Article A case of fundus albipunctatus in both eyes

Jianbo Mao
Wenzhou Medical University
Jingjing Lin
Wenzhou Medical University
Lijun Shen (ljshenysg@163.com)
Wenzhou Medical University Eye Hospital

Case report

Keywords: Fundus albipunctatus, optical coherence tomography, ERG

Posted Date: February 21st, 2019

DOI: https://doi.org/10.21203/rs.2.370/v1

Abstract

Background This case was first recorded in fundus albipunctatus with multimodal imaging (optical coherence tomography(OCT), angio-OCT, multicolor-OCT, fluorescence angiography), vision field and electrophysiological recordings. Case presentation The authors present a 52-year-old Chinese female who suffered night blindness for years. With multimodal images, the fundus images and full-field electroretinography after standard and prolonged dark adaption were consistent with fundus albipunctatus. Disease targeted gene test was not performed. Other imaging method seems to have minimal changes. Conclusions It is an observational case report about characteristic ophthalmic findings in fundus albipunctatus.

Background

Fundus albipunctatus (FA) is a rare autosomal recessive macular dystrophy, characterized by a myriad of numerous small white-yellow dots at the level of the pigment epithelium, sprinkled about the posterior pole and midperiphery of the retina. [1,2] FA patients suffer the night-blindness, with little visual acuity or visual field or color vision defect. The electrophysiological responses present that FA patient needs a long dark-adaptation period to obtain the maximum scotopic responses. With time, FA and its manifestations may progress. FA is caused mostly by mutations in the RDH5 gene, which encode the enzyme called 11-cis retinal dehydrogenase in the visual cycle. [3.4]

This case was aimed to display the fundus albipunctatus with multimodal imaging (optical coherence tomography(OCT), angio-OCT, multicolor-OCT, fluorescence angiography), vision field and electrophysiological recordings.

Case Presentation

Female patient, 52-year-old, has kept complaining about the night-blindness since childhood. Same symptoms were not found in her family. The best corrected vacuity was 20/25 in both eyes, with -3.00 DS in the left eye and -2.50DS/-0.50DC X110 in the right eye. Intraocular pressure was within the normal field. Through the slit-light examination, no positive sign was found. Fundus examination showed with well-defined optic disc (C/D ratio was about 0.3) and vessels, flattened macular area, no obvious pigmentation, while widely diffused white dots. The margin of the dots began from the nasal optic disc, and the temporal side outside the arch of the blood vessels, then reached the equator of the retina. These dots were detected symmetrical distribution in both eyes with almost same size. (Fig. 1) OCT revealed that in the dots lesion, multiple tiny hump-like substances with high reflective, some of which had ruptured the Ellipsoid zone, were found at the level of pigment epithelium. (Fig. 2) Multicolor-OCT revealed the distribution of the white, white and dark lesions in blue, green and red reflectance respectively, corresponded roughly to color photograph. (Fig. 3) The central 30° visual field in both eyes showed minor and local periphery visual defect, which may be caused by cataract. (Fig. 4) Angio-OCT in 6X6 mm field has not presented abnormal structure sign. (Fig. 5) Fluorescence angiography has showed

diffused hyper-fluorescence, some may correspond to the dots, and low background fluorescence, without leakage. (Fig. 6) Electroretinogram(ERG) showed in dark-adapted ERG the amplitude of a- and b-waves remarkably declined (almost no responses). In the light-adapted ERG white 30 Hz flicker showed reduced amplitudes as well. The scotopic ERG recorded after a long (3-hour) dark-adapted period in the left eye showed markedly improved rod-specific and combined ERG. (Fig. 7)

Discussion And Conclusions

FA, as a special kind of congenital stationary night blindness (CSNB) [5], characterized by its distinct fundus, dark-adaptation curve and ERG responses. As to its pathogen, present studies have focused on the Genes. Mostly, mutations in the RDH5 gene [6] (11-cis retinol dehydrogenase) affected retinoid metabolism (11-cis retinol dehydrogenase) in the visual cycle, leading to FA features. However, other genes mutation had been reported, as the RLBP1 gene [7] (retinaldehyde binding protein 1) and RPE65 gene [8] (RPE-specific protein). 11-cis retinol dehydrogenase, produced in the smooth endoplasmic reticulum of the pigment epithelium cells, has revealed great importance in the visual cycle and the production and accumulation of lipofuscin in the pigment epithelium cells. [9] So, the impairment of pigment epithelium cells accounts for not only the lesion position, but also the dark blindness symptoms. Strictly, FA is not totally stationary. Resent reports had detected the dysfunction of cone cells and the disruption of Ellipsoid zone in OCT. [10,11] Nonetheless, the autosomal dominant inheritance was reported before. However, in this report the family refused to perform genetic test. [12]

The most confusing differential diagnosis of FA is retinitis punctata albescens. In 1910, Lauber [1] firstly named FA and differentiate it from retinitis punctata albescens. The latter one, though shows similar dark blindness symptoms and white dots, has narrowing visual field, Retinitis Pigmentosa signs (pigmentation with bone-cells like, thin retinal vessels, disc with yellow-wax like) in the fundus, no recoverable ERG responses, and progressive visual impairment in both dark and light. The main points of FA diagnosis and its differential diagnosis were mostly found out by analysis of specific ophthalmic features. The psychological characteristics of the disease shows a dark adaptation delay—abnormal ERG, and declined amplitudes of cone and rod ERG, which would back to normal after 30-40 minutes. [13] Significant decline, but after a long enough period of dark adaptation can be to return to normal. In this report, we have presented multiple ophthalmic examinations to show the figure of FA more in detail. Besides traditional examinations (visual field, ERG, dark-adaption test, fluorescence angiography and OCT), we further performed multicolor-OCT and angio-OCT. As the pathology of FA goes, there were little vascular change sign in the macular area. However, multicolor-OCT revealed abnormal layers of retina enface, representing the accumulation of lipofuscin in retinal pigment epithelium cells, which corresponded to the hyperreflective lesions on OCT. The white dots in the fundus varied with age and genotype. [14] With time, it may fade away in patients with FA or after uveitis. Further observations were not included in this report.

Abbreviations

Fundus albipunctatus	FA
Optical coherence tomography	OCT
Electroretinogram	ERG

Declarations

Ethics approval and consent to participate: Not applicable.

Consent for publication：Written informed consent was obtained from the patient for publication of this Case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

Availability of data and material：Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

Competing interests: The authors declare that they have no competing interests.

Funding: The authors declare that there is no funding in this case report.

Authors' contributions: JJ L: collected and wrote the first manuscript; JB M: organized and revised the manuscript; LJ S: a major contributor in writing and revising the manuscript. All authors read and approved the final manuscript.

Acknowledgements: Not applicable.

References

1. Lauber H. Die sogenannte Retinitis punctata albescens. Klin Monatsbl Augenheilkd. 1910; 48(1): 133-148.
2. Marmor MF. Long-term follow-up of the physiologic abnormalities and fundus changes in fundus albipunctatus. Ophthalmology. 1990; 97(3): 380-384.
3. Sergouniotis PI, Sohn EH, Li Z, et al. Phenotypic variability in RDH5 retinopathy (Fundus Albipunctatus). Ophthalmology. 2011; 118(8): 1661-1670.
4. Skorczyk-Werner A, Pawłowski P, Michalczuk M, et al. Fundus albipunctatus: review of the literature and report of a novel RDH5 gene mutation affecting the invariant tyrosine. J Appl Genet. 2015; 56(3): 317-327.
5. Sidiki SS，Hamihon R，Dutton GN，Fear of the dark in children：is stationary night blindness the cause? BMJ. 2003; 326: 211-212
6. Yamamoto H, Simon A, Eriksson U, et al. Mutations in the gene encoding 11-cis retinol dehydrogenase cause delayed dark adaptation and fundus albipunctatus. Nat Genet. 1999 Jun;

22(2): 188-91.

7. Naz S, Ali S, Riazuddin SA, et al. Husnain T,Macdonald IM, Sieving PA, Hejtmancik JF, Riazuddin S. Mutations in RLBP1 associated with fundus albipunctatus in consanguineous Pakistani families. Br J Ophthalmol. 2011;95: 1019–1024.
8. Schatz P, PreisingM, Lorenz B, et al. Fundus albipunctatus associated with compound heterozygous mutations in RPE65. Ophthalmology. 2011; 118: 888–894.
9. Driessen CA,Winkens HJ, Hoffmann K, et al. Vugt AH,VanHooser JP,Wieringa BE, DeutmanAF, Palczewski K, Ruether K, Janssen JJ. Disruption of the 11-cis-retinol dehydrogenase gene leads to accumulation of cis-retinols and cis-retinyl esters. Mol Cell Biol. 2000; 20: 4275–4287.
10. Querques G, Carrillo P, Querques L, et al. High-definition optical coherence tomographic visualization of photoreceptor layer and retinal flecks in fundus albipunctatus associated with cone dystrophy. Arch Ophthalmol. 2009; 127(5): 703-706.
11. Makiyama Y, Ooto S, Hangai M, et al. Cone abnormalities in fundus albipunctatus associated with RDH5 mutations assessed using adaptive optics scanning laser ophthalmoscopy. Am J Ophthalmol. 2014; 157(3): 558-570.
12. Kranias G, Augsburger JJ, Raymond LA. Resolution of night blindness in fundus albipunctatus. Ann Ophthalmol. 1982; 13: 871–874.
13. Wang NK, Chuang LH, Lai CC, et.al. Multimodal fundus imaging in fundus albipunctatus with RDH5 mutation: a newly identified compound eterozygous mutation and review of the literature. Doc Ophthalmol. 2012; 125: 51–62.
14. Sergouniotis PI1, Sohn EH, Li Z, et al. Phenotypic Variability in RDH5 Retinopathy (Fundus Albipunctatus). Ophthalmology. 2011; 118(8): 1661-70.

Figures

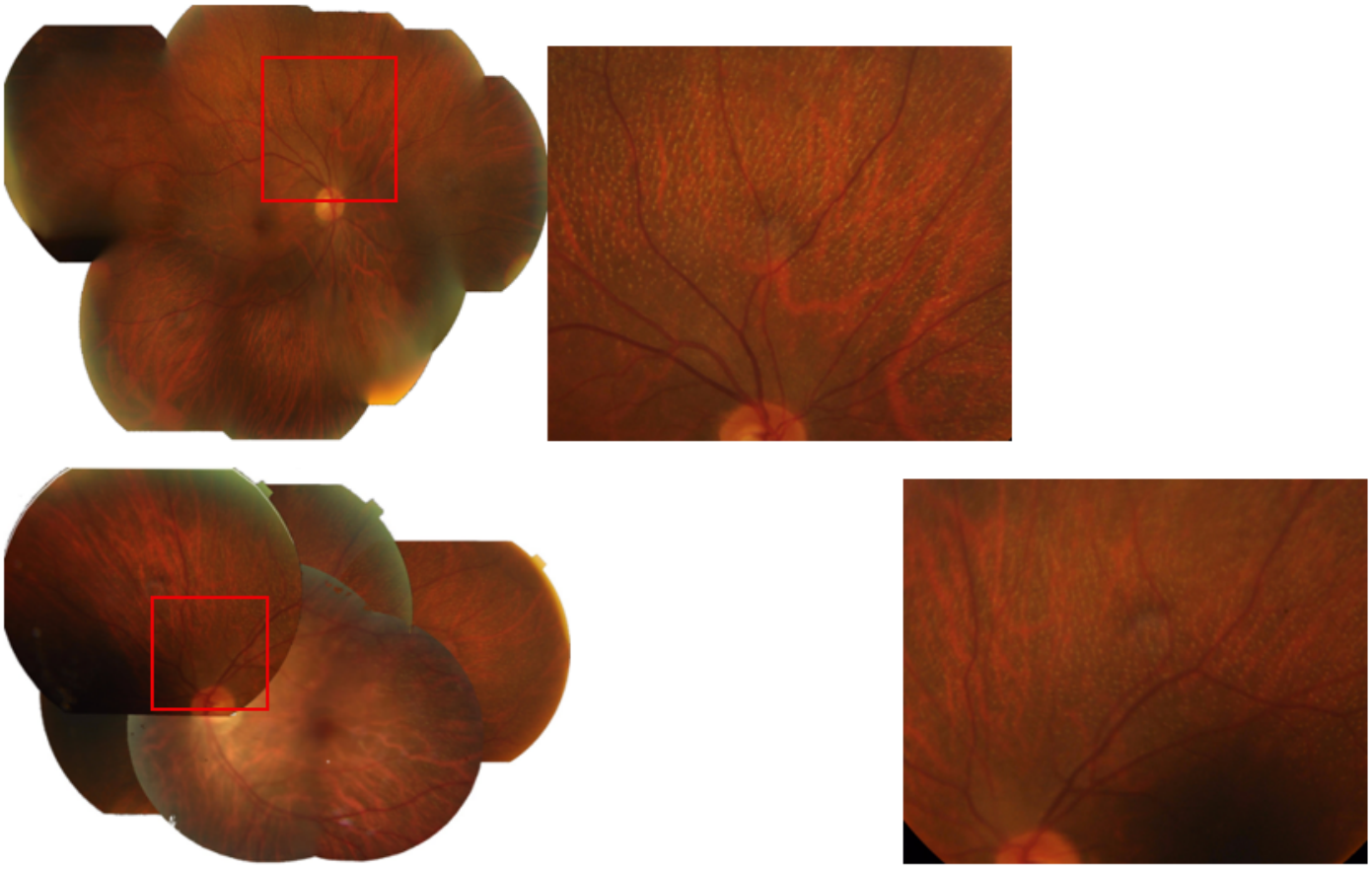

Figure 1

Fundus color photograph. Superior photo: OD; Interior photo: Left eye. Superior right and left photo were local enlarged of the right eye and left eye (red frame). Multiple white dots were revealed at the periphery area.

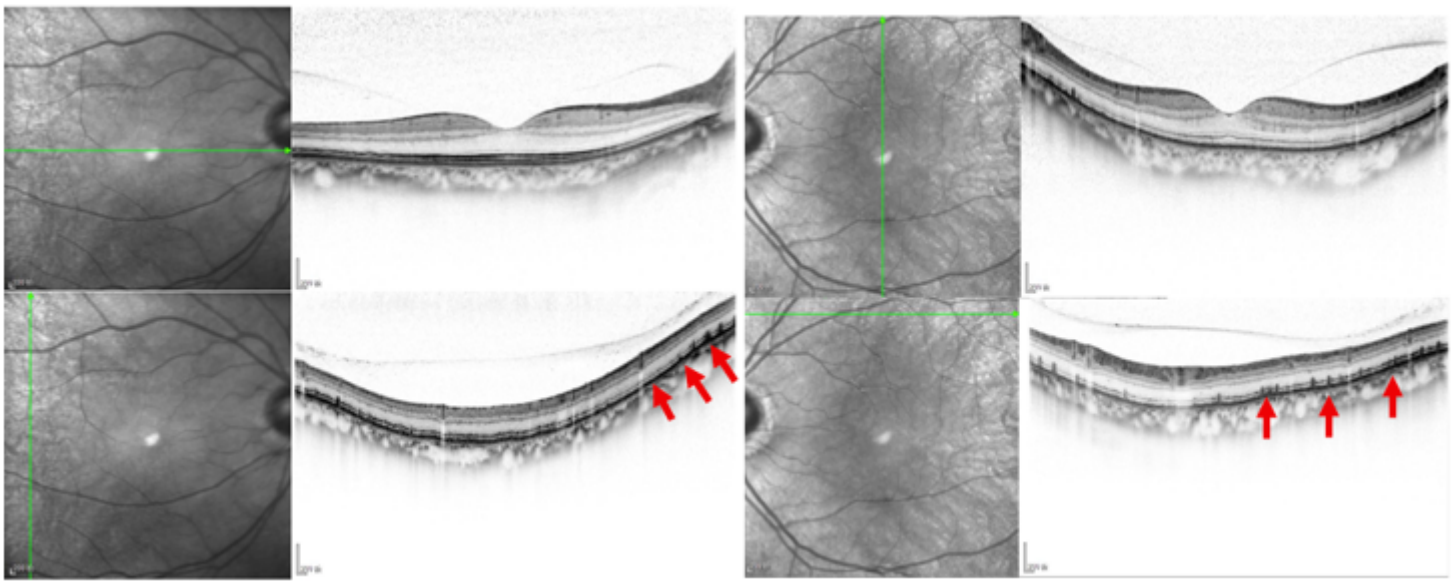

Figure 2

Optical coherence tomography. In the both eyes, macular retina structure were normal (superior right and superior left). Outside the macular area (interior right and interior left), at the level of pigment epithelium, there were some hump-like substances with high reflective, some of which had ruptured the Ellipsoid zone (red arrow).

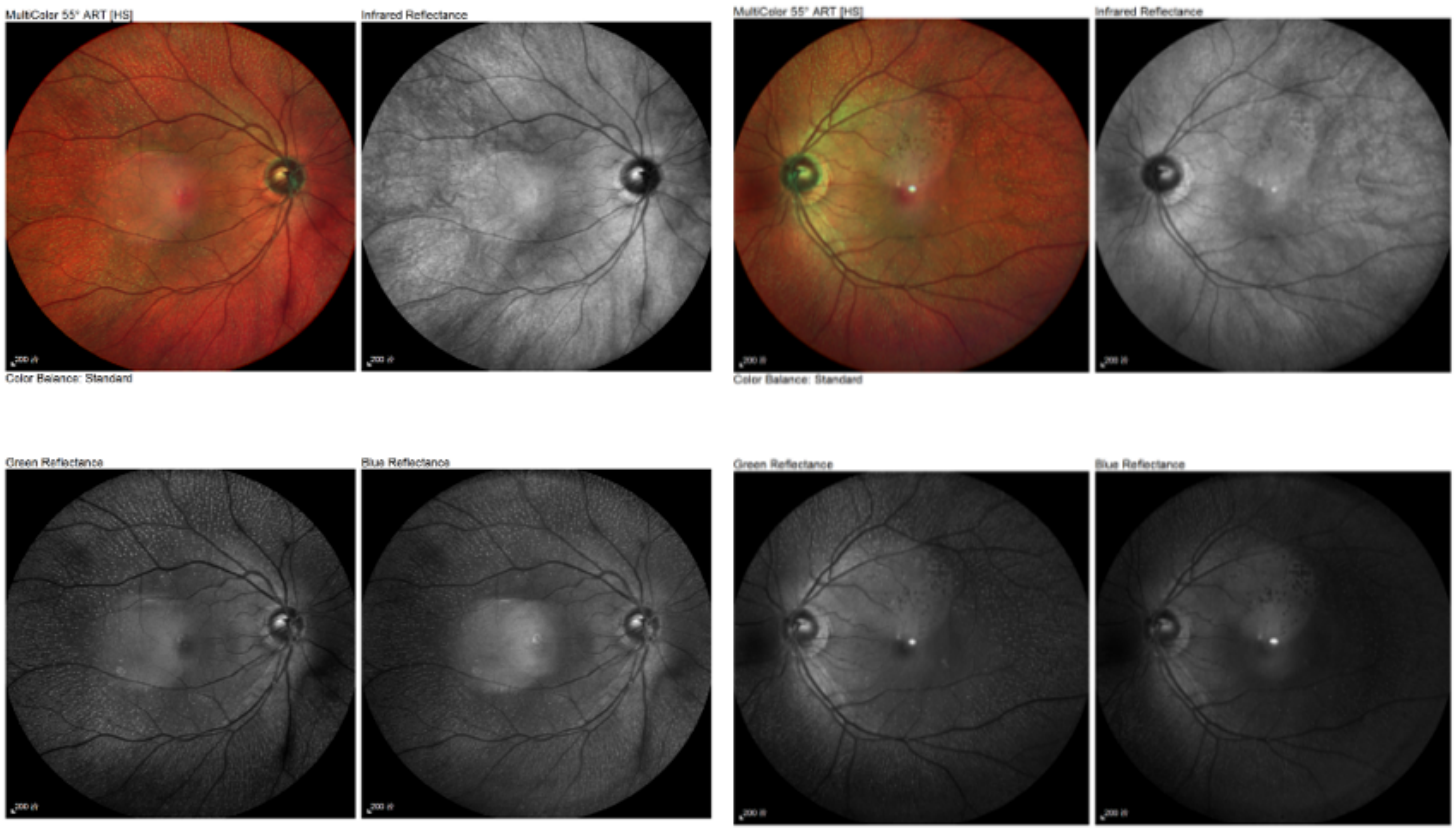

Figure 3

Multicolor-optical coherence tomography. Left photo: OD; Right photo: OS. Multicolor-OCT revealed the distribution of the white, white and dark lesions in blue, green and red reflectance respectively, corresponded roughly to color photograph.

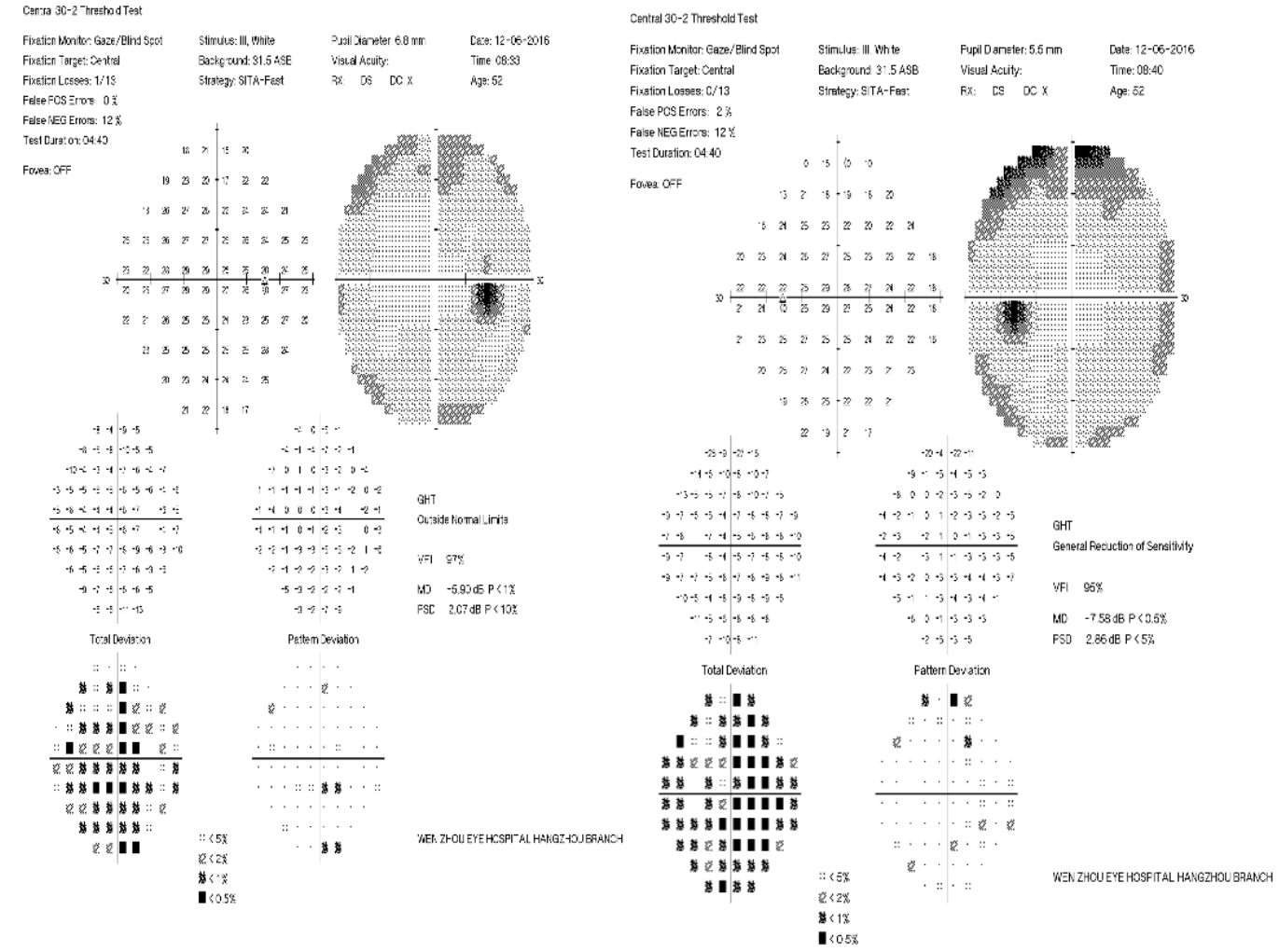

Figure 4

The central 30° visual field. Left photo: OD; Right photo: OS. The central 30° visual field in both eyes showed minor and local periphery visual defect.

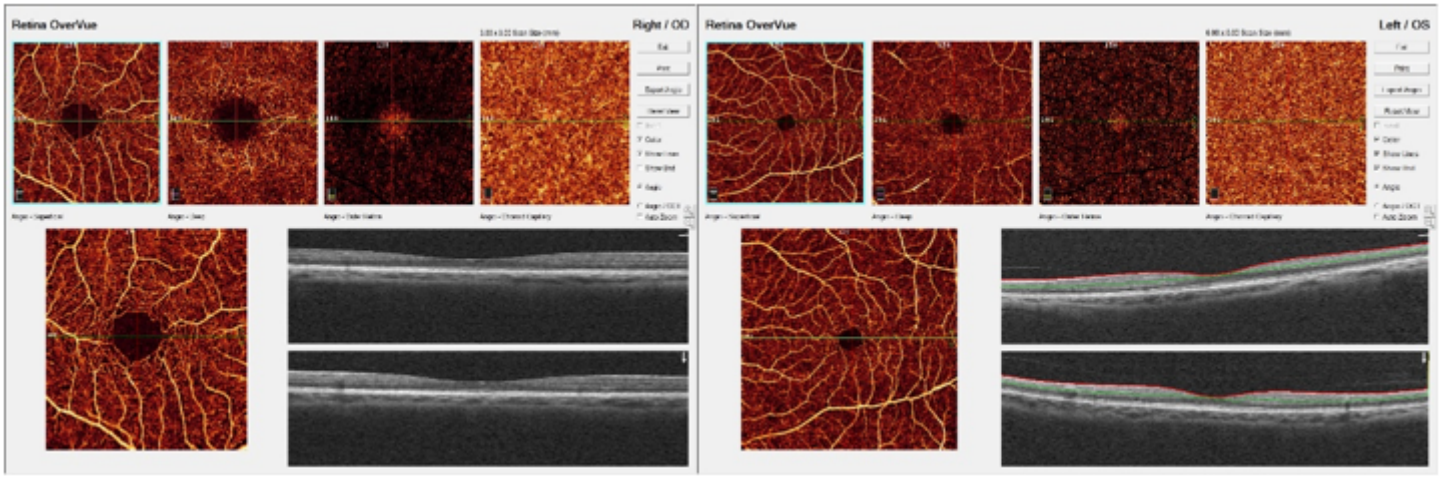

Figure 5

Angio-OCT in 6X6 mm field. Left photo: OD; Right photo: OS. Angio-OCT in 6X6 mm field revealed little changes in both eyes.

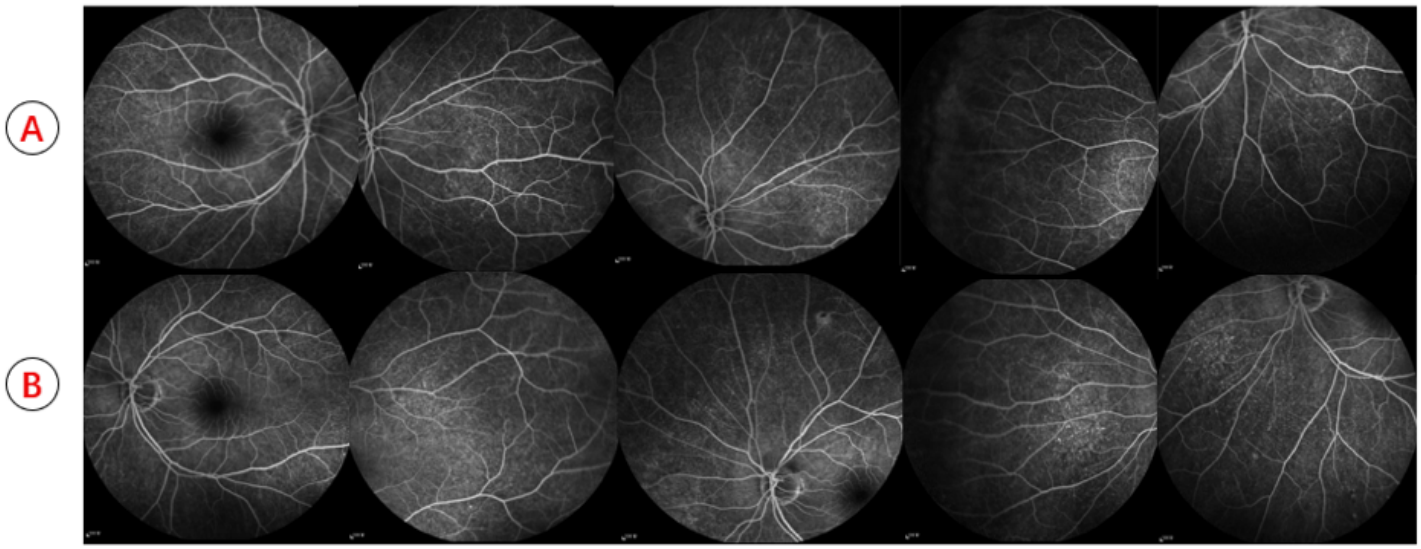

Figure 6

Fluorescence angiography (in the midturn). A: OD; B: OS. In both eyes, fluorescence angiography showed diffused minor hyper-fluoresces, and low background fluorescence, without leakage.

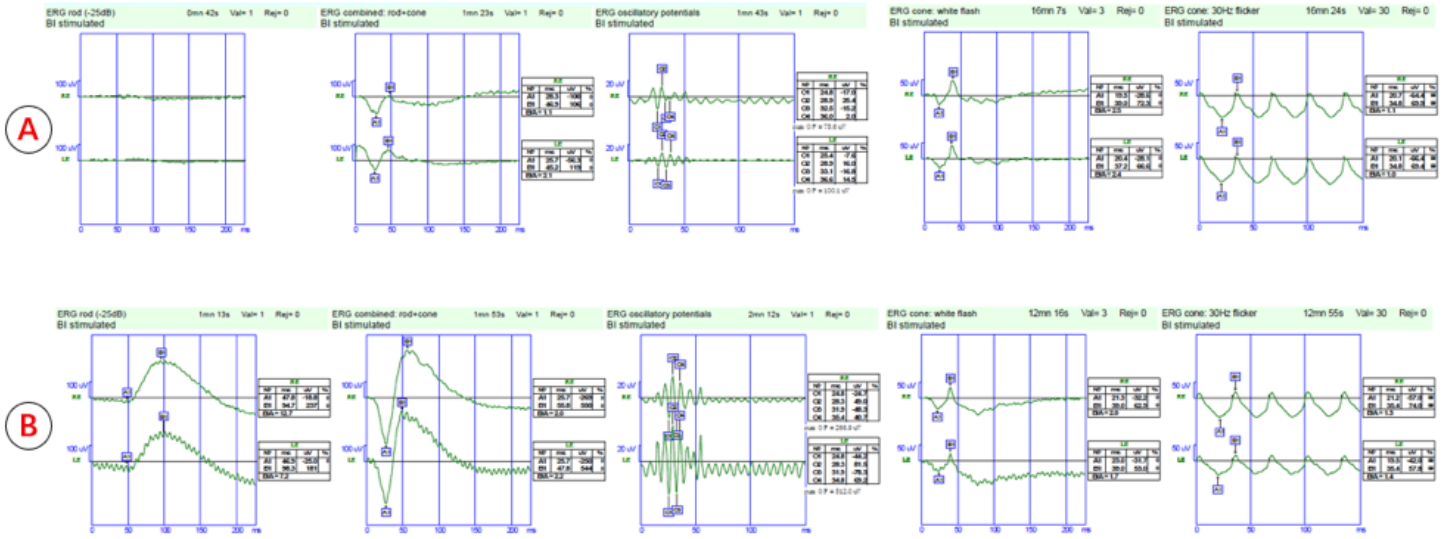

Figure 7

Electroretinogram. A: ERG- first time; B: ERG-second time, after 3 hours. In the first time, dark-adapted ERG, combined ERG, oscillatory potentials ERG: the amplitude of a-, b- and o- waves were remarkably declined (a-, and b- waves almost no responses). light-adapted ERG with 30 Hz flicker: minor reduced amplitudes of b- waves. Only cone-relied ERG: almost normal. In the second time, which was after 3 hours, the ERG recorded markedly improved rod-specific and combined ERG.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- CAREchecklistChinese2013.pdf
- CAREchecklistEnglish20131.pdf