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Multi-Modal Ultra-Widefield Imaging Features in Waardenburg Syndrome

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Abstract

Background—Waardenburg syndrome is characterized by a group of features including; telecanthus, a broad nasal root, synophrys of the eyebrows, piedbaldism, heterochromia irides, and deaf-mutism. Hypopigmentation of the choroid is a unique feature of this condition examined with multi-modal Ultra-Widefield Imaging in this report.

Material/Methods—Report of a single case.

Results—Bilateral symmetric choroidal hypopigmentation was observed with hypoautofluorescence in the region of hypopigmentation. Fluorescein angiography revealed a normal vasculature, however a thickened choroid was seen on Enhanced-Depth Imaging Spectral-Domain OCT (EDI SD-OCT).

Conclusion(s)—Choroidal hypopigmentation is a unique feature of Waardenburg syndrome, which can be visualized with ultra-widefield fundus autofluorescence. The choroid may also be thickened in this condition and its thickness measured with EDI SD-OCT.

Keywords

Waardenburg Syndrome; Choroid; Hypopigmentation; Enhanced depth imaging OCT; Ultra-Wide-field Imaging; Autofluorescence

Case description

A 45 year-old Caucasian female was referred for bilateral irregular fundus pigmentation. She denied any symptoms, past medical or ocular history. On clinical examination her best-corrected visual acuity was 20/20 OU with a normal slit-lamp examination. Dilated fundus

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examination revealed irregular hypopigmentation posterior to the equator in both eyes (Figure 1A-B). Ultra-widefield fluorescein angiography (UWFA) was normal in both eyes, (Figure 1C-D), while fundus autofluorescence (FAF) imaging demonstrated a bilateral hypoautofluorescence signal posterior the equator in the region of the hypopigmentation (Figure 2 A-B). Enhanced depth imaging SD-OCT (EDI-OCT) was performed revealing a thickened choroidal vasculature in both eyes (430 & 435 microns respectively) (Figure 2 E-F). The overlying retinal architecture was otherwise normal. Systemic evaluation revealed sensorineural deafness, telecanthus and a white forelock. Further investigation revealed a first-degree relative with Waardenburg syndrome and the diagnosis was confirmed.

Discussion

Waardenburg syndrome (WS) was first described as a developmental anomaly of the eyelids, eyebrows, nasal root, iris, scalp hair, and congenital deafness.¹ Waardenburg further delineated the six main characteristics comprising WS, including; (1) telecanthus, (2) a broad nasal root, (3) synophrys of the eyebrows, (4) a white forelock (piedbaldism), (5) heterochromia irides, and (6) deaf-mutism. The choroid was initially observed to be affected to a minor degree.¹

WS type 1 is inherited in an autosomal dominant pattern with a variable phenotype, even amongst family members.² In a series of 34 patients published by Dellman and Hageman, 10 of the 15 patients with pigmentary abnormalities of the iris also showed decrease pigmentation in the retina.³ Shields et al. recently described the anterior and posterior segment imaging findings in Waardenburg syndrome.⁴ In this series a similar hypopigmentation of the choroid was reported in all 9 eyes in two patterns: sectoral and diffuse.⁴ Similar to the reported case, all eyes had a normal retina, FAF signal demonstrated mild hypoautofluorescence (scleral unmasking), hypopigmented choroid without lipofuscin. In this series, the region of the hypopigmented foveal choroid was thinner, however in our patient, the hypopigmented foveal choroidal region in both eyes was thicker than normal (430 & 435 microns respectively). The small number of measurements in both reports (5 measurements from 2 eyes vs. 2 measurements from 1 eye) is too small to conclude a true distinction. There may be some degree of variation in this parameter in WS, however the relatively few numbers of patients precludes a true comparison. Moreover, the manual technique of choroidal segmentation may introduce variation in measurement. Thus in order to detect whether choroidal thickness in WS differs from normal subjects, more patients need to be studied.

Ultra-wide field imaging was not performed in the series published by Shields et al.,⁴ however in our patient UWF imaging reveals the extent to which the choroid is affected. Furthermore, examination of the choroid with red-filter highlights the contrast of hypopigmented choroid compared to normal choroid (Figure 2C-D).

The choroidal pigmentation variation in WS has been described as “hypopigmentation.”⁴ Review of the cases described earlier by Goldberg showed that some patients had choroidal “hyperpigmented areas.”⁵ Our case displayed variable pigmentation, with a darker choroid peripherally and a lighter pigmentation more posteriorly, which we termed as

“hypopigmentation” (Figure 1). Nevertheless, given the variability in the terminology described by Shields and Goldberg, we suggest using the term, “variable choroidal pigmentation,” to more accurately describe the fundus findings in WS.

Several conditions may resemble the choroidal features observed in WS such as choroidal nevus, choroidal melanoma, vitiligo and Vogt-Koyanagi-Harada Syndrome, ocular melanocytosis, and sectoral oculo (dermal) melanocytosis.⁶

This is first case to our knowledge of choroidal hypopigmentation in a patient with Waardenburg syndrome examined using ultra-widefield imaging. The manifestation of choroidal hypopigmentation is reflected as hypoautofluorescence, normal fluorescein angiography, clear demarcation with red-filter separation and an overall thickened choroid. Waardenburg syndrome is an important diagnosis to be considered in the differential diagnosis of a variably pigmented choroid.

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Figure 1. Ultra-wide field color fundus photograph of the right (A) and left (B) eyes demonstrated hypopigmentation of the choroid posterior the equator. Ultra-widefield fluorescein angiography of the right (C) and left (D) eyes demonstrating normal perfusion in late frames.

Figure 2.

Ultra-widefield fundus autofluorescence of the right (A) and left (B) eyes revealing, hypoautofluorescence (scleral unmasking) in the region of choroidal hypopigmentation. Red-filter separation of the fundus image of the right (C) and left (D) eyes highlighting the contrast between normal choroid and hypopigmented choroid. EDI-OCT of the right (E) and left (F) eyes, demonstrating a thickened choroid (430 & 435 microns respectively) with a normal overlying retina.