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Selective retina therapy for subretinal fluid associated with choroidal nevus

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ABSTRACT

Purpose: To report a case of a patient with subretinal fluid (SRF) associated with choroidal nevus (CN), who was treated with selective retina therapy (SRT) and ultimately achieved resolution of the SRF.

Observations: A 41-year-old man with SRF associated with CN in his right eye (RE) underwent ophthalmologic evaluation, including optic coherence tomography, fluorescein angiography (FA) and indocyanine green angiography. The best corrected visual acuity (BCVA) converted to the logarithm of the minimum angle of resolution (logMAR) was 0.00 in the RE. SRT (532 nm, 1.7 μs pulse duration, 30 pulses in 100Hz; Medical Laser Center Lübeck) was performed with the laser spots equally distributed across the FA leakage area. Until 20 months SRT was repeated several times because the SRF decreased every time in response to SRT, but was not completely resolved and sometimes increased with time. After performing 6 times of SRT session, leakage on FA stopped at 21 months follow-up and SRF was resolved at 31 months. At 60 months after the first SRT, there were no signs of malignant transformation, no SRF, and the BCVA in the RE was 0.22.

Conclusions and Importance: SRT seems to be a useful treatment and proper clinical studies are necessary to establish the best treatment protocol for SRF associated with CN.

1. Introduction

A choroidal nevus (CN) is a common benign choroidal tumor that arises from neural crest-derived melanocytes that is found a 1.4–2.9% prevalence in an Asian population.[1,2] Although it is usually asymptomatic, 10% of patients with CN develop symptoms of decreased visual acuity.[3] Vision loss should be anticipated in patients with subfoveolar CN, particularly those with overlying retinal pigment epithelial (RPE) detachment, orange pigment, and foveal edema. Choroidal neovascularization or subretinal fluid (SRF) that extends beneath the fovea also cause vision loss. Treatment methods include direct photocoagulation of the leakage site, photodynamic therapy (PDT), transpupillary thermotherapy (TTT) and intravitreal bevacizumab (IVB).[4–7] However, these may not be sufficiently effective or may induce malignancy,[4–6] and an effective method of treatment has yet to be established.

Selective retina therapy (SRT) was developed as a laser procedure in which the RPE is selectively broken down through a microbubble formation within RPE cells. This treatment does not induce thermal diffusion in surrounding tissues, which enables selective RPE disruption without affecting the neural retina or choroid.[8–11] Several reports have revealed that SRT was effective for central serous chorioretinopathy (CSC) and diabetic macular edema (DME).[12–15] Since thermal diffusion beyond the RPE melanosomes does not occur, and thus there is no thermal damage on the neurosensory retina in SRT, it can be expected that SRT may be suitable for the treatment of the central macular region.

Previously, we reported the safety of SRT for CSC of Japanese patients using microperimetry after three months.[15] This report describes a case of a patient with the CN-associated SRF who was treated with SRT and ultimately achieved resolution the SRF.

2. Case report

A 41-year-old man with metamorphopsia in his right eye (RE) for 4 years was referred to our department. At the first visit, best corrected

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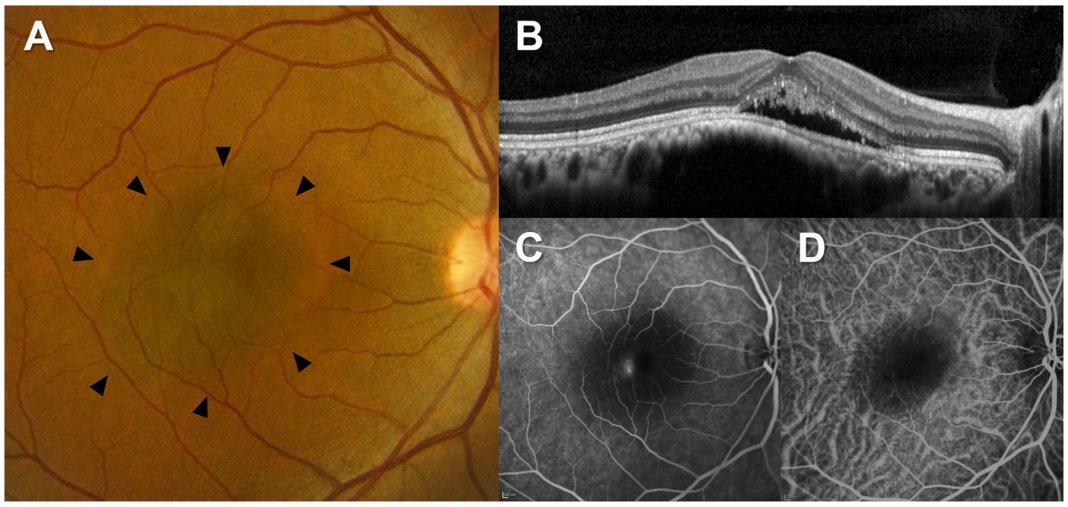

Fig. 1. Composite of photographs at pretreatment of SRT.
Color fundus photograph (A), optic coherence tomography (B) fluorescein angiography (C) and indocyanine green angiography (D). (A) Arrow heads indicate the approximate range of the choroidal nevus. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

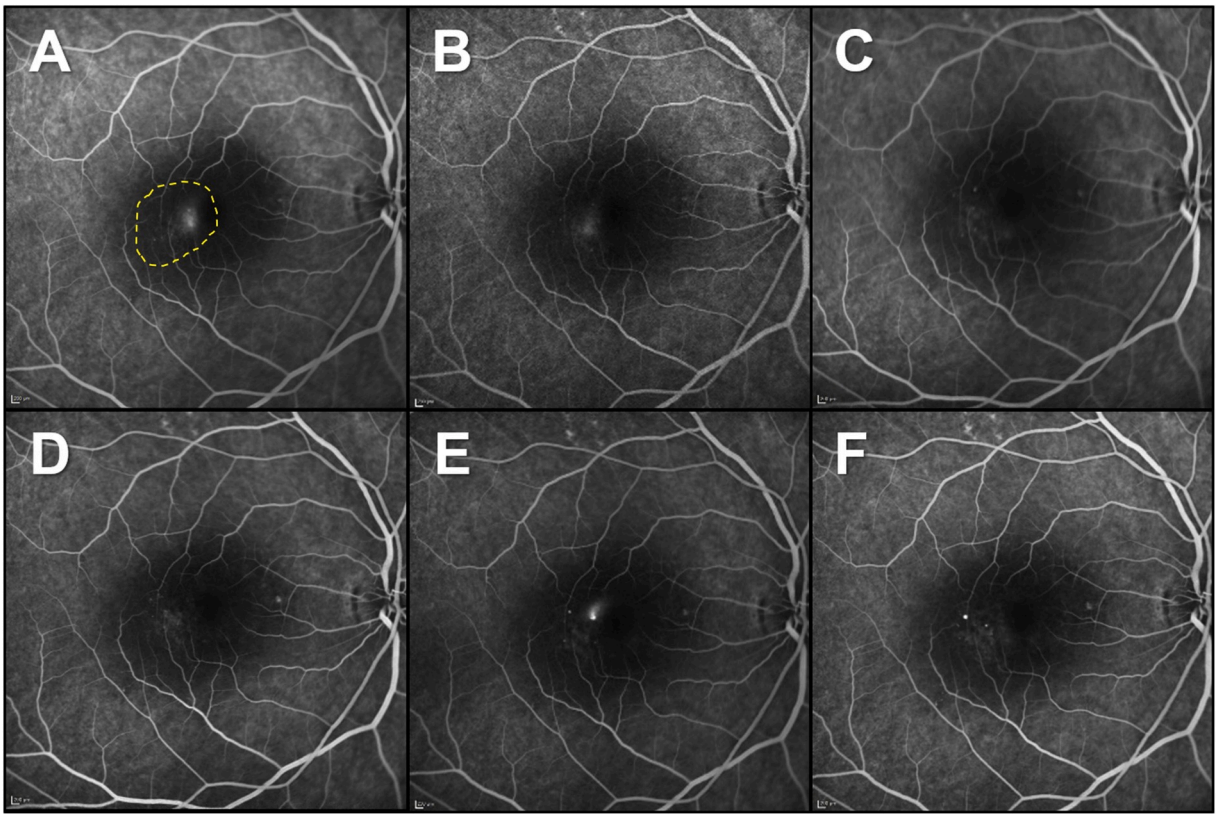

Fig. 2. Fluorescein Angiography at the time of SRT. Follow-up of pretreatment (A), at 3 months, before the second SRT (B), at 9 months, before the third SRT (C), at 12 months, before the fourth SRT(D), at 15 months, before the fifth SRT (E), at 18 months, before the sixth SRT (F).

visual acuity (BCVA) in logarithm of the minimum angle of resolution (logMAR) was 0.00 in the RE and −0.30 in the left eye (LE). Biomicroscopic fundus examination of RE disclosed a circular region of a darker pigmentation with a diameter of about 2 disc diameter in the macular region including fovea accompanied with the SRF (Fig. 1A, arrow head). Optical coherence tomography (OCT) showed SRF and a hyporeflective choroidal lesion beneath RPE suggesting CN (Fig. 1B). Fluorescein angiography (FA) showed hypofluorescence in the early phase and punctate hyperfluorescence in the late phase (Fig. 1C) at the CN, indicating diffuse dye leakage. Indocyanine green angiography (IA) showed hypofluorescence from early phase to late phase (Fig. 1D). Based on the angiography and the OCT findings with no choroidal neovascularization or the other fibrous membranes, we made a diagnosis of SRF associated with CN. Two months after the first visit, SRF still remained and thus any intervention was considered as desirable for the resolution of SRF. Since the leakage point was close to the subfovea, conventional laser photocoagulation was avoided, and SRT was selected. Written informed consent was obtained from the patient, and

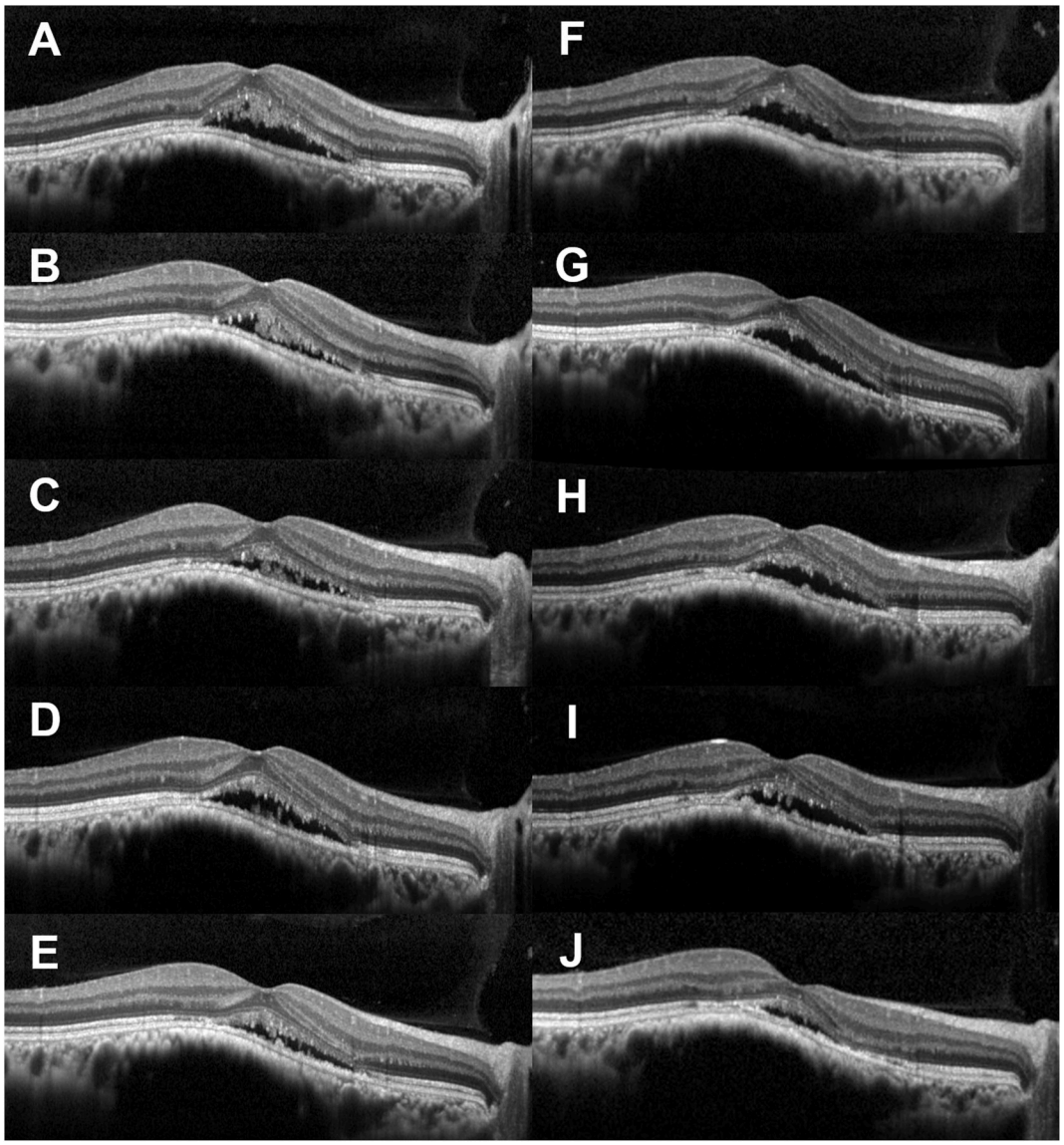

Fig. 3. Optic coherence tomography before and after selective retina therapy. Follow-up of pretreatment (A), at 1 month (B), 2 months (C), 3 months (D), 6 months (E), 9 months (F), 12 months (G), 15 months (H), 18 months (I), and 24 months (J).

SRT was performed. SRT was carried out with the approval of the local Ethics Committee of our hospital and registered with University hospital Medical Information Network (UMIN) (No. 000010471). The SRT laser system (Medical Laser Center Lübeck, Lübeck, Germany, prototype) utilizes a Q-switched pulsed, 527nm Nd:YLF laser with second harmonic generation. The pulse duration was 1.7 μs, with pulse frequency of 100 Hz, and 30 pulses per irradiation. A Mainster central field contact lens with a magnifying power of 1.05 was used and adjusted so that the spot size at retina becomes 200 μm. For the energy titration test irradiation was made outside the vascular arcade. The microbubble detection for each irradiation was conducted using an optoacoustic method as previously reported,[15] and the energy range for the selective RPE destruction can be indicated by the optoacoustic (OA) value. After deciding the treatment energy, the treatment was performed at and around the leakage points assessed with FA (Fig. 2A, dotted circle), giving an interval between spots of about one spot diameter.

Following the first SRT, the SRF decreased gradually, but increased after 3 months (Fig. 3B–D), while the leakage on FA decreased (Fig. 2B). A second SRT session was then therefore performed. The SRF again decreased, but still remained at 6 months (Fig. 3E). Nine months after the first SRT, the SRF increased again (Fig. 3F), thus two further SRT sessions were performed at 9 and 12 months after the first SRT (Fig. 2C and D). At 15 months after the first SRT, a different leakage site from the first one was observed on FA (Fig. 2E), and the SRF had also deteriorated (Fig. 3H). Two further SRT sessions were therefore performed at 15 and 18 months after the initial session (Fig. 2E and F). The SRF decreased again gradually (Fig. 3H–J), disappearing at 31 months after the first SRT with no leakage on FA (only window defect) (Fig. 4A–D). BCVA (logMAR) in the RE at this period was 0.30 and thinning of the outer layer of the central retina was observed. At 60 months after the first SRT, there were no recurrence of SRF, no signs of malignant transformation, such as an increase in size of the choroidal nevus or neovascularization (Fig. 4E and F). The BCVA (logMAR) in the RE had been slightly increased and showed 0.22 at 60 months, without any symptom of scotoma. Time courses of central macular thickness (CMT) and logMAR BCVA is shown in Fig. 5. Details of all SRT sessions are shown in Table 1.

3. Discussion

Ten percent of patients with CN develop symptoms of decreased visual acuity, and patients with subfoveolar nevus (26%) are significantly more likely to develop reduced visual acuity compared to those

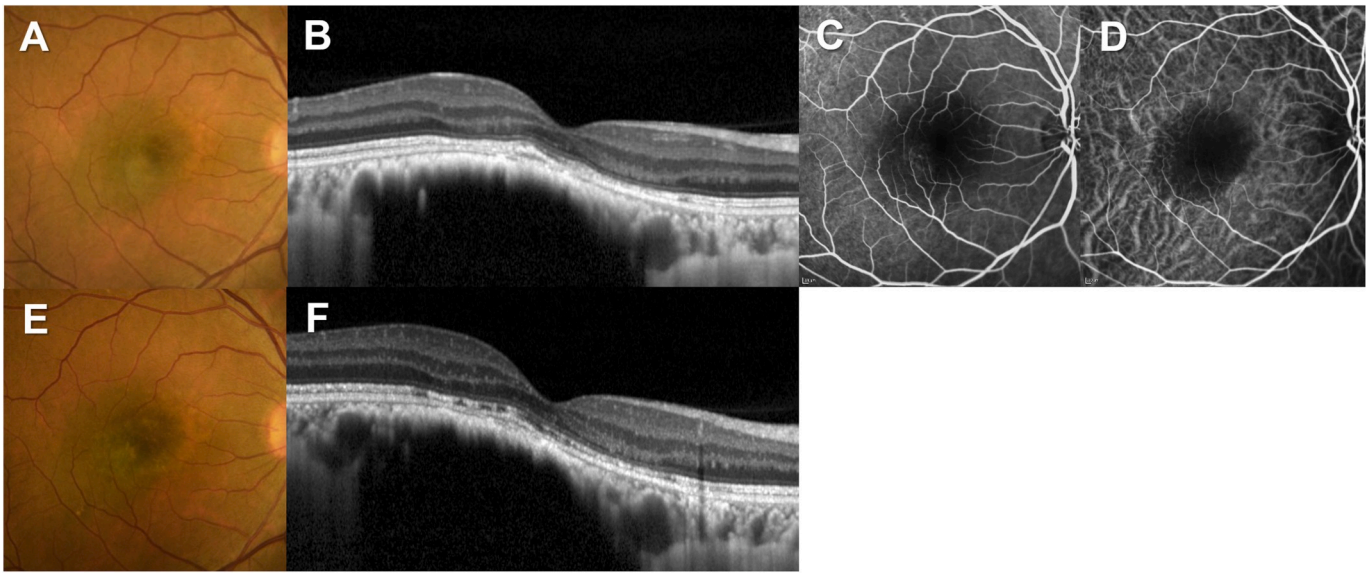

Fig. 4. Composite photographs after 31 months (A–D) and 60 months (E, F) of selective retina therapy. Color fundus photograph (A, E), optic coherence tomography (B, F), fluorescein angiography (C) and indocyanine green angiography (D). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

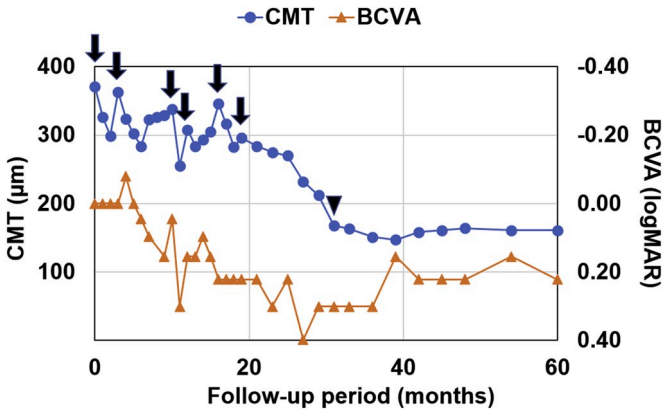

Fig. 5. The time course of changes in central macular thickness and best corrected visual acuity (in logMAR). Notes: The arrow shows the timing of SRT and the arrow head shows the timing of the complete resolution of subretinal fluid.

Table 1
Details of SRT sessions.

SRT session	Duration from initial SRT (Months)	Number of Irradiation (Spots)	Energy (μJ); Mean (Range)		OA value; Mean (Range)	
1	–	12	114	(100~132)	309	(102~825)
2	3	12	110	(89~126)	309	(105~557)
3	9	16	84	(69~92)	196	(52~775)
4	12	17	98	(80~127)	176	(30~645)
5	15	13	78	(70~105)	664	(96~1567)
6	18	20	84	(78~97)	274	(126~928)

with extrafoveolar nevus (2%) in 15 years.[3,16] Chronic SRF with CN may induce photoreceptor morphology change.[17] Several reports have proved the efficacy of PDT or TTT in the treatment of SRF with CN, while malignant transformation or tumor growth was seen in 18% to 35% of cases and required radiation therapy.[4–6] IVB was not effective in reducing SRF with CN but therapeutic response of SRF to IVB is suggested to be useful as an indicator between melanoma and nevus, where the SRF associated with melanoma may be highly possibly refractory to IVB.[7] In the present report, although it was only one case, complete resolution of the SRF was achieved by patiently treating leakage point at the RPE with repeated SRT, without malignant transformation and recurrence of SRF over 60 months follow-up.

It is conjectured that the primary reason for the occurrence of SRF in CN is the degeneration of the RPE by tumor cells.[17] These tumor cells cause the accumulation of lipofuscin in RPE cells, dedifferentiate, and generate mucoid inclusion bodies, causing SRF. RPE dysplasia is also associated with choroidal neovascularization and development of disciform scar. Another suggested reason is the destruction of the choriocapillaris by the tumor.[18] The decrease in the choriocapillaris induces secondary degenerative atrophy of the RPE, causing SRF accumulation. The persistent SRF may cause the degenerative atrophy of the RPE and photoreceptor, causing decreased visual acuity if it progresses around the foveola.[19] In the presented case, it took 31 months until the SRF has completely resolved since the patient began to be treated with SRT. Moreover, it had taken already 4 years with subjective symptoms without treatment before being referred to us. Therefore, the thinning of the outer retinal layer and the decrease of visual acuity in this case are considered to be due to the persistent SRF for years. Unfortunately, more detailed examination for retinal function such as microperimetry or multifocal electroretinogram was not performed during this follow-up. Recently, OCT angiography has been more common and less invasive for examining retinal circulation. These will be considered necessary for future clinical trials.

SRT disrupt the RPE cells only at the site of irradiation, stimulate RPE cell migration and proliferation into irradiated areas to improve the metabolism and function at affected areas. Although treatment was focused on the leakage sites in the presented case, SRF resolution could be accelerated through the modification of the method and the timing of additional SRTs.

In conclusion, SRT seems to be a useful treatment for the SRF associated with CN. However, further clinical studies would be desirable to establish the best treatment protocol.

Patient consent

The written consent was obtained from the patient.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

The following authors have no financial disclosures: (MY, YM, AK, KH,TK, DTK, RB, SH).

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