Supplementary Material

Prevalence and Clinical Characteristics of Dark Without Pressure Retinal Changes in a Chinese Hospital-Based Population

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Supplementary Online Content

Table S1. Case Series Review of Characteristics of patients with DWP

First Author	Age	Sex	Eye with DWP	Race	Diagnosis	Characteristic of DWP
Nagpal[1]	16	Male	OS	African-American	haemoglobin SS	left fundus showed a small dark brown area at 7.30 o'clock in the midperiphery; It was about I disc diameter in size and had sharply demarcated margins; This lesion appeared flat and was a uniform brown in color; Fluorescein angiography showed neither blockage of retinal or choroidal fluorescence nor any hyperfluorescence; this area was smaller and had disappeared in subsequent follow-up visits
Nagpal[1]	25	Male	OD	African-American	haemoglobin SS	There was a 3/2 disc diameter brown area at 2 to 4 o'clock in the midperiphery. The anterior margin was straight; the vertically oriented posterior margin had a dentate border. Fluorescein angiography of this brown area was normal. This area was smaller in subsequent follow-up visits, and the anterior margin had also become irregular. At

						12.30 o'clock another brown area j disc diameter in size and oval in shape was found.
Nagpal[1]	56	Male	OD	African-American	haemoglobin SC	A dark brown area 3 disc diameters above and nasal to the disc was about 7/3 disc diameters wide, with irregular margins and a flat appearance. Fluorescein angiography showed normal circulation and fluorescence. Follow-up examination of the dark brown area 8 months later showed that it was smaller and had faded to light brown.
Nagpal[1]	14	Female	OD	African-American	haemoglobin SC	a dark brown area at 2 o'clock in the midperiphery. It was flat, horizontally orientated, about 2 disc diameters long and I disc diameter wide, and had irregular but sharply outlined margins. Fluorescein angiography of this brown area showed normal perfusion. The area of the old salmon patch at its posterior edge showed possible occlusion of a small precapillary arteriole with faint blockage of choroidal fluorescence. One month later the dark brown area was smaller and had faded.
Nagpal[1]	26	Female	OS	African-	haemoglobin SS	a small oval, dark brown area (1 disc diameter) at 9.30 o'clock in the midperiphery.

				American		Fluorescein angiography of this area was normal. the dark brown area in the left eye had faded in subsequent follow-up visits. Fluorescein angiography showed that this area appeared normal.
Nagpal[1]	12	Female	OU	African-American	haemoglobin SS	Fundus examination showed several areas of peripheral arteriolar occlusion in both eyes. The right eye showed a flat dark brown area, about 2 disc diameters nasal to the disc, extending from 2.30 to 5.30 o'clock. Its width varied from 1 to 3 disc diameters and it had irregular but sharply demarcated margins. Fluorescein angiography showed normal circulation. The left eye also showed peripheral arteriolar occlusions and a dark brown area extending from 7 to io o'clock 2 disc diameters nasal to the disc. It was flat and 3 to 5 disc diameters wide. The distinct margins were surrounded by normal retina. Fluorescein angiography showed normal retinal circulation and normal choroidal fluorescence.
Nagpal[1]	46	Female	OD	African-	Hypertension;	Fundus examination revealed mild generalized narrowing of retinal arterioles and a

				American	haemoglobin AA	few linear flame-shaped haemorrhages. In the right eye 2 disc diameters below the disc there were two dark brown areas which were flat, irregular, and clearly demarcated. The surrounding retina was normal. Fluorescein angiography showed normal retinal circulation.
Fawzi[2]	25	Female	OD	African-American	myopia	Ophthalmoscopy revealed a flat discrete patch of darker retina with well-defined scalloped edges in the inferonasal periphery. No vascular abnormalities were present, and no evidence of vitreous separation or traction was identified. Spectral domain ocular coherence tomography revealed normal vitreoretinal interface and normal retinal and choroidal architecture in the patch of dark fundus. Scans centered on the border of the lesion demonstrated normal hyperreflectivity of the ellipsoid zone (inner segment and outer segment junction) outside the lesion, with a discrete transition to hyporeflectivity of the outer retinal bands within the dark fundus patch.
Fawzi[2]	14	Male	OD	Hispanic	retinal astrocytic	The right fundus showed an astrocytic hamartoma along the inferior arcade, with an

					hamartoma	unrelated, well-defined area of dark without pressure outside the arcade. Fundus autofluorescence showed intense hypo-autofluorescence within the lesion. Optical coherence tomography through the astrocytic hamartoma confirmed its location in the retinal nerve fiber layer. Nearinfrared reflectance and OCT through the dark without pressure lesion showed abrupt transition to hyporeflective outer segments in the lesion, which did not change with OCT beam direction change
Fawzi[2]	12	Female	OD	African-American	-	There was a 9- · 9-mm area of dark retina in the inferior posterior pole of her right eye with a distinct 360° border. Although darker than the surrounding retina, the absence of melanosis and presence of a sharp border suggested that the dark area was not a nevus. Hyporeflectivity of the ellipsoid zone on OCT, near-infrared, and hypo-autofluorescence were seen in the dark retinal area
Fawzi[2]	27	Female	OU	African	thyroid cancer; peripheral retinal tears; dot syndrome	Fundus color photographs also revealed brown–red geographic areas outside the arcades in the right eye and nasal to disk in the left eye. These lesions corresponded to

						near-infrared hyporeflective zones, corresponding to spectral domain OCT photoreceptor hyporeflectivity seen in the corresponding scans.
Fawzi[2]	37	Male	OS	African-American	myopia	a large well-defined dark patch in the superior temporal periphery of the fundus. No other fundus abnormalities were noted. Fundus autofluorescence demonstrated a large hypoautofluorescent patch with sharply demarcated borders. Spectral domain OCT demonstrated attenuation of the ellipsoid zone reflectance in the dark fundus lesion without any alteration of the vitreoretinal interface
Fawzi[2]	16	Female	OS	White	congenital hypertrophy of the retinal pigment epithelium	an incidental white without pressure lesion in the preequatorial retina of the left eye. Infrared reflectance imaging of the left eye in the region of white without pressure revealed a previously unrecognized rim of dark without pressure posterior to the lesion (hyporeflectivity on infrared). Optical coherence tomography showed that all the photoreceptor zones (ellipsoid and interdigitation zones and outer segments) showed a transition from mild hyperreflectivity (normal retina) to hyporeflectivity

						(dark without pressure) to intense hyperreflectivity (white without pressure)
Fawzi[2]	12	Male	OS	White	HLA-B27 anterior and intermediate uveitis	Fundus photography showed dark geographic lesions, more prominent on green (532 nm) reflectance, with mild hypoautofluorescence on green 532 nm autofluorescence. Optical coherence tomography showed abrupt transition to hyporeflectivity of the outer retina at the level of ellipsoid and interdigitation zones.
Fawzi[2]	20	Female	OD	African-American	unilateral increase in floaters	Dilated fundus examination disclosed unilateral patches of peripheral white without pressure, with a surrounding border of darker lesions in the symptomatic right eye. Fundus autofluorescence imaging revealed hypo-autofluorescence in both dark and white lesions. The infrared reflectance showed transition from hyporeflectivity to hyperreflectivity within the dark and white lesions respectively, which correlated with similar transition on OCT in the outer photoreceptor lines, compared with the surrounding fundus.
Fawzi[2]	9	Male	OU	Asian	myopia	Dilated fundus examination revealed bilateral, nasal dark without pressure lesions.

						Optical coherence tomography obtained through the lesions showed hyporeflectivity of the outer segments within the lesion, transitioning to normal reflectivity in unaffected regions. asymptomatic “dark lesions” in the fundus increased in size during follow-up.
Moysidis[3]	35	Male	OS	Asian	HIV infection	Dilated fundus examination revealed several areas of retinal darkening in the left eye, nasal, and superior to the disc that on spectral domain (SD)-OCT (Spectralis, Heidelberg, Germany) corresponded to hyporeflectivity localizing and limited to the EZ band. no qualitative difference of the vasculature within the area of darkening in the left eye compared with the adjacent vasculature and also compared with the corresponding image of the right eye in optical coherence tomographic angiography
Chang[4]	41	Female	-	Hispanic	CHRPE	Flat appearing uniformly pigmented lesion with a well-demarcated shadow anteriorly
Chang[4]	20	Male	-	African-American	Myopia; CHRPE	Flat appearing uniformly pigmented small lesion with a well-demarcated shadow anteriorly

Chang[4]	41	Female	-	Hispanic	Myopia; CHRPE	Flat appearing uniformly pigmented small lesion with a well-demarcated shadow anteriorly
Chang[4]	19	Male	-	Chinese	Myopia; CHRPE	Elevated appearing uniformly pigmented lesion with a well-demarcated area of shadow anteriorly, with disappearance after 3 years
Chang[4]	12	Female	-	African-American	Myopia; CHRPE	Elevated appearing uniformly pigmented lesion with a well-demarcated shadow anteriorly, with reduction in extent over 3 years
Chang[4]	31	Female	-	Hispanic	Myopia; CHRPE	Elevated appearing pigmented lesion with a well-demarcated shadow anteriorly, with disappearance after 3 years
Chen[5]	12	Female	OS	African American	NA	a well-demarcated, flat, hyperpigmented lesion in her left eye. Over 1.5 years, the superonasal border of the lesion was seen to regress, and the inferior border was seen to enlarge. Fundus autofluorescence showed hypoautofluorescence, and OCT showed hyporeflectivity at the level of the photoreceptors.
Gupta[6]	13	Male	OD	-	anterior uveitis	The fundus examination of the right eye showed a well-defined lesion darker than the

						surrounding area and sparing the macula, suggestive of a large, dark-without-pressure fundus lesion. There were no vascular abnormalities and no evidence of vitreous separation or traction. On spectral-domain OCT, an abrupt transition to hyporeflectivity of the ellipsoid and outer segments of the photoreceptors was seen within the dark fundus lesion. Visual fields and full fields via electroretinogram were normal, suggesting that the lesions represent structural changes without associated functional deficits.
Flores Pimentel[7]	2	Female	OU	Hispanic	Right sigmoid sinus thrombosis; history of sixth nerve palsy and bilateral papilledema	Location of DWP was nasal to disc (OD) and inferonasal to disc (OS). OCT showed hyperreflectivity of the ellipsoid zone outside the lesion, discrete transition to hyporeflectivity within the dark patch. FA showed normal choroidal and retinal vascular patter, no leakage
Flores Pimentel[7]	13	Male	OU	Hispanic	high risk-B acute lymphoblastic leukaemia	Location of DWP was nasal to disc (OU). Dark area showed attenuation of the outer hyperreflective band in the outer retina along the EZ line on the OCT. FAF showed

						hypo-auto fluorescence within the lesion
Flores Pimentel[7]	4	Female	OS	Hispanic	Developmental delay, Alopecia, ichthyosis, congenital vs. perinatal CMV infection	Location of DWP was nasal to disc (OS). FA showed normal retinal and choroidal vasculature pattern and flow
Flores Pimentel[7]	4	Male	OU	African-American	Familiar bilateral congenital cataract	Location of DWP was temporal to fovea (OD) and inferotemporal (OS)
Flores Pimentel[7]	7	Female	OS	Caucasian	Marfan syndrome	Location of DWP was superotemporal, end of the vascular arcade
Flores Pimentel[7]	9	Male	OU	Hispanic	Developmental delay, obesity, high myopia, likely CSNB	Location of DWP was temporal to macula anterior to equator, along the superior temporal arcade (OD). OCT showed transition to hyporeflectivity of the outer retinal bands across the dark areas. Full-field ERG showed diffuse inner retinal dysfunction, negative ERG.

Sherman[8]	21	Female	OD	African American	Choroidal Osteoma; myopia	In the mid-periphery an annular band of dark without pressure is visualized with sharply demarcated scalloped borders surrounding the tumor with abrupt change to normal appearing retina in the far periphery. There was a distinct, sharp transition in the outer-retinal reflectance pattern from hyporeflectance of the ellipsoid zone in the area of pigmentation to normal reflectance in normal-appearing retina.
Steptoe[9]	23	Male	OS	Brazilian origin	Ocular toxoplasmosis	a flat, delineated area of retinal darkening consistent with the clinical appearance of DWP could be seen on ultra-widefield retinal imaging. No corresponding change in fundus autofluorescence (FAF) was observed in the area of DWP. OCT through the area demonstrated a characteristic thinned, hyporeflective ellipsoid zone band in keeping with DWP.

Abbreviations: DWP, Dark Without Pressure; OD, Oculus Dextrus; OS, Oculus Sinister; OU, Oculus Unati; OCT, Optical Coherence Tomography; HLA, Human Leukocyte Antigen; HIV, Human Immunodeficiency Virus; SD, Spectral Domain; EZ, Ellipsoid Zone; CHRPE, Congenital Hypertrophy of The Retinal Pigment Epithelium; FAF, Fundus Autofluorescence; FA, Fluorescein Angiography; CMV, Cytomegalovirus; CSNB, Congenital Stationary Night Blindness; ERG, Electroretinogram.

Table S2. Demographic characteristics of the overall patients with and without DWP

	Patients with DWP	Patients without DWP	Total Patients	*P* Value
<30 years	231	421	652	<0.001
30-39 years	243	523	766	
40-49 years	188	694	882	
50-59 years	278	940	1218	
>59 years	542	2726	3268	

Abbreviations: DWP, Dark Without Pressure.

Table S3. Demographic characteristics of the control group patients with and without DWP

	Patients with DWP	Patients without DWP	Total Patients	*P* Value
<30 years	115	296	411	<0.001
30-39 years	98	289	387	
40-49 years	80	374	454	
50-59 years	98	407	505	
>59 years	174	1114	1288	

Abbreviations: DWP, Dark Without Pressure.

Table S4. Demographic characteristics of the AMD group patients with and without DWP

	Patients with DWP	Patients without DWP	Total Patients	*P* Value
<30 years	4	2	6	0.025
30-39 years	1	4	5	
40-49 years	6	12	18	
50-59 years	9	41	50	
>59 years	66	296	362	

Abbreviations: AMD, Age-related Macular Degeneration; DWP, Dark Without Pressure.

Table S5. Demographic characteristics of the DR group patients with and without DWP

	Patients with DWP	Patients without DWP	Total Patients	*P* Value
<30 years	4	2	6	0.008
30-39 years	13	12	25	
40-49 years	19	28	47	
50-59 years	37	75	112	
>59 years	38	147	185	

Abbreviations: DR, Diabetic Retinopathy; DWP, Dark Without Pressure.

Table S6. Demographic characteristics of the HM group patients with and without DWP

	Patients with DWP	Patients without DWP	Total Patients	*P* Value
<30 years	36	13	49	<0.001
30-39 years	46	38	84	
40-49 years	12	42	54	
50-59 years	15	50	65	
>59 years	12	85	97	

Abbreviations: HM, High Myopia; DWP, Dark Without Pressure.

Table S7. Demographic characteristics of the Uveitis group patients with and without DWP

	Patients with DWP	Patients without DWP	Total Patients	*P* Value
<30 years	16	10	26	<0.001
30-39 years	16	20	36	
40-49 years	8	26	34	
50-59 years	10	31	41	
>59 years	5	50	55	

Abbreviations: DWP, Dark Without Pressure.

Table S8. Demographic characteristics of the RH group patients with and without DWP

	Patients with DWP	Patients without DWP	Total Patients	*P* Value
<30 years	4	3	7	0.030
30-39 years	10	11	21	
40-49 years	7	11	18	
50-59 years	18	19	37	
>59 years	20	64	84	

Abbreviations: RH, Retinal Holes; DWP, Dark Without Pressure.

Table S9. Demographic characteristics of the RD group patients with and without DWP

	Patients with DWP	Patients without DWP	Total Patients	*P* Value
<30 years	9	6	15	0.022
30-39 years	9	14	23	
40-49 years	5	19	24	
50-59 years	9	28	37	
>59 years	10	40	50	

Abbreviations: RD, Retinal Detachment; DWP, Dark Without Pressure.

Table S10. Demographic characteristics of the RVO group patients with and without DWP

	Patients with DWP	Patients without DWP	Total Patients	*P* Value
<40 years	2	1	3	0.026
40-49 years	8	7	15	
50-59 years	6	22	28	
>59 years	21	73	94	

Abbreviations: RVO, Retinal Vein Occlusion; DWP, Dark Without Pressure.

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