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Case Report

Long-Term Outcomes following Intravitreal Ranibizumab for Choroidal Neovascularization Related to Nd:YAG Laser Macular Injury: A Case Report

Eleni Christodoulou[a] Georgios Batsos[b] Evita Evangelia Christou[c] Konstantina Gorgoli[d] Efstratios Parikakis[b] Dimitrios Karagiannis[b] Loukas Kontomichos[b] Maria Stefaniotou[c]

[a]Department of Ophthalmology, Tzaneio General Hospital of Piraeus, Athens, Greece; [b]2nd Ophthalmology Department, Ophthalmiatreio Eye Hospital of Athens, Athens, Greece; [c]Department of Ophthalmology, Faculty of Medicine, School of Health Sciences, University of Ioannina, Ioannina, Greece; [d]Iris and Retina Private Practice, Ioannina, Greece

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Abstract
Choroidal neovascularization (CNV) secondary to Nd:YAG laser macular injury consists of a rare condition without standardized treatment. Herein, we present the long-term outcomes of a case with a spontaneous closure of a laser-associated macular hole that was followed by late-onset CNV and was successfully treated with intravitreal ranibizumab. A 32-year-old man suffered a macula injury in his right eye after accidental exposure to an 800-nm wave length Nd:YAG laser pulse. Ophthalmological examination demonstrated deterioration in visual acuity along with parafoveal and post-hyaloid hemorrhage. After 1 month, fundoscopy indicated the formation of a full-thickness macular hole. A close observation revealed spontaneous closure of the hole and visual improvement within the next month. One and a half year later, the patient presented with sudden visual distortion, while optical coherence tomography and fluorescein angiography disclosed the development of CNV. The patient was successfully treated with a single intravitreal injection of ranibizumab. The patient's condition has remained stable during an 8-year follow-up period. In conclusion, laser-induced macular injury consists of an increasingly remarkable condition that may have a profound impact on visual outcomes. Our case provides insight into the potential mechanisms of Nd:YAG laser injury and its complications, indicating that CNV may

Correspondence to:
Evita Evangelia Christou, evitachristou@gmail.com

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occur even in the long term, while anti-vascular endothelial growth factor may help maintain stable anatomic and functional outcomes.

Introduction

The widespread use of lasers for medical, scientific, or commercial applications during the past decades has led to a sharp rise of reported adverse effects regarding vision. Patients typically present with visual disturbance and distinct clinical features, seldom masquerading as various retinal disorders, while the prognosis for functional and anatomical outcomes markedly depends on both the extent of exposure and the laser's characteristics (type, power, wavelength, spot size) [1–3].

Wavelength either less than 400 nm or more than 1,400 nm affects the anterior segment of the eye (cornea and lens), while that from 400 to 1,400 nm affects the retina. Damage is usually caused through direct exposure, and not uncommonly, it may be related to a reflected or scattered beam. It is crucial to recognize macular injuries as they consist of a potentially sight-threatening condition primarily encountered in young patients [3].

The purpose of this paper was to report a case of an accidental Nd:YAG laser (a solid state laser with a synthetic crystalline material – yttrium aluminum garnet [YAG] – doped with a chemical element – neodymium [Nd])-induced macular injury; early clinical findings, late complications, anatomical and functional status during an 8-year follow-up period are herein described. A similar case with an accidental Nd:YAG laser-induced macular hole followed by spontaneous closure and concurrent choroidal neovascularization (CNV) development has been previously described by Ying et al. [4]; in this case, CNV was successfully treated with two sessions of photodynamic therapy. To the best of our knowledge, our case is distinct in that CNV developed in the long term and was treated with intravitreal ranibizumab.

Case Presentation

A 32-year-old man suffered a macula injury in his right eye after accidental exposure to 800-nm wavelength Nd:YAG laser pulse. The incident took place in a physics laboratory while he was aligning the laser beam.

The patient was immediately admitted to the emergency department of our hospital due to visual disturbance of his right eye. On presentation, best-corrected visual acuity (VA) was 0.70 logMAR for his right eye and 0 logMAR for his left eye. Ophthalmological examination of the right eye demonstrated an unremarkable anterior segment, lens, intraocular pressure, and vitreous, while fundoscopic examination revealed parafoveal and post-hyaloid hemorrhage (Fig. 1a). Optical coherence tomography (OCT) showed a slight thickening of the macula, loss of fovea depression, disruption and migration of the retinal pigment epithelium (RPE), and alterations of the outer retina including attenuation of the ellipsoid zone, external limiting membrane, and outer nuclear layer and disruption of photoreceptors' inner segment/outer segment junction (Fig. 1b). Ophthalmological examination of the left eye indicated no pathological clinical findings.

Upon review 1 week later, although there was a considerable anatomical configuration of the fovea, the inner segment/outer segment junction disruption and RPE alterations were still present. After 1 month, fundoscopy disclosed the formation of a full-thickness macular hole

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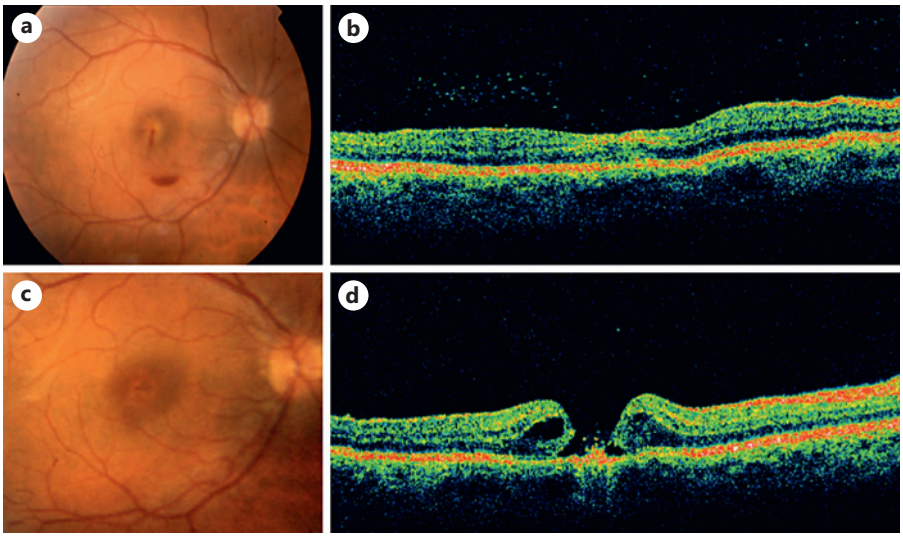

Fig. 1. At presentation, the fundus photograph showed parafoveal and post-hyaloid hemorrhage (**a**) and optical coherence tomography (OCT) demonstrated alterations at the macular area, such as slight thickening of the macula, loss of fovea depression, disruption, and migration of the retinal pigment epithelium (RPE) and alterations of the outer retina including attenuation of the ellipsoid zone, external limiting membrane, and outer nuclear layer and disruption of photoreceptors' inner segment/outer segment (IS/OS) junction (**b**). At the 1-month follow-up visit, the patient presented with a full-thickness macular hole that was evident in the fundus photograph (**c**) and OCT (**d**).

(FTMH) (Fig. 1c), which was also confirmed by OCT (Fig. 1d). Close observation along with topical nonsteroidal anti-inflammatory drugs to control inflammation was suggested as the best treatment option in this case, and the patient was willing for regular monitoring. Given the young age of the patient and the fact that the accident had happened recently, no surgical intervention was recommended at the time. Indeed, a spontaneous closure of the hole was observed within the next month with a subsequent visual improvement to 0.18 logMAR. Notwithstanding the fact that functional outcomes were satisfactory, fundus examination (Fig. 2a) depicted a distorted retinal morphology and structure, along with disruption of the RPE.

Clinical examination and multimodal imaging revealed a stable condition of the retinal morphology during the follow-up visits after both 2 and 6 months. OCT illustrated disruption and migration of the RPE (Fig. 2b), while intravenous fluorescein angiography (Fig. 2c) demonstrated associated window defects due to the RPE alterations at the macula, confirming chronicity, and indocyanine green angiography showed normal choroidal vasculature (Fig. 2d).

One and a half year later, the patient presented with sudden visual deterioration of his right eye. On examination, his logMAR VA was measured 0.70. Fundus examination revealed alterations at the level of the RPE (Fig. 2e). OCT of the macula demonstrated a central subretinal hyper-reflective region along with intraretinal and subretinal fluid that corresponded to signs indicating CNV (Fig. 2f). Fluorescein angiography displayed leakage which corresponded to the CNV lesion, confirming the diagnosis of classic CNV (Fig. 2g).

Following detailed counseling with the patient, an intravitreal injection of an anti-vascular endothelial growth factor (VEGF) agent was proposed. Unfortunately, the patient postponed the appointment for the injection and came back after 2 weeks with further deterioration of VA. Fundoscopic examination revealed extensive subretinal blood (Fig. 3a), while OCT imaging was worse than that of the previous visit (Fig. 3b). For this reason, a single

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Fig. 2. At 6 months, fundus photograph (**a**) and OCT (**b**) show macular hole closure with disruption and migration of the retinal pigment epithelium (RPE). Fluorescein angiography (FAG) demonstrated window defects due to the RPE alterations at the macula (**c**) and indocyanine green angiography showed normal choroidal vasculature (**d**). One and a half year later, the patient presented with RPE alterations on the fundus photograph (**e**), while intraretinal and subretinal fluids were present on the OCT (**f**). Early (**g**) and late (**h**) phase of FAG revealed leakage which corresponded to classic choroidal neovascularization.

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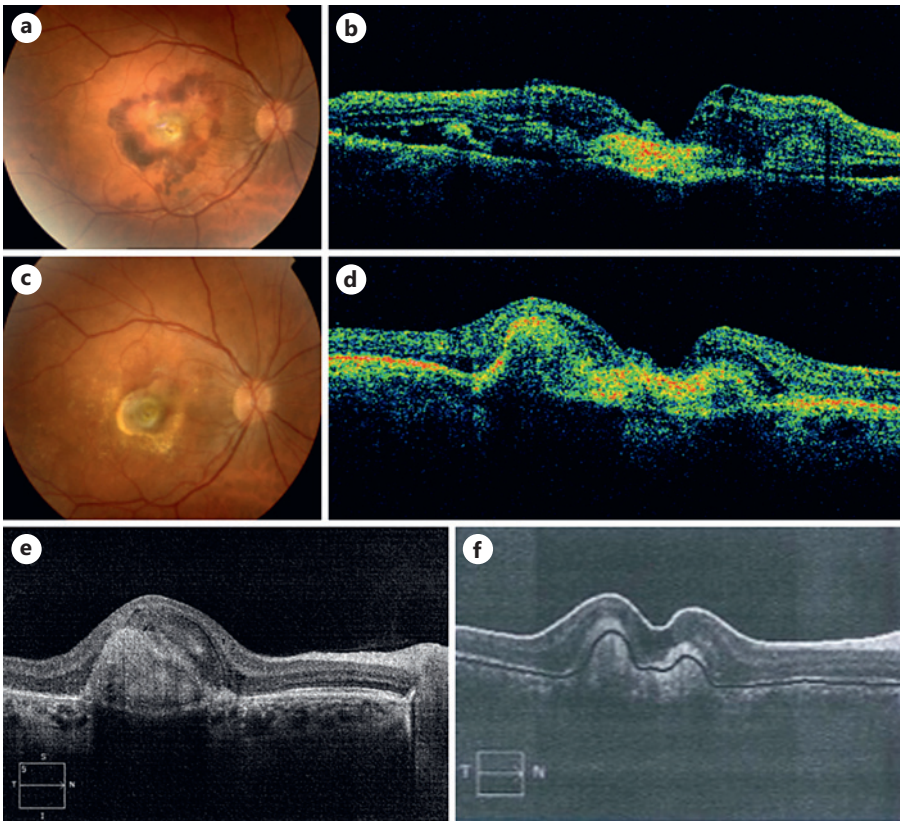

Fig. 3. Two weeks after the diagnosis of choroidal neovascularization, the patient came back with subretinal blood at the macular area, as shown at the fundus photograph (**a**) along with extensive intraretinal and subretinal fluid, as shown on OCT (**b**). The patient was treated with intravitreal ranibizumab injection. At the 4-week visit after the injection, fundus image (**c**) and OCT (**d**) illustrated absorption of blood, as well as intraretinal and subretinal fluid, with residual neovascular scarred tissue. OCT images (**e**, **f**) at 8-year of follow-up remained stable.

intravitreal ranibizumab injection 10 mg/mL was administered immediately. At the 4-week follow-up visit, VA improved to 0.48 logMAR. OCT illustrated absorption of the intraretinal and subretinal fluid with residual neovascular scarred tissue at the foveal area (Fig. 3d), which was also evident at the fundoscopy (Fig. 3c). The patient's condition has remained stable during a follow-up period of 8 years (Fig. 3e, f).

Discussion

Given that Nd:YAG laser is seldom utilized in the treatment of retinal conditions, its impact on retinal tissue is mainly derived from accidental injuries and in some cases is accountable to a profound detrimental effect. A number of complications have been associated with photodisruption, namely, vitreous, retinal, and subretinal hemorrhage; macular hole; epiretinal membrane; and CNV [2].

Based on its mechanism of action, the Nd:YAG energy is initially absorbed by melanin which is located in the RPE and causes tissue ionization, plasma formation, and an acoustic shock wave. The latter may spread centrifugally, leading to mechanical disruption of the surrounding retina, including the RPE and choroid. The initial injury notably causes a release

of inflammatory mediators from the directly damaged cells that subsequently leads to collateral damage of neighboring cells over time [3, 5, 6].

The pathophysiologic mechanism of a laser-induced FTMH differs from that implicated in an idiopathic FTMH, which is related to the tractional forces by an anomalous posterior vitreous detachment. In laser-induced cases, the posterior hyaloid is still partially attached with a localized detachment over the FTMH; however, tractional forces may still develop due to disruption of retinal tissue and retinal fibroglial formation. Conceivably, spontaneous closure of laser-induced holes may be related to either small initial hole size or the presence of hemorrhage secondarily acting as tissue glue that has potentially occurred in our case [1, 7].

The literature provides evidence of cases requiring surgical repair for the macular hole and others presenting with spontaneous closure. Admittedly, the decision should be personalized in each case depending on the anatomical features of the hole [6, 7]. Even cases with uncomplicated macular hole closure have the potential to present with future unfavorable outcomes such as CNV and therefore should be closely monitored [4, 8–10].

Our case was notable for a remarkable FTMH with spontaneous closure eventually followed by development of CNV; thus, the understanding of the underlying pathophysiology is quite intriguing. Macular hole formation was potentially the result of the photo-disruptive effect of Nd:YAG laser [6, 7]. Following that, it is a hypothesis that a small defect in Bruch's membrane occurred, owing to laser or developed at the atrophic lesions over time, leading to development of CNV [4, 8–10]. Another explanation of CNV formation may involve choroidal ischemia due to laser along with the wound healing process that may act as a stimulus for inflammation, matrix remodeling, and angiogenesis. Obviously, release of angiogenic factors from ischemic tissue may compensate for choroidal hypoperfusion, while suppression of these possible etiological parameters including VEGF may successfully stabilize the progression of CNV [4, 8–10]. Interestingly, there is a previous report in the literature with CNV development after FTMH closure that has been successfully treated with 2 sessions of photodynamic therapy [4]. In that case [4], choroidal neovascular membrane developed at 3 months after the injury. Nonetheless, in our case, CNV had evidently developed in the long term and responded to anti-VEGF treatment.

Undoubtedly, our case affords an insight into pathological processes that may be associated with visual impairment in the long term, providing evidence of late choroidal neovascularization as an issue that is mandatory to be promptly identified and treated. Overall, in cases of laser-induced macular injuries, it is critical to accurately diagnose the distinct macular pathology, closely monitor progression, and provide prognostication for future visual outcomes. In conclusion, our case highlights the fact that all personnel working with laser products should take the necessary precautions and use protective goggles. In the event of a macular hole formation, spontaneous closure can occur, and a close observation can be an alternative to the early surgical treatment. Our aim is to raise awareness that choroidal neovascularization can occur even in the long term, while anti-VEGF treatment may maintain stable anatomic and functional outcomes for a long period. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see www.karger.com/doi/10.1159/000529297).

Statement of Ethics

Ethical approval is not required for this case report in accordance with local or national guidelines. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of Interest Statement

The authors report that they do not have any conflict of interest regarding the presenting data.

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Author Contributions

Eleni Christodoulou contributed to writing, design, interpretation, and final approval of the manuscript and is accountable for accuracy and integrity of the work. Georgios Batsos and Evita Evangelia contributed to writing, interpretation, drafting, and final approval of the manuscript and are accountable for accuracy and integrity of the work. Konstantina Gorgoli contributed to interpretation, drafting, and final approval of the manuscript and is accountable for accuracy and integrity of the work. Efstratios Parikakis, Dimitrios Karagiannis, and Loukas Kontomichos contributed to interpretation, revision, and final approval of the manuscript. Maria Stefaniotou contributed to design, interpretation, drafting, and final approval of the manuscript and is accountable for accuracy and integrity of the work.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material files. Further inquiries can be directed to the corresponding author.

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