

# Bilateral Nonarteritic Anterior Ischemic Optic Neuropathy Following Intravitreal Injection of Pegaptanib

Mikiko Kimakura<sup>1</sup>, Akio Oishi<sup>1\*</sup>, Michiko Mandai<sup>1,2</sup> and Yasuo Kurimoto<sup>1</sup>

<sup>1</sup>Department of Ophthalmology, Kobe City Medical Center General Hospital, Japan

<sup>2</sup>Laboratory for Retinal Regeneration, Center for Developmental Biology, RIKEN, Japan

## Abstract

**Purpose:** To report a rare case with bilateral nonarteritic anterior ischemic optic neuropathy (NA-AION) that developed one week after the unilateral intravitreal injection of pegaptanib for the treatment of age-related macular degeneration (AMD).

**Methods:** A patient with AMD in the right eye and bilateral cataracts underwent phacoemulsification and aspiration with intraocular lens implantation (PEA+IOL) combined with an intravitreal injection of pegaptanib in the right eye. She also underwent PEA+IOL for the left eye three days after the procedure was completed on the right eye.

**Results:** She developed bilateral NA-AION one week after the injection of pegaptanib. Visual acuity declined to 0.02 OD and 0.1 OS.

**Conclusions:** Although anti-vascular endothelial growth factor (VEGF) therapy is generally safe and the causative relationship was not clear, severe side effects, even affecting the contralateral eye, should be kept in mind.

**Keywords:** Age-related macular degeneration; Anterior ischemic optic neuropathy; Anti-VEGF; Intravitreal injection; Pegaptanib

## Introduction

Anti-vascular endothelial growth factor (VEGF) therapy is now a first-line treatment for age-related macular degeneration (AMD). Although the treatment is generally safe, severe side effects, (e.g., endophthalmitis, lens injury, and retinal detachment) occasionally occur. The drug is also associated with systemic side effects, particularly thromboembolic events. Even though each injection contains very small risk, it can be a threat for patients who receive ongoing injections, which standard regimen demands.

Anterior ischemic optic neuropathy (AION) results from ischemic damage of the optic nerve including the optic nerve head. Although arteritic AION (i.e., AION associated with giant cell arteritis) sometimes involves the optic nerve bilaterally, simultaneous development of bilateral nonarteritic AION (NA-AION) is rare [1] and is reported only in particular situations, such as dialysis-induced hypotension [2] or hyperviscosity syndrome due to polycythemia vera [3]. Herein, we report a case with bilateral NA-AION that developed one week after the unilateral intravitreal injection of pegaptanib for the treatment of AMD.

## Case Report

A 70-year-old woman with hypertension and poorly controlled diabetes presented with metamorphopsia OD. Her visual acuity (VA) was 0.2 OD. Funduscopic examination and angiography confirmed the diagnosis of AMD. She was treated with photodynamic therapy, which stabilized her right VA. After a nine-month follow-up period, she had developed bilateral cataracts and the recurrence of exudative changes in her right eye. She underwent phacoemulsification and aspiration with intraocular lens implantation (PEA+IOL) combined with an intravitreal injection of pegaptanib in the right eye. She also underwent PEA+IOL for the left eye three days after the procedure was completed on the right eye. These procedures were performed without any complications and no abnormality was detected in postoperative examinations including fundus examination.

However, a week after the operation on the right eye, she noticed a sudden visual loss in both eyes. She came to our hospital one week after the visual loss. Her VA had declined to 0.02 OD and 0.1 OS. Funduscopic examination revealed optic discs swelling accompanied by hemorrhage. A serological test showed no abnormality; no inflammation markers and autoantibodies were detected. She did not have fever, weight loss, headache, or jaw claudication. A magnetic resonance imaging study showed only old lacunar infarcts. There was no enhancement of optic nerves. Fluorescein angiography revealed a filling delay and the leakage of the dye from bilateral optic nerve head. A visual field test showed central scotoma and altitudinal hemianopia, both of which were more severe in the right eye (Figure 1). She was diagnosed with bilateral NA-AION. Optical coherence tomography showed peripapillary retinal edema, which became atrophic in three months (Figure 2).

## Discussion

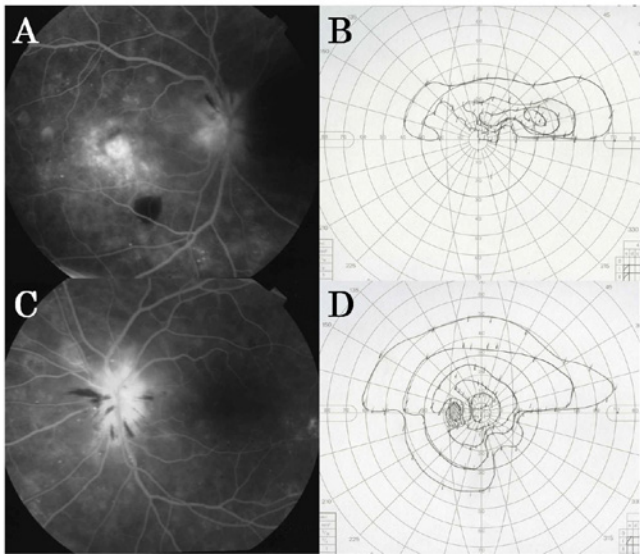
We report a case with bilateral NA-AION that developed one week after the unilateral intravitreal injection of pegaptanib for the treatment of AMD. NA-AION is most often a unilateral disease, and simultaneous involvement of both eyes is very rare [1]. Although a causal correlation is not clear because the patient had several predisposing risk factors and also underwent cataract surgery, bilateral development of NA-AION only a week after the treatment suggests some causality.

**\*Corresponding author:** Akio Oishi, Department of Ophthalmology, Kobe City Medical Center General Hospital, 4-6 Minatojima Nakamachi, Chuo-ku, Kobe, Hyogo 650-0046, Japan, Tel: (81)-78-302-4321; Fax: (81)-78-302-4321; E-mail: [aquio@kuhp.kyoto-u.ac.jp](mailto:aquio@kuhp.kyoto-u.ac.jp)

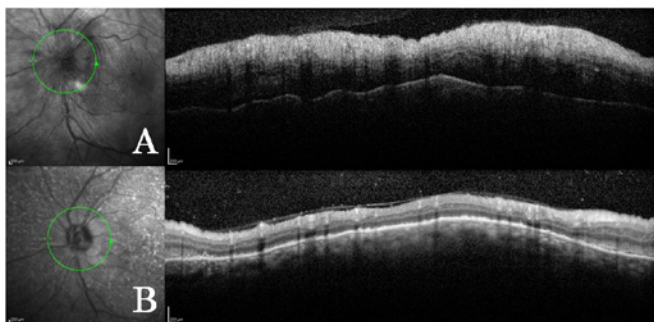
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**Figure 1:** Fluorescein angiography (FA) and Goldmann perimetry of a patient with bilateral AION. [A] FA of the right eye showed perfusion delay and fluorescent leakage from optic disc as well as from choroidal neovascularization in the macula. Microaneurysms due to diabetic retinopathy are observed. [B] Goldmann perimetry of right eye showed absolute inferior altitudinal defect, relative superior altitudinal defect with absolute superior nasal altitudinal defect, and central scotoma. [C] Splinter hemorrhages, dye leakage, and microaneurysms are also confirmed in the left eye. [D] Left eye also showed inferior altitudinal defect, of which was absolute defect in inferior nasal and inferior temporal.



**Figure 2:** Infrared image and corresponding OCT images of the patient in the left eye. [A] Just after AION appeared. Swelling of retinal nerve fiber layer is prominent. Analyzable image could not be obtained in the right eye because the patient had difficulty in fixation and the nerve fiber swelling was too severe. [B] Three months after the onset. The marked swelling of retinal nerve fiber layer in the peripapillary area resolved and atrophy develops instead.

Development of NA-AION several days after the intravitreal injection of anti-VEGF agents has been occasionally reported [4-8]. Although the cases were all unilateral and the causative drugs were bevacizumab or ranibizumab, these reports suggest that the anti-VEGF therapy was responsible for the development of NA-AION. Alternatively, some authors suggest that abrupt rise of intraocular pressure (IOP) following the procedure may be responsible for the development of AION [9].

AION has also been reported to occur after cataract surgery [10,11]. Abrupt rise of intraocular pressure (IOP) was again considered to be a cause of post-cataract-extraction AION [10]. In our case, right and left IOP was 18 and 17 mmHg postoperative day one, respectively. In addition, cases in the report of post-cataract extraction AION

underwent intracapsular cataract extraction, which is far more invasive than PEA. It was unlikely that current cataract surgery and such physiologic IOP cause bilateral AION. Other hypothesis include general anesthesia as a cause of post cataract surgery AION [11] but it is not applicable to the present case.

Pegaptanib is considered to be relatively safe when compared to ranibizumab or bevacizumab because it blocks only one subtype of VEGF. However, the case presented herein indicates that even the selective blockade of VEGF may affect ocular circulation and induce an ischemic event, such as bilateral NA-AION. The present case had several risk factors including hypertension and diabetes, which could influence the clinical course [1,9]. Although the causal relationship or the pathologic mechanism is not clear, care should be taken when using anti-VEGF agents in patients with thromboembolic risks (e.g., uncontrolled diabetes, high blood pressure, or recent stroke / myocardial infarction).

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