CASE REPORT

In vivo early retinal structural alterations following laser photocoagulation using three-dimensional spectral domain optical coherence tomography

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SUMMARY

To study the retinal structural alterations and surface topography of retinal pigment epithelium (RPE) immediately following laser photocoagulation up to day 7. Cross-sectional retinal imaging and RPE segmentation maps on spectral domain optical coherence tomography were obtained immediately at hour 1, day 1, day 4 and day 7 following 532 nm neodymium:YAG laser photocoagulation in a 56-year-old male patient for branch retinal vein occlusion. Immediately postlaser, loss of reflectivity of all the retinal layers was observed. At hour 1, hyper-reflectivity of outer retinal layers was observed with increase in hyporeflective spaces by day 1. Immediately postlaser, pitting of the RPE was observed on surface topography which regressed at day 1. On day 4, smooth RPE surface topography was observed with the occurrence of small elevated areas on day 7. The present report provides an insight into the in vivo changes in the retinal structure and RPE surface topography after laser photocoagulation.

BACKGROUND

Spectral domain optical coherence tomography (SD-OCT) provides high resolution in vivo imaging of the retina. The three-dimensional surface topography of retinal pigment epithelium (RPE) serves as a valuable tool in the analysis of the unique changes in this layer of the retina postlaser photocoagulation. RPE is the main target during laser photocoagulation due to the presence of melanin pigments.¹ Retinal microstructural changes on SD-OCT, seen immediately postlaser photocoagulation up to day 7, were documented. For the first time, three-dimensional SD-OCT-based RPE surface topography was evaluated during this time period.

CASE PRESENTATION

A 56-year-old hypertensive male patient noticed a rapid painless diminution of vision in the right eye for 2 days. At presentation, best-corrected visual acuity was counting finger 2 m right eye and 6/9 left eye. Examination of the left eye was unremarkable. Anterior segment examination of the right eye revealed clear cornea and lens. Slit lamp biomicroscopy of the right eye revealed inferotemporal branch retinal vein occlusion with macular oedema. SD-OCT imaging of the right eye was performed. Macular oedema and fine epiretinal membrane were observed. Hyper-reflectivity of the inner retinal layers was also observed. Macular central

subfield thickness of 479 μm , and cube average thickness of 456 μm was observed. Surface topography of the RPE, obtained using three-dimensional segmentation analysis, was unremarkable. Fluorescein angiography of the right eye revealed delayed filling of the inferotemporal veins. Macular oedema with late leakage of dye was visualised in the inferior half of the macula. No areas of capillary non-perfusion were visualised. Intravitreal bevacizumab was administered in the right eye. Twenty days later, a repeat SD-OCT imaging of the right eye revealed a macular central subfield thickness of 361 μm and cube average thickness of 348 μm .

Neodymium (Nd):YAG (532 nm) laser photocoagulation delivering low-energy to produce visible burns (100 μm spot size in the inferior macular area) was performed (figure 1). SD-OCT was performed immediately postlaser, at hour 1, day 1, day 4 and day 7.

Immediately postlaser, generalised hyporeflectivity of all the retinal layers along with intraretinal vacuoles in the outer retinal layers was observed (figure 2). At hour 1, the inner retinal layers

Figure 1 Scanning laser ophthalmoscopy images of the patient's right eye: pre-scatterer laser photocoagulation (A); postlaser after 24 hours (arrow indicates postlaser spots) (B).

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Figure 2 Cross-sectional spectral domain optical coherence tomography with the corresponding three-dimensional retinal pigment epithelium surface map Prelaser photocoagulation (A); immediately postlaser showing hyporeflective spaces (arrow) (B).

Figure 3 Cross-sectional spectral domain optical coherence tomography with the corresponding three-dimensional retinal pigment epithelium surface map postlaser at hour 1 showing hyper-reflective areas (A); day 1 (B).

regained reflectivity whereas hyper-reflectivity of the outer retinal layers at site of burn and presence of intraretinal vacuoles in the outer nuclear layer between the laser burns was observed. Obliteration of subretinal space with disorganisation of the outer retinal layers was observed. At day 1, hyporeflective spaces in the outer nuclear and inner plexiform layers of the retina were observed in between the prominent hyper-reflective areas of laser burn (figure 3). At day 4, the hyper-reflectivity decreased with the reorganisation of the disrupted outer retinal layers observed to regain at day 7 (figure 4).

Immediately postlaser, three-dimensional RPE surface maps showed topographical alterations. Pitting of the RPE layer was observed corresponding to areas of laser photocoagulation. These alterations were found to decrease after 24 hours with flattening of the RPE observed on surface maps at day 4. At day 7, small areas of RPE elevations were observed.

Figure 4 Cross-sectional spectral domain optical coherence tomography showing the reorganisation of retinal layers with a decrease in hyper-reflectivity (arrow). Corresponding three-dimensional retinal pigment epithelium surface maps showing alterations in surface topography postlaser photocoagulation at day 4 (A); day 7 (B).

INVESTIGATIONS

Cirrus high-definition SD-OCT imaging (Carl Zeiss Meditec Inc, California, USA) was carried out using macular cube 512×128 scan feature. Images with signal intensity 7 and above were considered.

Blood pressure: 144/78 mm Hg.

TREATMENT

Intravitreal bevacizumab was administered in the right eye with laser photocoagulation on follow-up after 20 days. Nd:YAG (532 nm) laser photocoagulation delivering visible burns (100 µm spot size in the inferior macular area) was performed.

DISCUSSION

Several studies, including those on animal models, document the effects of laser photocoagulation on different retinal layers.²

Regeneration of the retinal layers postlaser have also been documented.³ The present report documents for the first time the sequence of early retinal structural alterations and topographical changes of the RPE surface postlaser photocoagulation.

Immediate loss of reflectivity of retinal layers suggests the presence of local thermal reaction resulting in a haze at the level of all the retinal layers. Immediately postlaser, RPE segmentation maps showed topographical alteration with surface pitting corresponding to the area of treatment. The high amount of melanosomes intrinsic to the RPE absorbs the energy delivered by the laser. Histological studies have documented the damage of the RPE with associated coagulative tissue changes in the photoreceptors and neurosensory retina postlaser photocoagulation.⁴ This substantiates the hyper-reflectivity of the outer retinal layers observed in our case after 1 hour of the laser photocoagulation.

Several studies have documented the activation of Muller cells under pathological conditions.⁵ The activation of Muller cells has protective as well as detrimental effects. Dysfunction of Muller cells is associated with the development of retinal oedema and cystic degeneration, as seen in cases of diabetic retinopathy with diabetic macular oedema.⁶ The protective effect of the reactive Muller cells has been evidenced by the attribute of Muller cells to function as intrinsic progenitor cells.⁷ Experimental studies on mouse eyes have documented that retinal laser photocoagulation stimulates Muller cells to adopt characteristics of progenitor cells by re-entering the cell cycle and dedifferentiating. This results in reorganisation of the retina postlaser photocoagulation. Increase in molecular biomarkers like glial fibrillar acidic protein and cyclin D1 and D3 after 24 and 48 hours of laser photocoagulation further substantiates this role of Muller cells.⁶ Muller cell dysfunction provides a plausible explanation for the hyporeflective spaces visualised in the outer retinal layers in the present case. The reorganisation of the retinal layers that is visualised to begin after 24 hours is explained by the activation of cell cycle progression and dedifferentiation of Muller cells.

Laser irradiation induces necrosis and apoptosis of the RPE cells. This is followed by a reparative process. The repair of the laser lesions involves migration and proliferation of the damaged as well as the neighbouring RPE cells. Neighbouring RPE cells and macrophages of choriocapillary origin migrate to phagocytose the cell debris of damaged RPE cells.⁸ In vitro studies have observed the process of cell migration at 24 hours. This would explain the decrease in RPE pitting observed on the surface map at day 1. This precedes the process of cell proliferation which resumes in 48 hours. This proliferative response leads to regeneration of the RPE in the following days. Uncharacteristic surface topography on day 4 corroborates with these findings. Further RPE cell proliferation takes place for a week.⁸ This provides a plausible explanation for the occurrence of RPE elevations observed on the surface topography maps at day 7.

With the advent of subthreshold laser photocoagulation, it has been shown that ophthalmoscopically invisible burns are detectable on OCT images. These changes, however, may show a temporal delay. The retinal structural changes may not be visible on early OCT images, but are visible on the follow-up images.⁹ Koinzer *et al* have documented an OCT-based classification of laser-induced retinal morphological changes. The classification also takes into consideration the temporal delay in visibility of these changes with variation in irradiation time and diameter.¹⁰ Various studies have emphasised the advantage of

shorter pulse duration, smaller spot size, and low-intensity laser on healing of retinal lesions postlaser photocoagulation.^{11 12} Deák *et al* have documented the morphological changes in the retina, and the reorganisation of the outer retinal layers and RPE after half-fluence laser photocoagulation. The characteristics were observed to be similar to threshold burns. They also proposed the supplementary role of cytokines in the beneficial outcome of laser.¹³

The present report provides an unparalleled account of 'in vivo' structural alterations in retina, and change in the surface topography of RPE postlaser photocoagulation.

Learning points

- ▶ Laser photocoagulation is associated with structural alterations of the retinal layers and changes in surface topography of retinal pigment epithelium (RPE).
- ▶ Early changes include generalised hyporeflectivity of all the retinal layers. This is followed by hyper-reflectivity of the retinal layers corresponding to areas of laser photocoagulation. Hyporeflective spaces are observed in the outer nuclear layer in between the laser burns.
- ▶ Reparative process of reorganisation of the retinal layers is observed by 24 hours.
- ▶ Immediately postlaser photocoagulation, surface pitting of RPE corresponding to areas of laser are observed. These regress by day 1, resulting in an uncharacteristic RPE surface by day 4. This is followed by occurrence of areas of surface elevations by day 7.

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