



Polypoidal choroidal vasculopathy in a case of retinitis pigmentosa, successfully treated with intravitreal aflibercept

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ABSTRACT

Purpose: Polypoidal choroidal vasculopathy (PCV) is a subtype of age-related macular degeneration that is seen frequently in Asians. Nevertheless, it is rare for this condition to be combined with retinitis pigmentosa (RP). The purpose of this paper is to present findings from this rare combination in a Japanese patient, and to describe its successful treatment with intravitreal aflibercept (IVA).

Observations: The patient was a 71-year-old Japanese woman with RP (diagnosed at the age of 30) and PCV. She noticed a decrease in vision in her right eye 6 months previously. Decimal best-corrected visual acuity (BCVA) was 0.05 in her right eye. Optical coherence tomography and indocyanine green angiography (IA) revealed serous retinal detachment (SRD) and PCV in her right eye. The SRD was initially resolved after 3 monthly treatments with IVA, but recurrences began 5 months later, requiring four more treatments with IVA, performed about every 4 months within the next 12 months, for successful resolution. There were no recurrences of PCV in 7 more months of follow-up, as confirmed with IA at the final appointment. Final decimal BCVA in the right eye improved to 0.15. Furthermore, macular retinal sensitivity, measured with microperimetry, increased after the treatment, and RP-related visual field narrowing, determined by Goldmann perimetry, did not progress throughout follow up of 26 months.

Conclusion: More than 2 years of follow up showed that IVA may be effective for treating PCV, even in RP patients, and can increase central visual function without causing progression of RP-related visual field narrowing.

1. Introduction

Polypoidal choroidal vasculopathy (PCV) is a subtype of age-related macular degeneration (AMD) that is seen frequently in Asians. It is a severe disease that threatens central vision. Recently, treatment with anti-vascular endothelial growth factor (VEGF) drugs has been introduced to control PCV. Another retinal disease, retinitis pigmentosa (RP), is a genetic disorder that causes night blindness and concentric constriction of the visual field. Currently, there is no treatment for RP, but research is ongoing. Approaches being investigated include gene therapy, either to suppress or delay rod photoreceptor degeneration or to regenerate the outer retinal structures.¹

PCV is very rarely combined with RP. However, if RP patients with loss of peripheral vision develop PCV, which affects central vision, the

combination can severely affect quality of vision. Therefore, treatment for PCV with anti-VEGF drugs is essential to preserve central vision. However, a search of the PubMed system revealed only one report of such a case, which was treated with the intravitreal injection of ranibizumab (IVR) and followed for about 1 year.² The current report describes a case of RP combined with PCV, and describes how the patient was successfully treated with intravitreal aflibercept (IVA) during a follow-up period that lasted more than 2 years.

2. Case report

A 71-year-old Japanese woman presented with blurred and distorted vision in her right eye. The onset occurred six months previously and was sudden. The patient had been diagnosed with RP at the age of 30. No

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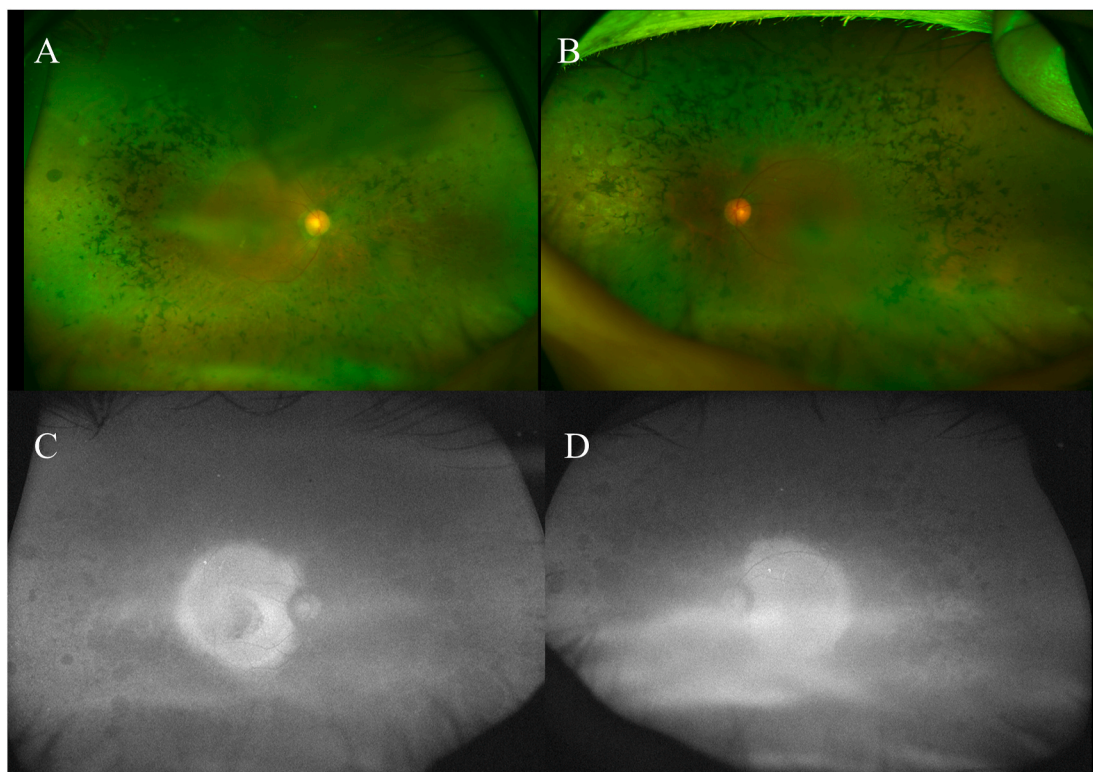


Fig. 1. Pre-IVA wide-field fundus and FAF images from both eyes. A: Wide-field fundus image of the patient's right eye showing bone spicule-like pigmentation and attenuated retinal vessels. B: Wide-field fundus image of the left eye showing bone spicule-like pigmentation and attenuated retinal vessels that are similar to the right eye. C: Wide-field FAF image of the right eye. Abnormal FAF patterns of ring hyper-autofluorescence and patchy hypo-autofluorescent areas are present in the posterior pole and peripheral regions, respectively. D: Wide-field FAF image of the left eye, showing abnormal patterns similar to the right eye: ring hyper-autofluorescence and patchy hypo-autofluorescent areas in the posterior pole and peripheral regions, respectively.

other members of her family had been diagnosed with RP. There was no past history of trauma, smoking, infection, consanguineous marriage, or intake of any medication for a prolonged period. At our initial examination, best-corrected visual acuity (BCVA) was 0.05 in her right eye. A fundus examination revealed retinal features typical of RP, such as bone spicule-like pigmentation and attenuated retinal vessels in both eyes (Fig. 1A and B). The macula of the right eye showed orange-reddish, elevated, well defined polypoidal lesions in the fovea surrounded by hemorrhage (Fig. 2A). Wide-field fundus autofluorescence (FAF) imaging of both eyes (Fig. 1C and D) showed abnormal FAF patterns of ring hyper-autofluorescence and patchy hypo-autofluorescent areas in the posterior pole and peripheral regions, respectively. Fluorescein angiography (FA) in the right eye showed faint leakage from polypoidal lesions (Fig. 2B). Indocyanine green angiography (IA) showed polypoidal lesions and reticulated hyper-fluorescence, indicating an abnormal choroidal vascular network (Fig. 2C). Laser speckle flowgraphy (LSFG) of the right eye before treatment showed reduced ocular blood flow, indicated by cooler colors in the LSF color map (Fig. 3B). Optical coherence tomography (OCT) showed a serous retinal detachment (SRD), retinal pigment epithelial detachment (PED) and polypoidal lesions (Fig. 3A). Central choroidal thickness (CCT) was 241 μm . Goldmann perimetry (GP) examination of the overall visual field showed concentric constriction of the field bilaterally and central scotoma in the right eye (Fig. 4A). Microperimetry examination of the visual field in the macula, based on fundus image tracking (MP-3, Nidek Co, Japan), showed a decrease in macular retinal sensitivity (Fig. 4B). Based on these findings, the patient was diagnosed with PCV combined with RP.

The patient was treated with three IVA treatments (0.05 ml), and was regularly monitored every month. The polypoidal lesions in the OCT images became flattened and the SRD disappeared after 3 IVA treatments. After the third IVA treatment, the SRD remained suppressed,

without any additional IVA, for the next 5 months (Fig. 3C). The elevated CCT also decreased from 241 μm to 214 μm . After 3 IVA treatments, decimal BCVA had improved from 0.05 to 0.1 in the affected eye, and macular retinal sensitivity, measured with MP-3, had also improved (Fig. 4D). Total macular retinal sensitivity increased from 471 dB to 570 dB. Average sensitivity increased from 11.8 dB to 14.8 dB, and total sensitivity in the four central points improved from 16 dB to 50 dB. The number of points with a sensitivity of 1 dB or less decreased from 9 to 5. However, compared to LSF before treatment (Fig. 3B), LSF after 3 IVA treatments showed an increase in areas with cooler colors, indicating decreased blood flow after the treatments (Fig. 3D).

The SRD began to recur beginning 5 months after the third IVA treatment. Due to this recurrence of PCV, four more IVA treatments were required and were performed about every four months over the next 12 months. The patient received no further IVA treatments during the last 7 months of follow-up (Fig. 3E). The absence of PCV was confirmed at the last appointment with IA. Compared to pre-treatment findings, findings from a color fundus examination, FA and IA had all improved after 26 months of follow-up (Fig. 2D, E and F, respectively). Decimal BCVA had improved to 0.15. LSF findings 7 months after the final 7th IVA treatment, i.e., at the final follow-up, showed increased areas with warmer colors, indicating increased blood flow. Indeed, LSF findings had recovered to a level similar to findings before IVA treatment (Fig. 3F). RP-related visual field narrowing, determined by GP, had not progressed, and the central scotoma had reduced at the final follow-up exam (Fig. 4C). There were no remarkable changes in night vision or the peripheral visual field during or after IVA treatment. There were no severe post-treatment complications.

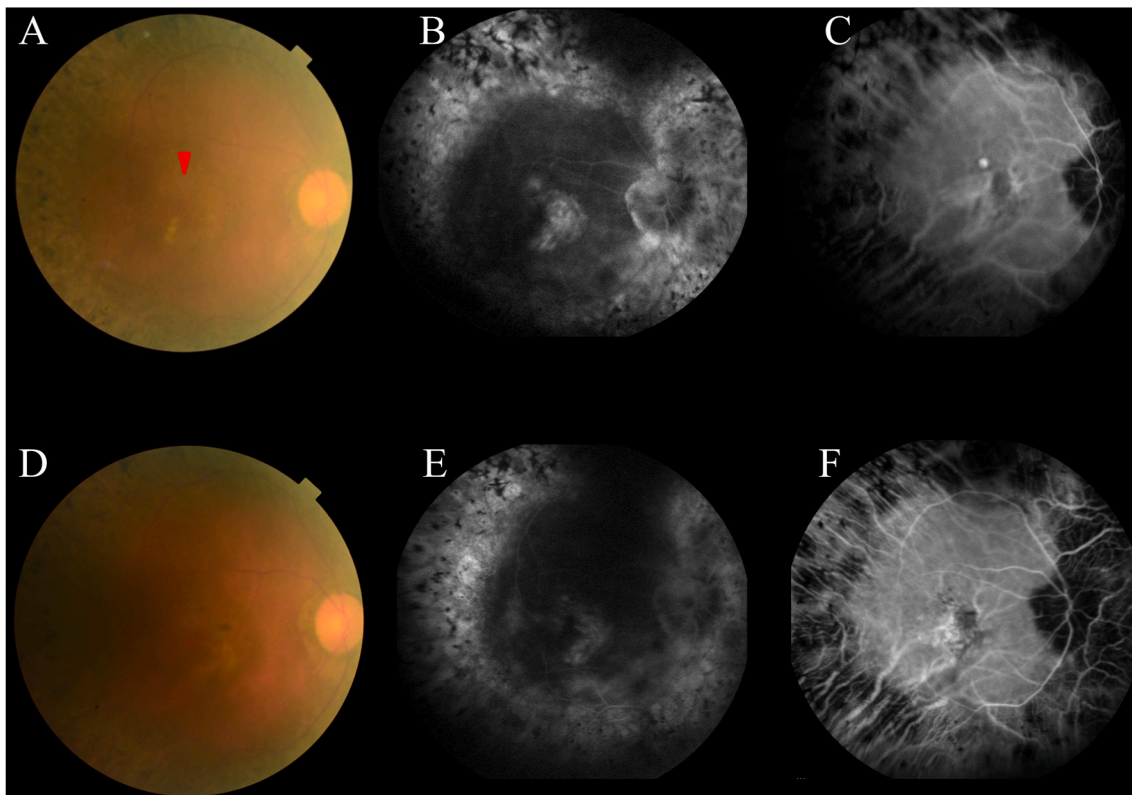


Fig. 2. Fundus, FA and IA images of the right eye before and after IVA treatment. A: Fundus image before IVA treatment. The macula shows orange-reddish, elevated, well defined polypoidal lesions in the fovea (shown by a red arrowhead). B: FA image before IVA treatment, showing faint leakage from polypoidal lesions in the late arteriovenous phase. C: IA image before IVA treatment, showing polypoidal lesions and reticulated hyper-fluorescence in the late arteriovenous phase. These findings indicate an abnormal choroidal vascular network. D: Fundus image after 7 IVA treatments. Abnormal pre-treatment features have diminished. E: FA image after 7 IVA treatments. The faint leakage from polypoidal lesions in the late arteriovenous phase has diminished. F: IA image after 7 IVA treatments, showing no polypoidal lesions in the late arteriovenous phase. Some regions in the macula have an appearance similar to retinal pigment epithelium mottling, but they were caused by decreased or absent IA staining due to choroidal vascular abnormalities, which became apparent after a polypoidal lesion and SRD disappeared after IVA. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

3. Discussion

Patients with combined PCV and RP are at risk of severe visual impairment if the central visual field, generally spared in RP, is lost due to PCV. Thus, these patients have a special need for PCV treatment to restore their quality of vision. To our knowledge, there has only been one previous report of a patient with RP combined with PCV.² This patient was treated with three consecutive IVR treatments and a single application of photodynamic therapy (PDT). Though the PED remained unchanged in that patient, the polypoidal lesions became flattened and BCVA (decimal BCVA: 0.2) was maintained without progression of the constricted visual field during a follow-up period of about 1 year. In the current case, BCVA and macular sensitivity improved slightly and were maintained after IVA treatment. RP-related visual field narrowing did not progress during 26 months of follow-up. Our favorable results, even after a long-term follow-up period of more than 2 years, might be related to the lack of subretinal hemorrhage at baseline as well as the use of IVA alone, without PDT.

Decreased choroidal blood flow and choroidal thickness have been reported in RP.^{3,4} This might explain the rarity of combined PCV and RP, because PCV is considered to belong to the pachychoroid spectrum disorders of the macula.⁵ Contrarily, decreased choroidal thickness has been reported in classic macular choroidal neovascularization (CNV), a change that might be considered more compatible with RP. There are two previous reports of RP cases that developed classic CNV, both of which responded well to intravitreal bevacizumab.^{6,7} Though the current case had a long history of RP and showed patchy hypo-fluorescent lesions in FAF, which might reflect the long duration of RP,⁸ choroidal

thickness was relatively preserved. It remains unclear why PCV became combined with RP in this case.

In certain circumstances, anti-VEGF drugs can adversely affect the systemic and ophthalmic circulation.^{9,10} However, the use of anti-VEGF drugs in eyes with RP has not been reported to cause these effects during treatment for macular edema¹¹ and CNV.^{6,7} Fortunately, previous and current reports on treatments for eyes with PCV in RP showed no clear adverse events during follow-up.² Furthermore, the current study showed positive effects on visual function after the administration of an anti-VEGF drug, even after more than two years of follow-up. However, anti-VEGF drugs, particularly aflibercept, can cause a reduction in choroidal thickness,^{12,13} and our finding of a temporary decrease in ocular blood flow after IVA should be considered as supplementary information in treating RP patients with PCV. The nature of changes in ocular blood flow after injection with anti-VEGFs remains a controversial topic. Studies of eyes with AMD that received IVA reported that choroidal blood flow was stable, but that retinal perfusion underwent a short-term reduction.^{14,15} Another study of AMD found that peripapillary choriocapillary flow decreased after injection with an anti-VEGF.¹⁶ Thus, past and current results lead us to speculate that, to some degree, the injection of anti-VEGFs affects ocular blood flow. Considering the potential risks associated with ocular ischemia, anti-VEGF drugs should be used for long-term treatment only after careful consideration and on a case-by-case basis, to preserve ocular blood flow.

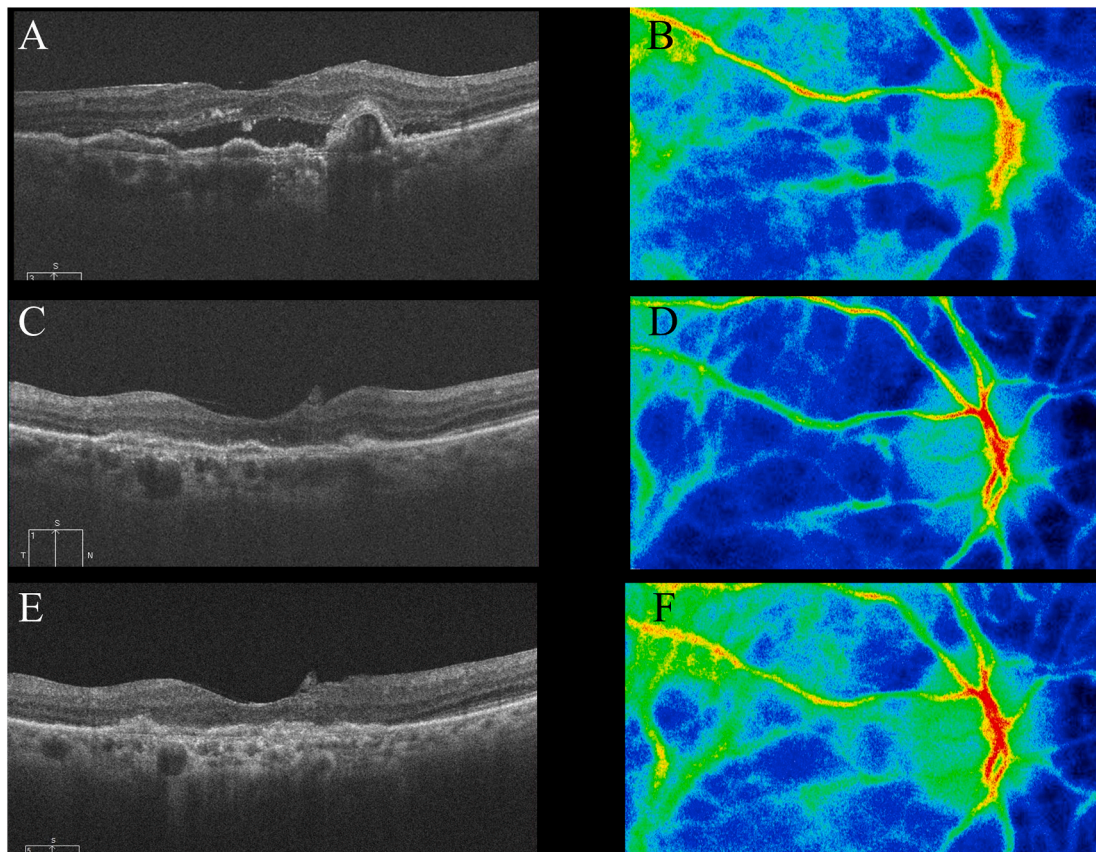


Fig. 3. OCT and LSFG images of the right eye before and after IVA treatment. A: OCT image before IVA treatment showing an SRD, a retinal PED and polypoidal lesion. B: LSFG color map before IVA treatment. The colors represent average blood flow during a single heartbeat. Warmer colors represent higher blood flow. C: OCT image after 3 IVA treatments. There is no SRD and no polypoidal lesion, although a slight PED remains. D: LSFG color map after 3 IVA treatments. Cooler-colored areas have increased compared to Fig. 3B, indicating decreased blood flow, including in the macula. E: OCT image 7 months after final IVA treatment, i.e., after 7 IVA treatments. There is no SRD and no polypoidal lesion, although a slight PED remains. F: LSFG color map 7 months after final IVA treatment, i.e., at the final follow-up. Warmer-colored areas have increased compared to Fig. 3D, indicating blood flow has returned to a similar level to Fig. 3B, including in the macula. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

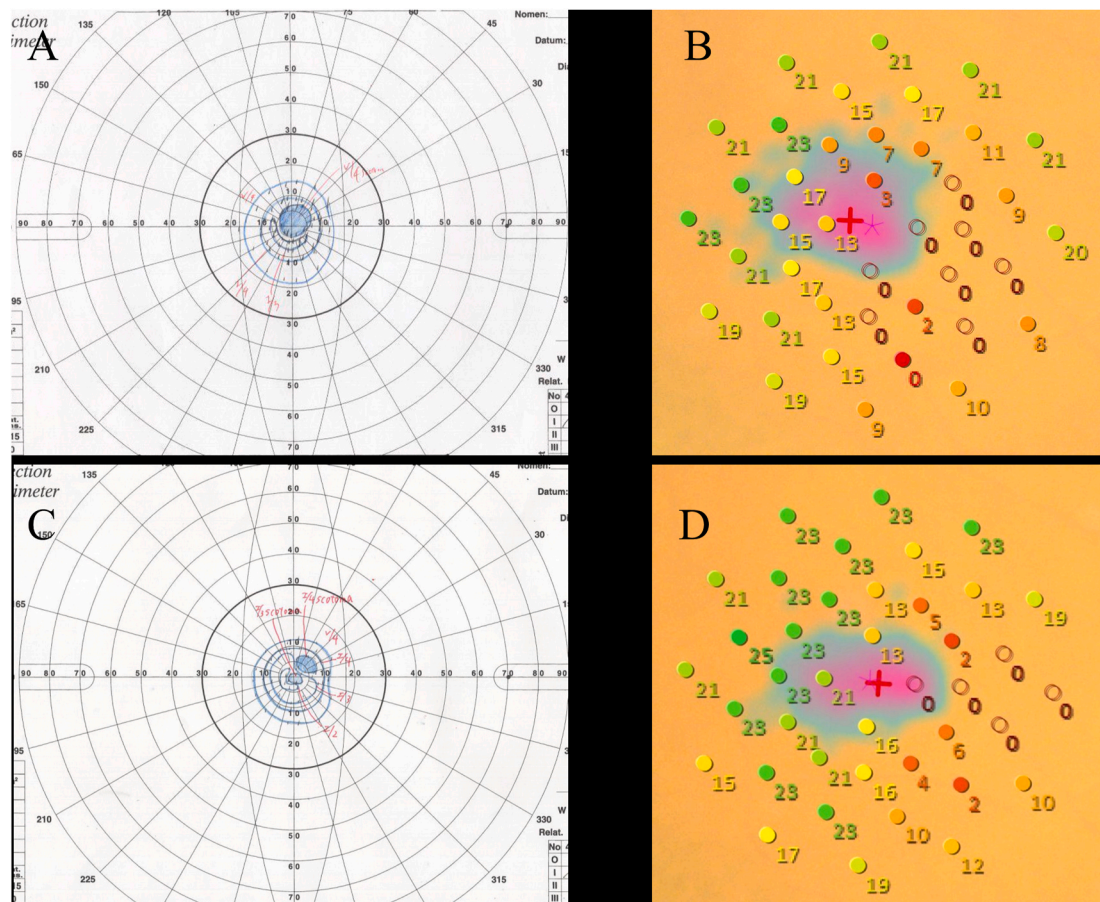


Fig. 4. Visual field overall and in the macula, before and after IVA in the right eye. A: GP-measured overall visual field before IVA, showing concentric constriction and central scotoma. B: Microperimetry-measured macular visual field before IVA, showing some points with decreased retinal sensitivity. C: GP-measured overall visual field after IVA, showing an improved visual field. D: Microperimetry-measured macular visual field after treatment, showing a remarkable number of points with increased retinal sensitivity.

In conclusion, more than 2 years of follow up showed that IVA may be effective for treating PCV, even in RP patients, and can increase central visual function without causing progression of RP-related visual field narrowing. We consider that further clinical experience will be necessary to develop the most suitable treatment regime for patients with RP combined with PCV, as well as with AMD in general.

Patient consent

Consent has been obtained from the patient.

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Author contributions

Involved in the design and conduct of the study were (H.K.); collection, management, analysis, and interpretation of the data (N.T., H.K., M.Y., T.H., and K.N.); drafting of the manuscript (N.T., and H.K.); and review, or approval of the manuscript (T.N.).

N.T., and H.K. wrote the main manuscript text and prepared all figures. All authors reviewed the manuscript.

Authorship

All authors attest that they met the current ICMJE criteria.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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