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Pigmentation Artifact of "True-Color" Fundus Photography in Circumscribed Choroidal Hemangiomas

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Keywords
Choroidal hemangioma · Fundus photography · Photo artifact

Abstract

Introduction: Color characterization plays an important role in the diagnosis of choroidal hemangiomas. Hence, fundus photography is a critical ancillary test in the recognition of this disease. We report a color artifact with "true-color" fundus imaging that can lead to a more pigmented appearance of these lesions resulting in incorrect diagnosis. ***Methods:*** This was a single-center retrospective study with chart and imaging review of patients with a diagnosis of choroidal hemangioma from October 2007 to October 2024. Fifteen cases with multimodal confirmation of the diagnosis with fundus photography, indocyanine green angiography, standardized echography, and optical coherence tomography were identified. All cases had fundus imaging with at least 2 different cameras. Pigmentation was graded by a retina specialist and the different fundus photography modalities as well as fundus examinations were compared. ***Results:*** Nine cases had artifactual "true-color" fundus photography with pigmentation. Six cases had a referring diagnosis of choroidal nevus or melanoma. All cases had multimodal imaging with a diagnosis confirming the diagnosis of choroidal hemangioma. Ten of 15 patients received photodynamic therapy, while 5 were observed. The average follow-up for patients was 36 months. ***Conclusion:*** Pigmentation artifact can be present in fundus photography of choroidal hemangiomas even with "true-color" fundus cameras. The Xenon lamp-based cameras tend to produce the most clinically accurate photos. This paper highlights the critical value of the clinical exam for the evaluation of choroidal hemangiomas.

Introduction

Choroidal hemangiomas are one of the more common intraocular vascular tumors with a characteristic reddish-orange color. This color, in addition to other characteristics such as high internal reflectivity and early hyper fluorescence with late washout on indocyanine green (ICG) angiography can distinguish circumscribed choroidal hemangiomas from other entities such as choroidal melanomas, nevi, or metastases [1, 2]. Recognizing

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choroidal hemangiomas is important given the benign nature of these tumors and the overall good response with interventions such as photodynamic therapy when visual function is compromised [3]. With the unique color of choroidal hemangiomas, fundus photography plays a significant role in guiding diagnosis and the clinician's decision-making.

While confocal scanning laser ophthalmoscopy (cSLO)-based ultra-wide-field imaging modalities such as Optos (Dunfermline, UK) are recognized as "pseudo-color" images, modalities with broader wavelength illumination ranges such as Clarus (Jena, Germany) and Topcon (Oakland, NJ, USA) have the theoretical advantage of capturing more true-to-life colors [4–6]. In the commonly used Clarus 500 fundus cameras, red, blue, and green light-emitting diodes (LEDs) sequentially illuminate to generate color images that are more comparable to images obtained with full-spectrum light sources. This includes red LED, 585–640 nm, green LED, 500–585 nm, and blue LED, 435–500 nm channels. The broad bandwidth of LEDs renders "true color" [6]. Topcon devices such as TRC-50DX, use a 300W Xenon flash bulb with a full spectrum and a color temperature of 5,000–6,000 K, which is similar to daylight [4, 5]. Xenon lamps are distinct in that they produce a largely continuous and uniform spectrum across the entire visible spectrum (380–700 nm) [7].

The artifact of pigmented appearance of choroidal hemangiomas in pseudo-color fundus photography via cSLO modalities has been described before [2]. In this paper, we describe 15 cases of choroidal hemangioma, confirmed with ICG angiography and echography, with multimodal fundus photography showing the artificial pigmented appearance that can occur even with "true-color" broad-wavelength LED illumination Clarus pictures. This tended to be less prominent with full-spectrum Xenon lamp-generated Topcon photos.

Methods

This was a retrospective study of clinical records and imaging acquired at a single tertiary referral center (University of Iowa Hospitals and Clinics) between 10 January 2007 and 10 January 2024. The study complied with the Health Insurance Portability and Accountability Act and the Declaration of Helsinki and was approved by the Institutional Review Board at the University of Iowa.

We reviewed patients seen within subspecialty retina clinics (E.B., H.C.B.) and included patients who had multimodal imaging with fundus photography of at least two of the following three modalities: Topcon 50DX (Topcon Inc.), Clarus 500 (Zeiss Inc.), Optos (Optos Inc.). All patients had diagnostic testing with ICG angiography and standardized echography, showing findings consistent with the diagnosis of circumscribed choroidal hemangioma. In all cases with follow-up, the clinical course remained consistent with the initial diagnosis. None of the lesions had diagnostic biopsy. Optical coherence tomography imaging was also performed in all cases using Spectralis (Heidelberg Inc.). The thickness of the lesions was measured via standard echography (ABSolu, Lumibird Medical) from the apex of the tumor to the inner sclera. When there was symptomatic subretinal fluid or the tumor led to metamorphopsia, full-fluence photodynamic therapy was performed with intravenous verteporfin administered at 6 mg/m^2, and 689 nm laser delivered at 50 J/cm^2 for 83 s covering the entire area of the lesion as described elsewhere [8].

Results

Six of the 15 cases had a referring diagnosis of a pigmented lesion such as choroidal nevus or melanoma (Table 1). Of these, 4 had brown pigmentation on Clarus photography at our center as well, one of which did not reveal such pigmentation on Topcon imaging. Nine cases in total, regardless of initial diagnosis, had a brown appearance on Clarus photography. Six cases had both Clarus and Topcon imaging of the lesion (note one had Clarus photography only post-treatment and is not shown in Fig. 1 due to the post-treatment artifact) (Fig. 1). Of note, on indirect fundus ophthalmoscopic examination, none of these lesions had brown pigmentation. ICG angiography revealed the previously described pattern of partial arterial filling with a dark center that fills in from periphery of the lesion during the venous choroidal filling [9]. On OCT, the previously described pattern of a smooth choroidal elevation with enlarged large choroidal vessels without displacement of the choriocapillaris was seen [10] (Fig. 2a). However, we also noted vascular cavitation in five tumors that tended to be more hypo-reflective than Haller's layer choroidal vessels and were relatively close to the choriocapillaris (Fig. 2b–e). Additionally, 5 cases revealed a lobular or lumpy surface of the tumor and not all cases had the completely smooth surface described before [10] (Fig. 2f). Twelve cases had subretinal fluid and five cases had prominent cystoid edema over the tumor. The tumor thickness on echography ranged from 1.4 to 3.9 mm. There were 6 females and 9 males, with ages from 38 to 90 years (mean 66). Ten patients received PDT therapy, while 5 were observed. The follow-up interval was 1–112 months (mean 36 months).

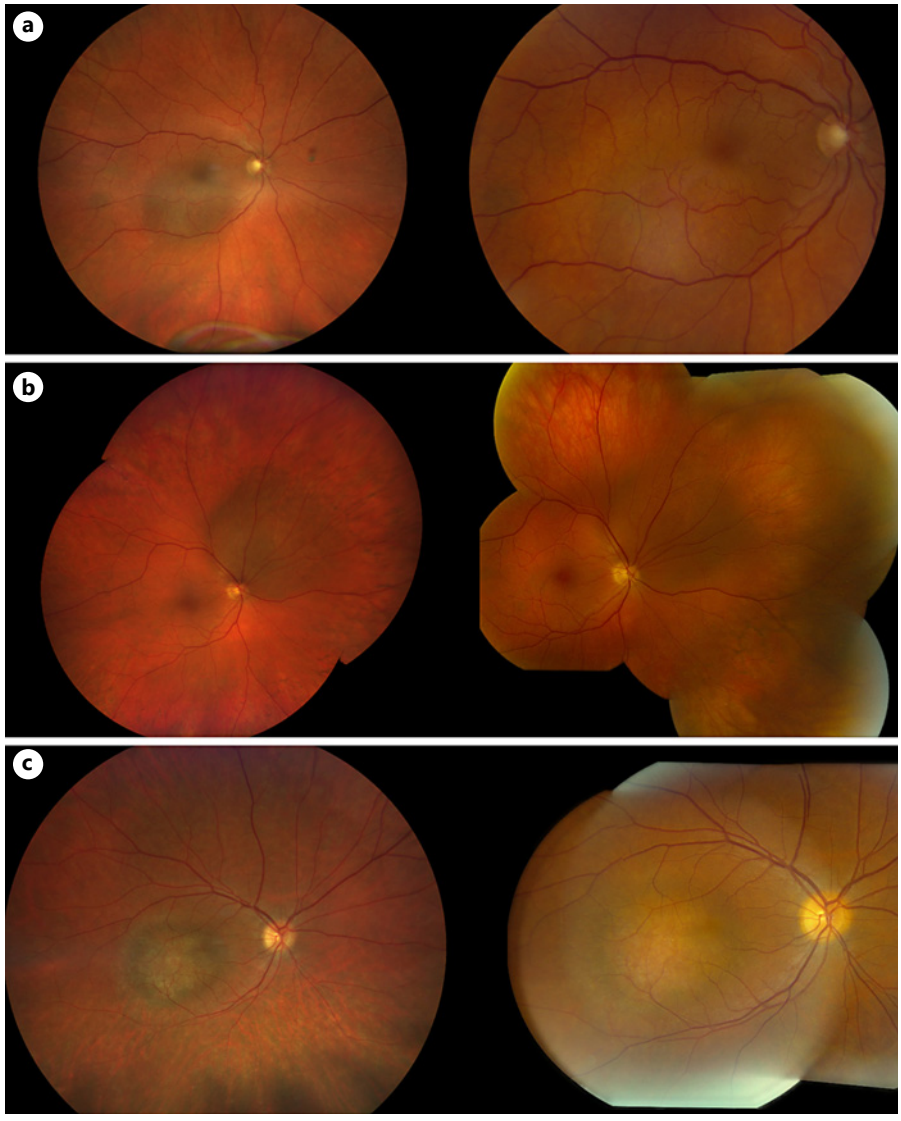
Table 1. Clinical characteristics and imaging findings of included patients

Case	Age	Referring diagnosis	Thickness, mm	Imaging	Pigment grade, Clarus	Pigment grade, Optos	Pigment grade, Topcon	Pigment grade, ophthalmoscopy	Treatment
1	90s	CSCR, amelanotic choroidal mass	2	Clarus, Optos	Moderate	Low	–	None	PDT
2	70s	Choroidal nevus	2.1	Clarus, Optos	None	None	–	None	PDT
3	80s	Eccentric CNVM vs. melanoma	2.9	Clarus, Optos	Moderate	Moderate	–	None	Observe
4	60s	Possible melanoma	3.9	Topcon	–	–	None	None	Observe
5	60s	Amelanotic choroidal melanoma	2.5	Topcon, Clarus	Moderate	–	Low	Low	Observe
6	50s	CH	3.3	Topcon, Optos	–	Moderate	Low	None	PDT
7	40s	CH	1.4	Topcon, Clarus	Low	–	Low	None	PDT
8	60s	CH	1.9	Topcon, Clarus	None	–	None	None	PDT
9	70s	Melanoma vs. met (hx of ca)	2.2	Topcon, Clarus	Moderate	–	None	None	Observe
10	60s	Choroidal melanoma	1.9	Clarus, Optos	Moderate	Moderate	–	None	PDT
11	30s	Choroidal mass	3.1	Clarus, Optos	Low	–	–	None	PDT
12	70s	Choroidal lesion	2.6	Topcon, Clarus, Optos	None	Low	None	None	PDT
13	70s	CH	2.5	Topcon, Clarus, Optos	Low	Low	None	None	PDT
14	70s	Choroidal nevus	2	Clarus, Optos	Moderate	Moderate	–	None	Observe
15	60s	CSCR, CH	1.4	Topcon, Optos	None	Low	–	None	PDT

CH, choroidal hemangioma; OCT, optical coherence tomography; ICG, indocyanine green angiography; PDT, photodynamic therapy; CNVM, choroidal neovascular membrane; CSCR, central serous chorioretinopathy; Echo, standardized echography.

Discussion

In this retrospective study, we highlight the phenomenon of brown pigmentation artifact in fundus photography for circumscribed choroidal hemangiomas. While this artifact has been previously described in pseudo-color cSLO-based imaging, it also can be seen with "true-color" LED-based illumination imaging, as used by the Clarus 500. This tends to occur less with full-spectrum Xenon illumination-based Topcon modalities. Hence, Topcon imaging may be the preferred fundus camera when the diagnosis of choroidal hemangioma is suspected. Similar to the previously reported brown pigmentation artifact of Optos images, "true-color"



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(Figure continued on next page.)

Clarus imaging can also produce erroneous brown pigmentation in choroidal hemangiomas that would lead to incorrect diagnosis of melanocytic lesions [1]. This may be due to the wider field of view obtained by the Clarus 500, leading to the capture of more color variations. This, in turn, may contribute to a more notable color differences as opposed to the smaller field of capture, and less color variance, of the Xenon based Topcon cameras. Additionally, the fact that the visible ranges of 380–435 nm and 640–700 nm are not utilized on the Clarus cameras LED illumination may also play a role.

Although a good fundus examination will typically allow for the recognition of the classic orange-colored appearance of choroidal hemangiomas, preliminary photography with brown pigmentation artifact can lead to pre-examination bias and erroneous diagnoses, especially given the relative rarity of choroidal hemangiomas. We could see this error in 6 of 15 referrals to our center with a primary diagnosis of choroidal melanoma or nevus. We suspect that this pigmentation artifact in various fundus photography modalities may have contributed to the incorrect preliminary diagnoses. The misdiagnosis of choroidal melanoma can be devastating to patients who have been informed of malignancy potential, while in fact their tumor of choroidal hemangioma is benign in nature. Our findings highlight the importance of a careful clinical exam with attention to the

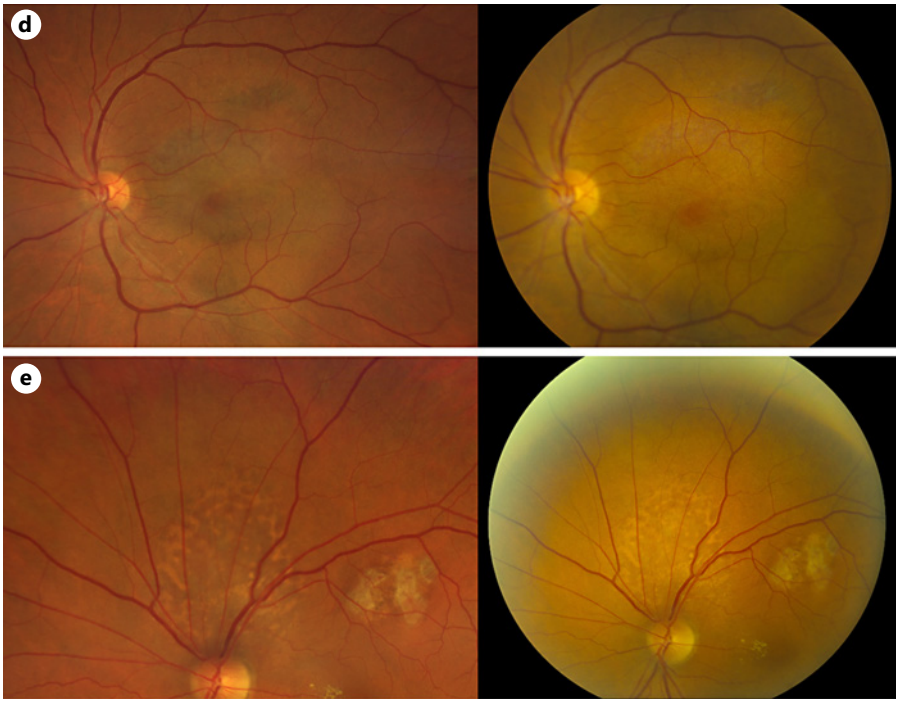

Fig. 1. a–e Clarus versus Topcon fundus images of choroidal hemangiomas. Images on the left of each pair show choroidal hemangiomas captured by Clarus 500 cameras, Topcon fundus photos are shown on the right. There appears to be a brown pigmented appearance to the Clarus 500 "true-color" images that could lead to an incorrect diagnosis of melanocytic lesions.

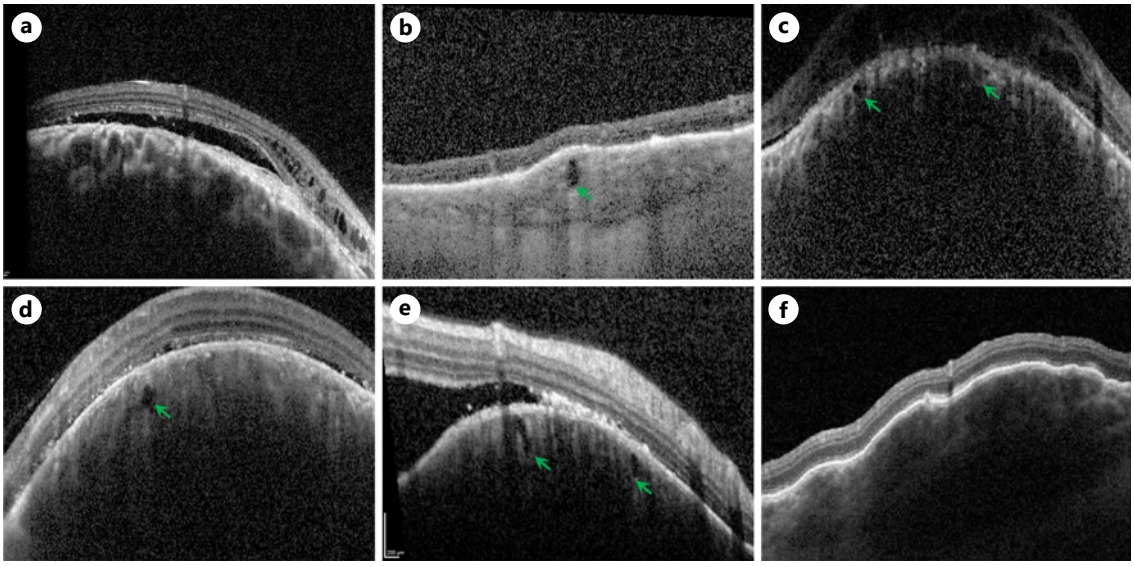

Fig. 2. Various optical coherence tomography (OCT) findings of choroidal hemangiomas noted. **a** The classic smooth choroidal elevation with enlarged large choroidal vessels. **b–e** Choroidal cavitations (green arrows) that are very hypo-reflective and relatively close to the surface of the lesions. Several cases demonstrated a lumpier, non-smooth, surface as exemplified in (**f**).

color of choroidal lesions. Even with a careful clinical examination, it can sometimes be difficult to distinguish choroidal hemangiomas from melanocytic lesions. Multimodal imaging that includes ICG angiography and echography are essential in addition to color fundus photography.

We also identified OCT features of choroidal hemangioma that have not been emphasized in the literature.

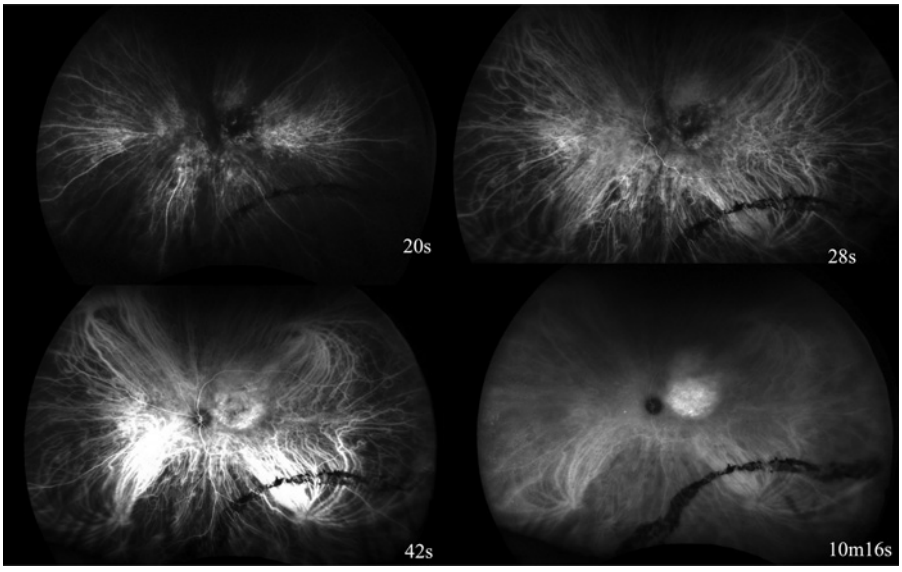

Fig. 3. Every case was confirmed by indocyanine green angiography (ICG) to have a pattern compatible with a diagnosis of choroidal hemangioma. In this exemplary case, four frames from the injection of the dye into the antecubital vein are displayed with the time indicated in the bottom right corner of each image. In the early phases, there is arterial flow into the choroidal hemangiomas with late pooling of cyanescens into a circumscribed space that tends to increase in intensity as the choroidal vascular cyanescens fades elsewhere in the later frames. Note artifact from prior laser inferotemporally that is unrelated to the hemangioma.

This includes the possibility of a lumpy or multilobular appearance to the lesion as well as the presence of unique hypo-reflective cavities within these lesions. The exact nature of these choroidal cavitations is unknown but could represent collapse or congestion of normal choroidal vasculature around intact Haller's vessels. On ICG angiography, we noted the previously reported small arterial flow into the choroidal hemangiomas with late pooling of cyanescens into a circumscribed space that tends to increase in intensity even as the choroidal vascular cyanescens fades (Fig. 3). This suggests a slow flow system and possibly a primarily venular composition of these vascular tumors.

In conclusion, this paper highlights a fundus photography artifact of a pigmented appearance to choroidal hemangiomas that can lead to incorrect diagnoses and the possibility of significant psychological and physical burden to patients. The clinician must be aware of these artifacts even in "true-color" imaging. Whether in triaging cases remotely or examining patients, a detailed clinical examination and appropriate additional ancillary testing is still vital for the accurate diagnosis of intraocular tumors. This becomes of increased importance in clinical applications of artificial intelligence where fundus photography is being used as a surrogate for clinical examination [11]. Our study highlights a potential limitation of reliance on fundus photography in ocular oncology, cautioning against less sophisticated artificial intelligence algorithms that would rely on pigmentation as a differentiating feature for tumors.

Statement of Ethics

This study protocol was reviewed and approved by the Institutional Review Board at the University of Iowa, Approval No. 202401210. The Institutional Review Board at the University of Iowa granted a waiver of written informed consent given the retrospective nature of the study.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Each author meets the ICMJE requirements for authorship. Research design: F.J. and E.B.; data acquisition/research execution: F.J., A.G., C.H., and E.B.; data analysis/interpretation: F.J., A.G., C.H., H.C.B., and E.B.; and manuscript preparation: F.J., A.G., H.C.B., and E.B.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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