


Case Report

Low-Level Laser Therapy Improves Visual Function in Occult Macular Dystrophy

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Abstract

Background: Occult macular dystrophy (OMD) is a binocular hereditary macular disease caused by Retinitis pigmentosa 1-like 1 (RP1L1) gene variation. Currently, there is no effective treatment for OMD. Low-level laser therapy (LLLT) is an innovative treatment for ophthalmological conditions by stimulate mitochondrial function. In this paper, we report a case of OMD and the effects of LLLT on this patient. **Case Presentation:** A 20-year-old man was diagnosed with OMD by genetic diagnosis. At presentation, the best corrected visual acuity (BCVA) was 3 letters (ETDRS) in his right eye (RE) and 12 letters in his left eye (LE). Spectral domain-optical coherence tomography (SD-OCT) revealed a blurred Elipsoid zone (EZ) and interdigitation zone (IZ) at the macular area of both eyes. The multifocal electroretinogram (MF-ERG) response amplitudes were reduced, and physiological blind spots were expanded in both eyes detected by perimetry. The full field electroretinogram (FF-ERG) examination, fluorescein angiograms (FFA), and fundus examination were normal. After an adequate evaluation of the safety of LLLT and with the patient's consent, the patient was treated with LLLT for 4 weeks (twice a day). For LLLT, the fundus was irradiated through the cornea for 180 sec with laser light (wavelength 650nm; average power 2.0 ± 0.5 mW). The BCVA increased to 20 letters in both eyes, and the MF-ERG amplitude and vision sensitivity detected by the perimeter increased too. However, the morphology of the EZ and IZ measured by SD-OCT didn't change. **Conclusions:** LLLT was shown to improve and maintain vision in a patient with OMD and may have contributed to improving the function of photoreceptor cells.

Keywords

Occult Macular Dystrophy, Low-Level Laser Therapy, Retinopathy, Case Report

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1. Introduction

Occult macular dystrophy (OMD) is a binocular hereditary macular disease that occurs in people about 20 years old and is characterized by normal fundus and progressive loss of vision [1]. In addition to the visual function decline, other abnormalities of OMD including a decrease in multifocal electroretinogram (MF-ERG) amplitude and blurred of the Ellipsoid zone (EZ) and interdigitation zone (IZ) as measured by Spectral domain-optical coherence tomography (SD-OCT), whereas fluorescence fundus angiography (FFA) and full-field electroretinogram (FF-ERG) often show normal results [2-6].

OMD is mainly caused by a heterozygous variant of the Retinitis pigmentosa 1-like 1 (RP1L1) gene, like the retinitis pigmentosa (RP) gene variant [7-9]. RP1L1 protein exists in cones and rods and may be involved in maintaining photoreceptor cell morphology and function [10, 11]. Currently, no effective treatment is known for the OMD.

Low-level laser therapy (LLLT) using red to near-infrared (NIR) light is an innovative treatment for a wide range of conditions. Red/NIR light can stimulate complex IV of the mitochondrial respiratory chain (cytochrome c oxidase, CCO) and increase ATP synthesis [12-17]. Recently, LLLT was

shown to improve visual function in patients with age-related macular degeneration (AMD), diabetic macular edema (DME), Amblyopia, and Retinitis pigmentosa (RP) [18-21]. Based on these findings, we describe the effects of LLLT in a patient with OMD.

2. Case Presentation

A 20-year-old Chinese man, without any prior significant medical history, referred to our department, complaining for visual deterioration for 5 years. At presentation he underwent a complement ophthalmological examination. Best corrected visual acuity (BCVA) was 3 letters (ETDRS) in his right eye (RE) and 12 letters in his left eye (LE), and multiple visual acuity examinations in other departments were lower than 12 letters of both eyes before referred to our department. Slit lamp examination did not identify any abnormalities in the anterior or posterior segments in both eyes. His intraocular pressure was normal bilaterally. Spectral domain-optical SD-OCT revealed blurred EZ and IZ of the binocular macular area (Figure 1).

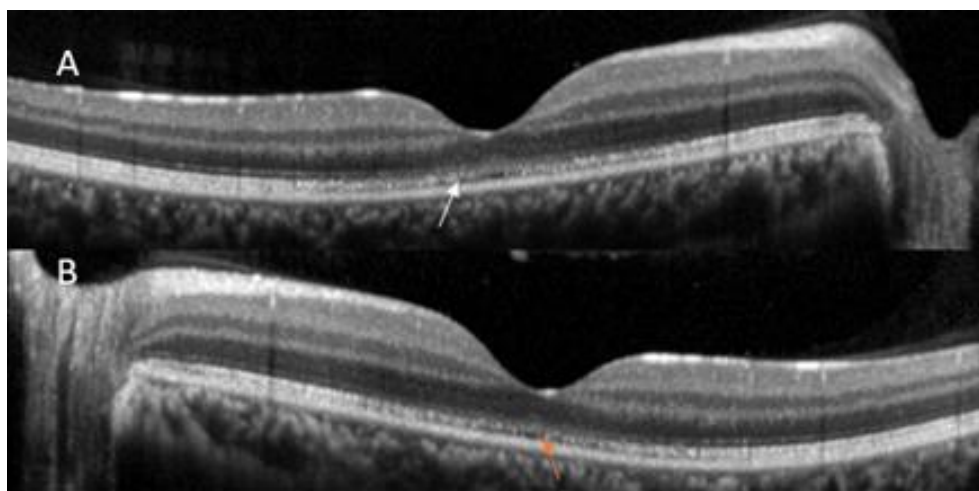


Figure 1. SD-OCT of the RE (a) and SD-OCT of the LE (b) before treatment.

A. The patient's right eye presented granular atrophy and poor continuity in EZ and IZ in macular area (as shown by the white arrow). B. The patient's left eye presented granular atrophy and poor continuity in EZ and IZ in macular area (as shown by the yellow arrow). EZ: Ellipsoid zone. IZ: interdigitation zone.

The FFA examination was normal. The FF-ERG were

within the normal range for both rod and cone components. However, MF-ERG with the 5 concentric rings were severely reduced. Perimetry showed the physiological blind spot enlarged with central dark spot of RE, and enlarged physiological blind spot of LE. The figure of MF-ERG and perimetry were shown in Figure 2.

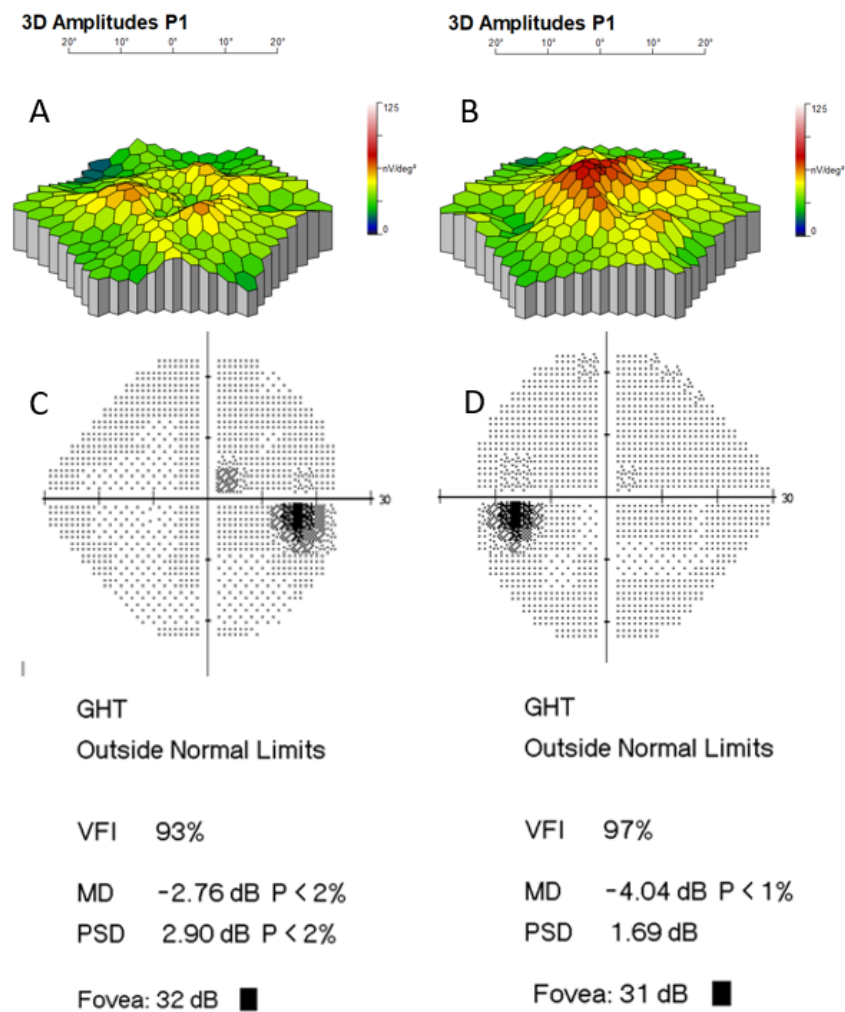


Figure 2. The figure of MF-ERG and perimetry.

A. 3D amplitudes P1 of MF-ERG of RE. B. 3D amplitudes P1 of MF-ERG of LE. c. perimetry examination of RE. d. perimetry examination of LE.

The genetic test identified RP1L1 gene C. C133T: P. R45W heterozygous variation of the patient (Figure 3), the result of genetic test of his mother was VRP1L1: NM_178857: exon2: c. C133 T: p. R45 w for hybrid type, his father was normal.

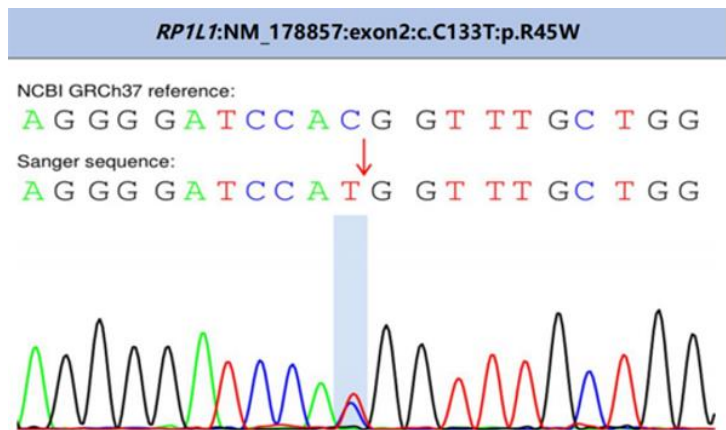


Figure 3. The result of genetic test of the patient. a point mutation of C mutated to base T at base 133 of the gene coding region.

A diagnosis of OMD was made.

LLLT was performed in compliance with the Declaration of Helsinki after the patient had given his informed consent. LLLT employed a continuous wave semi-conduct laser diode (RS-200-2A, EYERSING, Suzhou, China). Wavelength was 650 nm, average power output was 2.0 ± 0.5 mW, collimating optics were housed in a desk that produced a 1 cm diameter spot size. The patient was asked to look front while the eyelids were kept open, and the fundus was irradiated. Irradiation

treatment was performed for 180 sec and twice a day for 4 weeks.

Every week since beginning of the treatment, the patient's BCVA was re-examined. The BCVA increased to 20 letters of RE and 30 letters of LE after 1 weeks of LLLT, but there is no more improvement with further 3 weeks of treatment. Then finished LLLT and re-examined BCVA after 1 month, the BCVA was 20 letters in RE and 15 letters in LE. All BCVA is shown in Table 1.

Table 1. Summary of BCVA change before and after treatment.

BCVA (ETDRS)						
	before treatment	Treatment for 1 week	Treatment for 2 week	Treatment for 3 weeks	Treatment for 4 weeks	1 month after ended treatment
RE	3 letters	20 letters	20 letters	21 letters	20 letters	20 letters
LE	12 letters	30 letters	20 letters	24 letters	20 letters	15 letters

The binocular amplitudes of MF-ERG were examined at baseline and the end of the 4 weeks of LLLT. These amplitudes (response densities) of the 5 concentric rings of both eyes were improved after treatment as show in table 2.

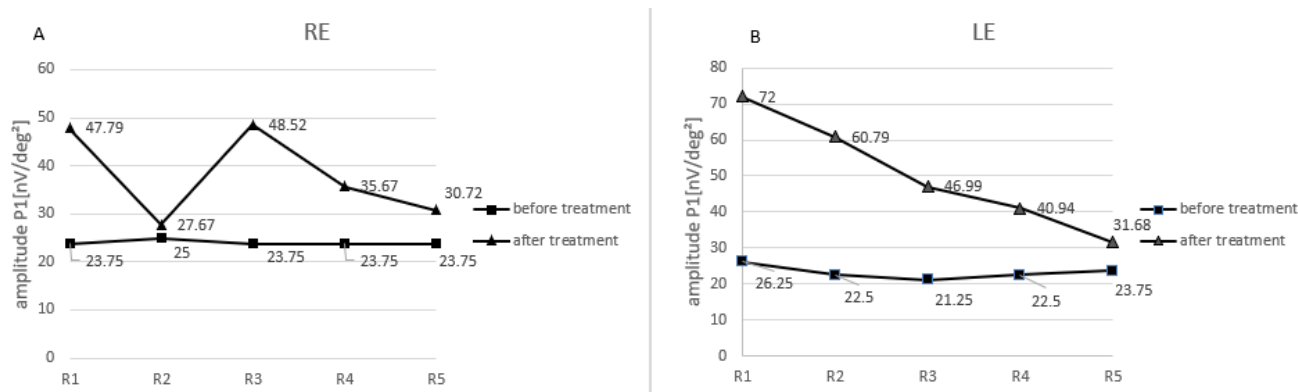


Figure 4. Amplitude (response densities) of the 5 concentric rings of the RE (A) and LE (B) before and after treatment.

For perimetry (central 24-2 threshold test), it was examined at baseline and re-examined at end of 4 weeks of LLLT. The foveal threshold represents the original value of the photo-sensitivity of the detection site, the lower the threshold, the higher the sensitivity, it was improved from 32 dB to 29 dB in RE and from 31 dB to 30 dB in LE after LLLT. The visual field indices (VFI) represent the Global visual function, it was improved from 93% to 94% in RE and from 97% to 99% in LE after LLLT. Mean deviation (MD)/Pattern standard deviation (PSD): MD represents a decrease in average visual acuity due to various factors, PSD reflects a decrease in av-

erage visual acuity by filters out the opacity optical media. The higher the absolute value of both, the more serious the decrease of visual acuity. The MD was improved from -2.76 dB (2%) to -2.46 dB ($p < 5\%$) of the RE and -2.27 dB ($p < 5\%$) from -4.04 dB (1%) of LE after LLLT. The PSD was improved from 2.90 dB (2%) to 2.29 dB ($p < 5\%$) of the RE and from 1.69 dB (1%) to 1.35 dB ($p < 5\%$) of the LE after LLLT. Although perimetry examination data did not change much before and after treatment, they all improved. All perimetry check data are shown in Table 2.

Table 2. Summary of Perimetry check data before and after LLLT.

Perimetry Test	RE		LE	
	Before	After	Before	After
Foveal threshold	32 dB	29 dB	31 dB	30 dB
VFI	93%	94%	97%	99%
MD	-2.76 dB P<2%	-2.46 dB P<5%	-4.04 dB P<1%	-2.27 dB P<5%
PSD	2.90 dB P<2%	2.29 dB P<5%	1.69 dB	1.35 dB

VFI: visual field indices, MD: Mean deviation, PSD: Pattern standard deviation.

The morphology of EZ and IZ measured by SD-OCT didn't change.

3. Discussion

This is the first report in literature presenting a rare clinical case of OMD, in which the applied LLLT treatment and its clinical outcomes are described, and the findings of genetic test, which diagnosis the clinical disease more accuracy, is provided.

Both OMD and RP are caused by heterozygous Retinitis pigmentosa 1-like 1 (RP1L1) gene [7-9], IVANDIC B T [21] used LLLT improved vision to 20/20 from 20/50 and maintained the vision in a single patient with RP. In this case, both subjective and objective visual function improved after LLLT treatment, but it wasn't as so significant as that obtained by IVANDIC B T. The possible reasons maybe as follows: 1. Differences in the response of the disease itself to the treatment; 2. Differences in optical parameters. due to the biphasic effect of LLLT, the different optical parameters, such as wavelength, energy density and irradiation time, may lead to different treatment results [22].

The impact of LLLT is intricate and not yet completely comprehended. At the cellular level, laser light positively influences the energy levels of cells. LLLT induces a photochemical reaction in the cell rather than producing a heat effect, a process known as biostimulation or photobiomodulation [31]. Photobiology operates on the idea that when light interacts with specific molecules known as chromophores, the energy of the photons excites electrons, prompting them to transition from lower-energy orbits to higher-energy orbits. The absorption of photon energy by brain mitochondria results in several neuroprotective effects [32]. Red and near-infrared (NIR) light pose far fewer safety risks compared to shorter wavelength light, making them the preferred option for retinal irradiation [33]. Maiya et al [34]. reported analogous findings in diabetic rats, indicating that laser-treated subjects exhibited superior and more rapid healing compared to the control group. Low-level laser therapy (LLLT) enhances wound healing in ischemic rat and murine diabetic models, mitigates the retinotoxic effects of methanol-derived formic acid in rat models, and reduces the developmental toxicity of dioxin in chicken

embryos. Red/NIR light has exhibited significant neuroprotective effects in multiple forms of retinal injury, while human research providing evidence of its capacity to enhance visual function are lacking. Enhanced neuronal mitochondrial activity, augmented blood supply to brain tissue, elevation of cell survival mediators, and restoration of normal microglial function has all been suggested as potential processes underlying red/NIR light [35]. The molecular and cellular mechanics of low-level laser therapy indicate that photons are absorbed by the mitochondria. They enhance ATP synthesis and reduce ROS levels, thereby activating transcription factors including NF- κ B, which induces several gene transcripts accountable for the advantageous effects of LLLT. Reactive oxygen species (ROS) are recognized for their ability to promote cellular proliferation at low concentrations, whereas at elevated levels, they inhibit proliferation and induce cell death. Nitric oxide participates in low-level laser therapy (LLLT) and may be photo-released from its binding sites within the respiratory chain and other locations. It is conceivable that minimal emission of NO at low light doses may be advantageous [36].

LLLT is a simple, safe and non-invasive treatment. Basic studies have shown that this treatment can effectively reduce cell apoptosis and improve cell function [23-26]. Clinical studies have also shown that LLLT can improve the visual function or abnormal retinal morphology of AMD, DME, Amblyopia and RP patients [18, 20, 27-29]. It's an innovative treatment with great potential value for treating eye diseases in the future [30]. In view of the effectiveness and safety of LLLT, more clinical studies should be designed to examine patients with OMD in the future, and consider more treatment modalities, to determine the best treatments respect to normalization and long-term stability of visual function.

4. Conclusions

In conclusion, to the best of our knowledge, this is the first report in literature that LLLT improved and maintained vision in a single patient with OMD. LLLT is simple, and without adverse effects. The results are promising but require independent confirmation before one may claim a benefit for patients with OMD.

Abbreviations

OMD	Occult Macular Dystrophy
LLLT	Low-Level Laser Therapy
MF-ERG	Multifocal Electroretinogram
SD-OCT	Spectral Domain Optical Coherence Tomography
RP1L1	Retinitis Pigmentosa 1-Like 1
BCVA	Best Corrected Visual Acuity
ETDRS	Early Treatment Diabetic Retinopathy Study
RE	Right Eye
LE	Left Eye
IZ	Interdigitation Zone
FF-ERG	Full-Field Electroretinogram
FFA	Fluorescence Fundus Angiography
CCO	Cytochrome C Oxidase
ATP	Adenosine Triphosphate
DME	Diabetic Macular Oedema
EZ	Ellipsoid Zone
VFI	Visual Field Indices
MD	Mean Deviation
PSD	Pattern Standard Deviation
RP1L1	Retinitis Pigmentosa 1-Like 1
AMD	Age-Related Macular Degeneration

Consent

Written informed consent was obtained from the patients for publication of this case report and any accompanying images, and no competing financial interests exist.

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Conflicts of Interest

The authors declare no conflicts of interest.

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