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Unsuccessful transscleral cyclophotocoagulation in oculocutaneous albinism

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ABSTRACT

Purpose: To report a case of unsuccessful transscleral cyclophotocoagulation in a patient with OCA1A tyrosinase-negative oculocutaneous albinism.

Observations: A 35-year-old Asian female with molecularly diagnosed OCA1A (tyrosinase-negative) oculocutaneous albinism and unilateral severe mixed mechanism glaucoma underwent transscleral cyclophotocoagulation on two separate occasions to treat elevated intraocular pressure. The intraocular pressure remained markedly elevated approximately 1 month following two separate treatments of transscleral cyclophotocoagulation while using high energy settings. The poor efficacy of both cyclophotocoagulation treatments was most likely due to a lack of melanin in the setting of oculocutaneous albinism.

Conclusions and importance: Cyclophotocoagulation in patients with oculocutaneous albinism is less likely to yield a desired lowering of intraocular pressure due to the absence of melanin.

1. Introduction

Transscleral cyclophotocoagulation (CPC) is a commonly used option for the treatment of refractory glaucoma via the destruction of ciliary body secretory epithelium, ultimately leading to the reduction of aqueous humor production.[1–3] We present a case of unsuccessful transscleral CPC, despite high energy levels, in a patient with OCA1A (tyrosinase-negative) oculocutaneous albinism. Understanding the melanin-dependent pathophysiology of CPC is important in determining patient candidacy. Based upon our case, CPC may be ineffective in patients with oculocutaneous albinism.

2. Case report

A 35-year-old developmentally delayed Asian female with presented to clinic with classic amelanotic features of oculocutaneous albinism (Fig. 1). She has a molecular diagnosis of autosomal recessive OCA1A (tyrosinase negative) oculocutaneous albinism that is consistent with her clinical findings. She has been followed for mixed mechanism glaucoma of the right eye (Fig. 1). Her left eye had been enucleated for end-stage neovascular glaucoma. In her right eye, she has a past surgical history of phacoemulsification with intraocular lens insertion that was complicated by medically-treated intraoperative aqueous misdirection, and later had an emergent Ahmed Seton with corneal patch graft for an intraocular pressure (IOP) spike to 70 mmHg. Although she had temporary IOP control following this surgery, her IOP increased to 27 mmHg on maximum medical therapy including timolol, netarsudil, latanoprost, and brimonidine. She previously developed a severe case of Steven- Johnson syndrome from methazolamide, so all carbonic anhydrase inhibitors have subsequently been avoided. Her visual acuity is stable at 20/400. Due to her developmental delay, we are unable to obtain visual field or optical coherence tomography to assess the progression her glaucoma.

Given the prior history of aqueous misdirection in this monocular patient, incisional surgery was felt to be risky. A “slow burn” transscleral CPC of the right eye was performed. A total of 21 spots were applied at a power of 1250 mW and duration 3500–4000 milliseconds sparing only the area over her prior Seton implant. She was placed on a weekly prednisolone taper starting from four times a day. One month following the CPC, her IOP had increased to 40 mmHg. The patient underwent repeat CPC, this time using 24 spots with a power raging from 2000 to 3000 mW at a duration of 2000–2500 milliseconds, again only sparing the area over the prior Seton implant. Despite increasing energy, no pops

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Abbreviations

CPC	Cyclophotocoagulation
IOP	Intraocular pressure
Nd:YAG	Neodymium: yttrium-aluminum-garnet
ACMG	American College of Medical Genetics

were heard. She was again placed on a weekly prednisolone taper starting at four times a day. One week following the second CPC, her IOP was 34 mmHg, and by her one month follow up appointment, her IOP was still slightly higher than her pre-operative IOP at 30 mmHg. No post-operative complications were seen at any of her post-operative visits, including prolonged anterior chamber inflammation. After a second unsuccessful CPC despite high energy, the decision was made to proceed with a second Ahmed Seton.

3. Discussion

This patient with oculocutaneous albinism was adopted and no family medical history is available. Genetic testing with a 30-gene Pigmentation Panel was obtained from a CLIA-approved commercial lab (Molecular Vision Laboratory, Hillsboro, OR), which revealed two tyrosinase (*TYR*) gene variants, c.863delT p.Leu288Tyrfs*31 and c.1283C > T p.Pro428Leu. The c.863delT mutation is a frameshift mutation that disrupts several functional domains in the encoded tyrosinase protein[4] and has been previously reported as a loss-of-function, pathogenic mutation in a Korean patient with OCA1A.[4] A different *TYR* frameshift mutation that affects the same codon has also been reported, c.862_863delTT p.Leu288Metfs*12.[5] Analyses of the novel missense variation (p.Pro428Leu) with 5 different algorithms, suggests that it is likely pathogenic (Table 1). Both *TYR* variants are absent from a large control population,[6] as would be expected for rare, albinism-causing mutations. Finally, the p.Leu288Tyrfs*31 and p.Pro428Leu *TYR* gene variations are classified as pathogenic (PSV1, PS1, PM2, PP4) and of unknown significance (PM2, PP3, PP4) respectively by American College of Medical Genetics (ACMG) standards[7,8] and are the likely cause of her albinism.

Since its development in the 1930's, cyclodestructive therapy has been a viable option for refractory glaucoma by reducing aqueous humor production through the destruction of the ciliary body secretory epithelium.[1,2] Modern-day cyclodestructive therapy most commonly involves CPC that is delivered either endoscopically or transsclerally.[2,3]

CPC uses a diode laser with a 810nm wavelength, which has been shown to be the wavelength that has the maximal absorption by melanin within the ciliary processes compared to prior CPCs performed with neodymium: yttrium-aluminum-garnet (Nd:YAG) lasers.[2,9,10] Through this mechanism, focused energy is selectively delivered to the ciliary processes with low risk for damaging neighboring ocular tissue.[9,10]

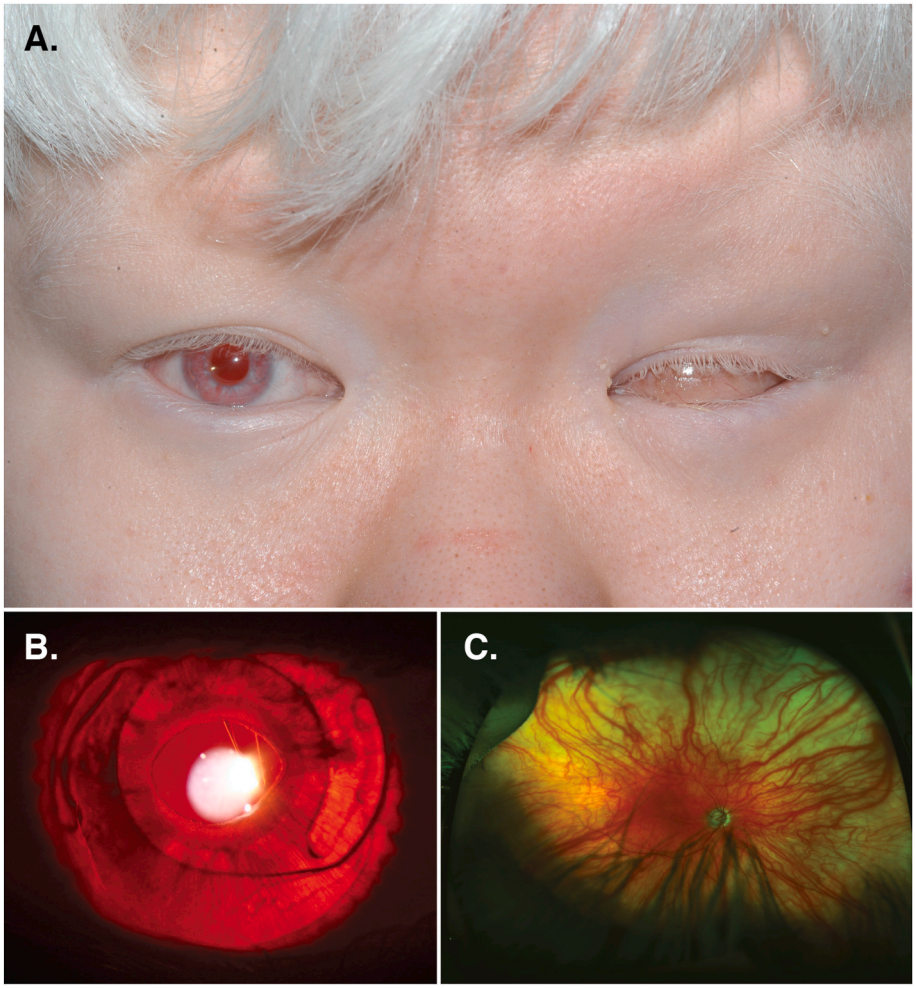

Fig. 1. A. External photograph demonstrating amelanotic features, including skin, hair, and irides. Her left eye has a conformer in place following enucleation. **B.** Complete transillumination of the right iris with underlying posterior chamber intraocular lens fully visible. **C.** Wide-field fundus photograph of non-pigmented retina.

Table 1
Analysis of the novel missense variation with five separate algorithms evaluating for likelihood of pathogenicity.

OCA1 variant		SIFT	PolyPhen2	Blosum62	MutationTaster	CADD
c.1283C > T	p.Pro428Leu	Deleterious (0)	Probably damaging (1.0)	−3	Disease-Causing (98)	26.6

Cantor et al. demonstrated this pigment-dependent mechanism in rabbits. Transscleral CPC performed on control rabbits with normal pigmentation revealed robust necrosis of the ciliary body's pigmented epithelium which ultimately led to complete obliteration of the ciliary processes, while albino rabbits were unchanged histologically.[11]

Our case showed transscleral CPC to be ineffective, despite high energy levels, in a patient with OCA1A tyrosinase-negative oculocutaneous albinism. We hypothesized that the increased vascularity of the ciliary body would contain enough non-melanin pigment within the hemoglobin to absorb energy, but the 810nm wavelength of CPC is within the red spectrum and least absorptive for blood.

4. Conclusion

In this patient with OCA1A tyrosinase-negative oculocutaneous albinism, CPC was attempted but found to be ineffective despite high energy levels. Understanding the melanin-dependent pathophysiology of CPC is important in determining patient candidacy. This case suggests that CPC may be ineffective in cases of oculocutaneous albinism, and these results should be considered in similar cases with little or no melanin.

Patient consent

A written informed consent was obtained from the patient's parents.

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Authorship

All authors attest that they meet the ICMJE criteria for authorship.

CRediT authorship contribution statement

Aaron D. Dotson: Writing – review & editing, Writing – original draft, Methodology, Investigation, Data curation. **John H. Fingert:** Writing – review & editing, Resources, Investigation, Formal analysis, Conceptualization. **Erin A. Boese:** Writing – review & editing, Writing – original draft, Supervision, Resources, Methodology, Investigation, Data curation, Conceptualization.

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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