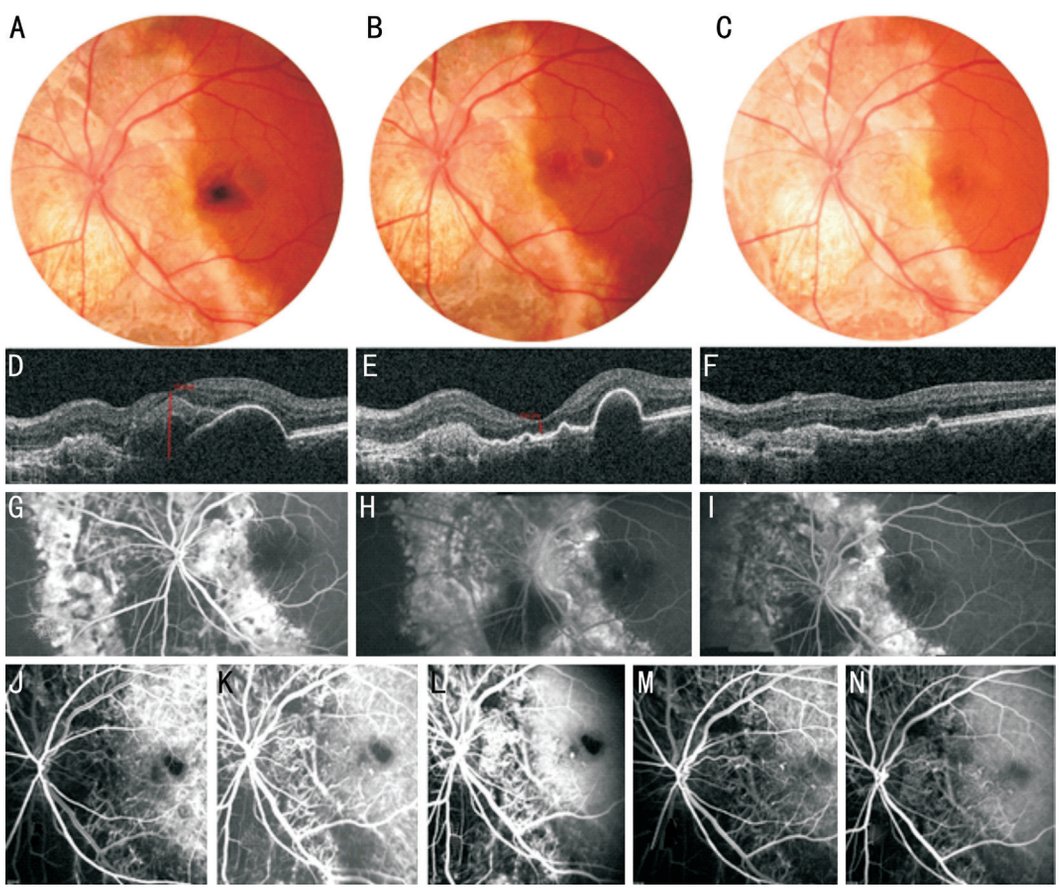

Figure 2 Left eye before (A, D, G, J-L), after the first injection (B, E, H) and after the third injection (C, F, I, M, N) of conbercept during the first visit Color photos showed obvious resolution of submacular hemorrhage after the injection (B, C). At the same time, after the first injection, the mean central foveal thickness and the hemorrhagic PED decreased on OCT (E). OCT showed total regression of exudation after the third injection of conbercept (F). FFA showed two dotted hyperfluorescence at the location of hemorrhagic PED after the injection (H). ICGA showed characteristic dotted hyperfluorescence, branching vascular network, aneurysmal dilations and polyps (J-L). After another two injections, the dotted hyperfluorescence disappeared (I), the polyps partially regressed, but the vascular networks remained (M, N).

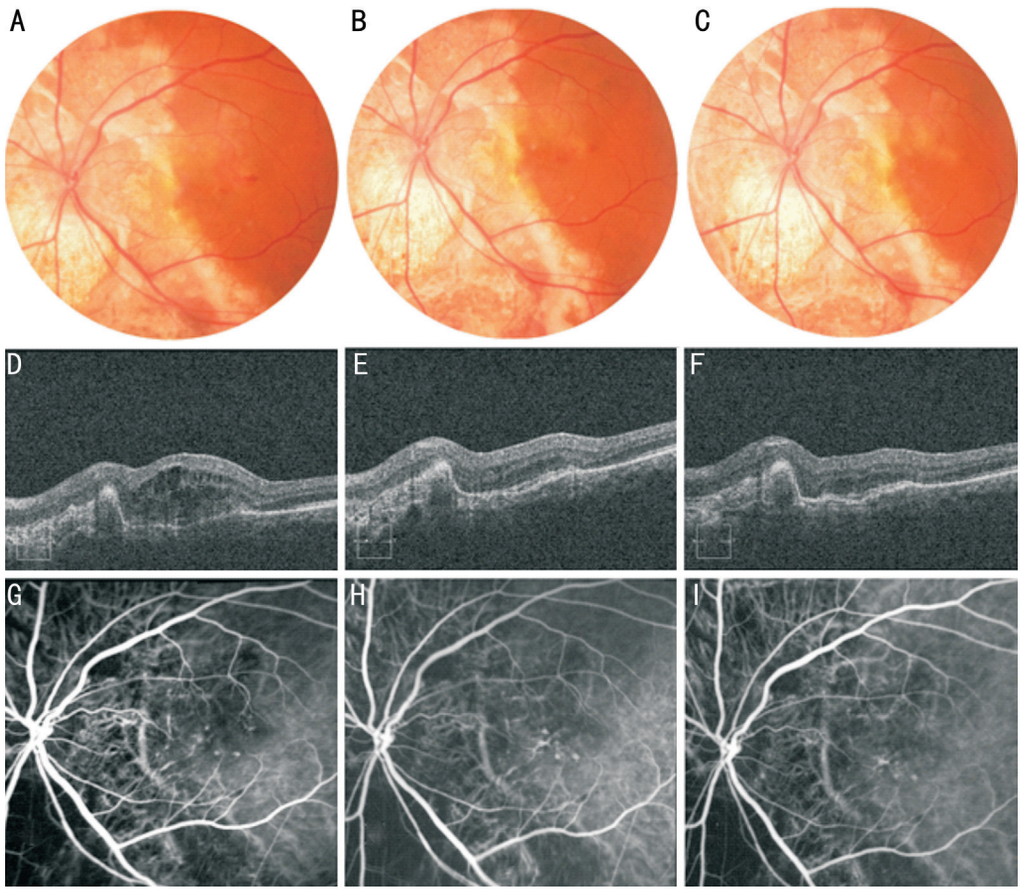

Figure 3 Left eye before (A, D, G), after the first injection (B, E, H) and after the third injection (C, F, I) of conbercept in the second visit Color photos showed expansion of the osteoma, changes in RPE and two deep retinal hemorrhages (A). At the same time, OCT revealed obvious macula edema (D) and ICGA revealed recurrence of polyps (G). After the first injection of conbercept, obvious resolution of macular edema (E) and hemorrhage absorption were observed (B). ICGA showed partial regression of the polyps (H). After the third injection, no further improvement was seen in OCT (F). ICGA revealed partial regression of polyps and branching of vascular networks (I).

adjacent to the fovea (Figure 3A). Further examinations showed obvious macular edema (Figure 3D) and recurrence of polyps (Figure 3G). He underwent additional three consecutive treatments with conbercept in the left eye. He responded very well to the first injection in terms of OCT image finding and showed obvious resolution of macular edema (Figure 3E) and hemorrhage absorption (Figure 3B). Vision acuity was elevated to 20/125. ICGA showed partial regression of the polyps. Another two injections of conbercept were given to the patient in the following two months. At 1-month follow up after the third injection, vision acuity was 20/100. However, no further improvement was seen in OCT (Figure 3F). ICGA revealed partial regression of polyps and branching vascular networks (Figure 3I).

DISCUSSION

CO is a rare, benign tumor, first reported by Gass *et al*[3] in 1978. CNV occurs in 31%-47% of patients affected by CO within 10y and is the major cause of sudden visual loss[4]. In this case of bilateral CO, no leakage was observed on FFA before treatment. According to previous literature, CNV might be the reason of sudden vision loss in the left eye. At 1-month follow up after the first injection of conbercept, FFA showed two dotted hyperfluorescence temporal to the macula fovea. Further ICGA revealed characteristic signs of PCV. Thus, the exact cause of submacular hemorrhage in the left eye of the patient is PCV instead of CNV. Upon review of the literature, we found only one case of bilateral CO with bilateral PCV in a middle-aged Japanese woman, reported by Fine *et al*[5]. Together, these two cases highlight the need for ICGA when CO presents with submacular hemorrhage. The hemorrhage could block the choroidal lesions beneath it in FFA. This might lead to the misdiagnosis of PCV associated with CO. In this case, further ICGA should be performed to achieve a correct diagnosis. The intrinsic nature of CO is cancellous bone, which lies between an altered choriocapillaris and the outer choroidal layers. Tumor growth requires abundant oxygen for the generation of branching vascular networks and polyps. The most significant feature of polyps is hemorrhage. If the barrier function of the RPE remains normal, it manifests as reddish PED. This was the case at the patient's first visit. If the function of RPE is

affected by the tumor, as was the case in the second visit, the hemorrhage might be in the neural retina.

The proper management of CNV associated with CO is still debated. Traditional therapies such as laser photocoagulation, surgical removal of CNV, transpupillary thermotherapy (TTT), and photodynamic therapy (PDT) have showed limited success for CNV associated with CO[4]. Recently, increasing reports showed that intravitreal injection of antivascular endothelial growth factor (anti-VEGF) antibodies such as bevacizumab and ranibizumab was effective for CNV secondary to CO[6]. In this case, although we were not sure whether it was CNV causing the hemorrhage, intravitreal injections of conbercept were used, which showed remarkable effectiveness. Conbercept is a naturally made recombinant human VEGF receptor-Fc fusion protein in China which has shown excellent effects in the treatment of wet-AMD. In the other case of bilateral PCV associated with CO reported by Fine *et al*[5], they considered that the natural course of PCV is related to a better visual prognosis than classic CNV, and PCV responds favorably to photodynamic therapy.

The patient was referred to the eye clinic due to a sudden decline in vision in the left eye. In addition, his right eye had also suffered a sudden decline in vision twenty years ago. The patient ignored the decline in vision; thus, there was no medical record regarding this incident. Fundus examination showed that the CO involved the macula of the right eye, and obvious RPE proliferation and accumulation were also noted. OCT showed elevated fovea, irregular RPE, and neural retina in the right eye. FFA showed no leakage in the macula. We wanted to determine the cause behind the sudden decline in vision and the structural change of the macula in the right eye. More specifically, we want to determine whether these changes were caused by CNV or PCV. The major cause of CO related vision decline includes gradual neural retinal atrophy and CNV. Gradual neural retinal atrophy resulting from RPE changes usually leads to a gradual decline in vision. Submacular hemorrhage associated with CNV or PCV usually leads to sudden vision decline. Elevated fovea, irregular RPE, and neural retina in the right eye are signs of untreated submacular hemorrhage associated with CNV or PCV. Thus, CNV or PCV might have been potential reasons of sudden vision loss in the right eye 20 years ago.

With the progression of the osteoma and repeated macular edema, the patient's left eye could have ended up in a state similar to that of the right eye. Anti-VEGF treatments could effectively improve the patients' visual acuity and delay the progression of disease; however, they could not change the patient outcome.

ACKNOWLEDGEMENTS

Foundation: Supported by the National Basic Research of China (No.81600758).

Conflicts of Interest: Huang YM, None; **Zhang L,** None; **Liang J,** None; **Yuan RD,** None.

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