



# Choroidal Neovascularization in a Female Carrier of Ocular Albinism with a *GPR143* Mutation: A Case Report

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Dear Editor,

Ocular albinism type 1 (OA1) is a genetic disorder that is related to the melanin pigment and affects only the eyes. OA1 is caused by mutations in a G protein-coupled receptor 143 (*GPR143*) gene, which is specifically encoded on Xp 22.2 [1].

OA1 is a milder form of albinism that is characterized by reduced visual acuity, nystagmus, photophobia, reduced iris pigmentation, foveal hypoplasia, and abnormal development of the visual pathway [2]. Because OA1 is an X-linked disorder, OA1 usually manifests in males, while females act as carriers. Female carriers are mostly asymptomatic, but they occasionally may have “mud-splattered” or peripheral “mottled” retinal pigment changes, and rarely iris translucency or hypopigmentation. Herein, we report a case of incidental choroidal neovascularization in an ocular albinism carrier with a *GPR143* mutation. Written informed consent for publication of the study details and clinical images was obtained from the patient.

A 37-year-old woman and a 4-week-old girl visited Keimyung University Dongsan Medical Center (Daegu, Korea) for the evaluation of multiple retinal pigmentary changes in both eyes. The infant did well with fixation and following, and had no other unusual findings. A dilated

fundus examination revealed multiple “mud-splattered” hyperpigmentation in both eyes (Fig. 1A, 1B). The rubella immunoglobulin M and rubella polymerase chain reaction tests were negative, but next-generation sequencing based gene panel testing revealed a heterozygous mutation in the *GPR143* c.733C>T (p.Arg245\*), which is known as a pathogenic variant causing OA1.

Her mother also underwent an eye exam. The uncorrected visual acuity of the mother’s right eye was 20 / 20, the uncorrected visual acuity of her left eye was 20 / 40, and the refractive error was −0.50 cylindrical diopter 180° axis in the right eye and −0.25 spherical diopter in the left eye. Since the age of 20 years, her vision in left eye deteriorated due to macular degeneration. The fundus examination showed macular scar in the left fovea and blotchy pattern of retinal pigmentations in the peripheral retina of both eyes (Fig. 1C, 1D). Autofluorescence (AF) images showed a mixed pattern of hyper- and hypo-AF consistent with scattered areas of pigmentation (Fig. 1E, 1F). Swept-source optical coherence tomography (OCT) horizontal cross-section scan showed a hyper-refractive nodule with photoreceptor disruption above pachychoroidal vessels (Fig. 1G), and *en face* OCT angiography showed irregular choroidal neovascular vessels in the outer retina and choriocapillaris slab (Fig. 1H). The genetic test detected the same heterozygous mutation (c.733C>T) in *GPR143* (Fig. 1I).

To date, there have been no reports related to macular changes, other than case reports of a smaller than normal foveal depression and a narrow foveal avascular zone in OA1 carriers [3,4]. So, this is questionable whether choroidal neovascularization occurs frequently in OA1 patients

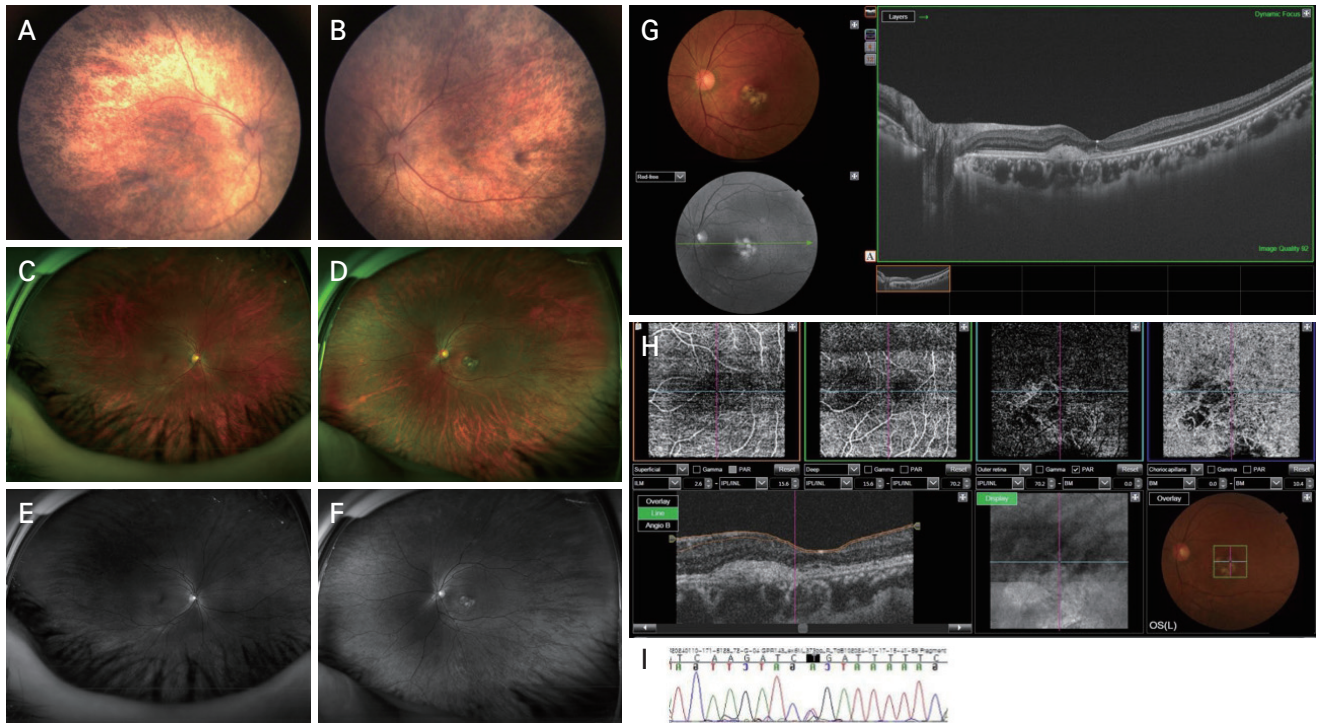
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**Fig. 1.** Multimodal imaging and genetic findings in a mother and daughter with ocular albinism. (A, B) Fundus photography of a daughter carrier with ocular albinism showing multiple “muddy” hyperpigmentations in both eyes. (C-F) Fundus photography of a mother carrier with ocular albinism showing peripheral pigmentary changes in both eyes and macular scarring in left eyes. (G) Horizontal cross-section of swept-source optical coherence tomography showing a hyper-refractive nodule with photoreceptor disruption above pachychoroidal vessels. (H) Optical coherence tomography angiography showing a thread-like vascular network of choroid neovascularization in the outer retina and choriocapillaris slab. (I) G protein-coupled receptor 143 (*GPR143*) genetic mutation profile in the mother carrier. The genetic test detected the same heterozygous mutation (c.733C>T) in *GPR143*.

as well as carriers.

In the retina, expression of *GPR143* was found only in the retinal pigment epithelium (RPE) [1]. If the activity of *GPR143* is abnormal or insufficient, the melanin synthesis process in RPE cells may still be normal, but the melanosome has an irregular shape and increases in size, eventually forming a “macro-melanosome” [1,2]. Therefore, if there is an abnormality in the pigment formation pathway of the RPE, various changes in the level of paracrine secretions from the RPE may occur.

One of the important agonists of *GPR143* protein is L-dihydroxyphenylalanine (L-DOPA). It is the first by-product converted from L-tyrosine by tyrosinase during melanin synthesis [1,2]. RPE cells produce and release L-DOPA on their own, and *GPR143* signaling in response to L-DOPA binding increases the secretion of pigment epithelium-derived factor (PEDF), which is a potent neurotrophic factor, decreases the secretion of vascular endothelial growth factor (VEGF), which is a potent angio-

genic factor. Many studies have suggested that decreased *GPR143* activity due to genetic differences or the aging process leads to decreased PEDF and increased VEGF secretion, which in turn leads to lesions such as macular degeneration [1,2,5].

In conclusion, this is the first case of choroidal neovascularization in a young OAI female carrier with a *GPR143* mutation. Although the association between *GPR143* abnormalities and choroidal neovascularization is uncertain at present, it is recommended that patients with OAI or female carriers undergo follow-up examinations to identify macular changes.

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