Original Article

Optic nerve head melanocytoma: Optical coherence tomography/angiography features

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Purpose: The objective of this study was to identify the diagnostic features of optic nerve head melanocytoma (ONH-MCT) on spectral domain optical coherence tomography (SD OCT) and OCT angiography (OCT-A). **Methods:** Retrospective study of 11 patients for their demographic, clinical features and imaging including SD OCT (tumour location, extent and interface) and OCT-A (surface and intrinsic vascularity) were reviewed. Flow rate percentage (FR %) was calculated over the lesion and compared to fellow eye and similar pigmented lesions. **Results:** The average age was 52.8 ± 10.9 years. ONH-MCT tumors occupied 3-tissue spaces- optic disc (n = 2), retinal layer (n = 5) and retina-choroidal layers (n = 4). SD OCT (11 eyes) showed elevated hyper reflective disorganized retinal layers with posterior shadowing (9 eyes) and hyper reflective dots within the tumor (all eyes). Microvascular features on OCT-A (8 eyes) in radial peripapillary capillary slab showed surface vascularization (7 eyes) and intrinsic vascularity in choroidal slab (8 eyes) with surrounding hypo reflective boundary. The mean FR % was higher at 65.1 ± 3.77% (CI: 61.9-68.2) compared to mean FR at 60.4 ± 1.06% (CI: 59.5-61.2) in the fellow eye (p = 0.01). Comparison with nevus and melanoma SD OCT showed a high reflective choroidal layer with normal or irregular outer retinal layers respectively; OCT-A showed hypo reflective area at the center with hyper reflective boundary and iso reflective area at center with hyper reflective boundary respectively. **Conclusion:** SD OCT and OCT-A features may help to differentiate ONH-MCT from clinically similar looking pigmented lesions like nevus and melanoma.

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Optic nerve head melanocytoma (ONH-MCT) is a benign dark brown to black pigmented lesion located either within or adjacent to the optic disc.[1] In majority of instances the tumor remains stable throughout the life and only observation is warranted.[2,3] A 10-year longitudinal study has shown that the tumor size could increase in up to 32% of cases and malignant transformation to melanoma could occur in 1-2% of cases.[2,4,5] The tumor is usually located over the optic disc and grows horizontally involving either the retinal and/or choroidal layers. In these situations, differentiating it from similar pigmented lesions like juxtapapillary choroidal nevus or malignant melanoma poses a diagnostic challenge.

Imaging modalities like B-scan ultrasonography, autofluorescence (AF), fundus fluorescein angiography (FFA) and optical coherence tomography (OCT) help in understanding the tumor morphology and in confirming the diagnosis.[6] But the factors that could predict a malignant transformation into melanoma or exponential growth causing tumor necrosis are ill understood.

Since the optical coherence tomography angiography (OCT-A) unravels the structural and microvascular characteristics as well as flow rates within the tumor and the surrounding retina and choroid[7,8] we studied OCT-A features of ONH-MCT along with flow rate characteristics that may help us in differentiating from similar pigmented choroidal lesion.

Methods

We included 11 consecutive patients (11 eyes) of confirmed clinical diagnosis of ONH-MCT seen in ocular oncology clinic at two tertiary eye care institute between January 2017 and March 2019. The informed consent was taken from all the subjects and appropriate institutional review board approval was obtained. Demographic details included patient's age, sex and eye involved. A complete and comprehensive ophthalmologic examination included the presenting and best-corrected visual acuity (BCVA), tumor characteristics (size, color, margin, extent of involvement- retinal/choroidal) and presence of associated optic disc edema or subretinal fluid. Ophthalmic imaging included fundus photograph, AF, and SD OCT in all eyes; OCT-A in 8 eyes; FFA in 4 eyes. The extent of tumor was classified into 3 types based on clinical examination and AF

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imaging: type 1- within the optic disc, type 2- involving the retinal layers, and type 3- involving retina-choroidal layers.

A SD OCT (DRI-OCT Triton Swept-source, Topcon, Tokyo, Japan) 5 line-raster was performed over the tumor and its surrounding areas to determine its location (inner or outer retina), posterior shadowing, overlying retinal structures, presence of hyper reflective dots, intraretinal or subretinal fluid and tumor-retinal interface.

OCT-A (DRI-OCT Triton Swept-source, Topcon, Tokyo, Japan) 6 × 6 mm scan over the tumor and surrounding area was performed to study the microvascular patterns in radial peripapillary capillary slab (RPC) and choroidal slab. A validated semi-automated segmentation algorithm was applied to identify relevant retinal layers, and manual corrections were performed as necessary to ensure accurate segmentation. The RPC slab was segmented with an inner boundary at 3 μm beneath the internal limiting membrane (ILM) and an outer boundary set at 70 μm beneath the ILM, imaging the peripapillary capillary network. The angiography of retina/choroid was segmented with an inner boundary 130 μm beneath the ILM and an outer boundary beneath the Bruch's membrane. In particular, we also evaluated en face angiograms of the choroidal slab, limited between the outer boundary of Bruch's membrane and approximately 20 μm beneath Bruch's membrane for tumors involving retina-choroidal layers. The OCT-commercial software calculated the flow area per 1 mm^2 in 6 × 6 mm scans in the RPC slab over the lesion. The flow rate percentage was calculated in 1 mm^2 radius by dividing the measured flow area by the selected area and then multiplying by 100 on the 31–69 μm section below the level of ILM over the lesion and the corresponding part of unaffected normal eye. Two experienced investigators (SN, AK) independently graded the flow percentage in the RPC slab over the tumor. All patients were followed for minimum duration of 6 months to look for any change in BCVA, size, color, extent of involvement or associated features like subretinal fluid, optic disc edema or vascular occlusions.

One classical case of juxtapapillary choroidal nevus and choroidal melanoma with fundus photograph, SD OCT and OCT-A was reviewed from published literature[8-10] and compared with our series of ONH-MCT to identify specific features which could help in differentiating these lesions.

Results

The mean age of the 11 patients was 52.8 ± 10.9 years (range: 35-69 years). There were 4 males and 7 females. The BCVA ranged from 20/20 to 20/80; 7 patients had vision of 20/20. Pupil examination was normal in all eyes. The mean intraocular pressure was 14.2 mm Hg (range 12-18 mm Hg). The tumor size ranged from approximately 1/3 DD to 2 DD with mean surface area of 2.70 mm^2 (range 1 – 5.4 mm^2). The tumor surface had dark brown pigmentation in 7 eyes and faint brown pigmentation in 4 eyes. The tumor margins extending into surrounding layers were irregular with fimbriae like appearance in 7 eyes and well-defined margins in 4 eyes. Seen clinically and confirmed on AF imaging, the tumor occupied 3-tissue spaces – limited within the optic disc only (n = 2), extended into retinal layer (n = 5) and extended into retina-choroidal layers (n = 4). There was associated optic disc edema in 2 eyes. There was no subretinal fluid (SRF) surrounding the tumor in any eye. FFA showed blocked fluorescence in all 4 eyes. Fig. 1 shows image of case # 11- dark brown pigmented tumor involving the retina-choroidal layers; Fig. 2 shows images of case #10- faint brown pigmented tumor involving the retinal layers.

The complete demographic details and clinical features are mentioned in Table 1.

SD OCT showed an elevated tumor mass arising from the optic disc with increased reflectivity at its anterior margins and a dense optically empty space at its posterior margin due to tumor shadowing. The overlying and adjacent retina layers were completely disorganized making it difficult to appreciate in 9 of the 11 eyes. In 4 eyes with faint brown surface pigmentation, the underneath posterior shadowing of tumor was incomplete with homogenous reflectivity and few scattered dots within the tumor. In all 11 eyes multiple hyper reflective dots were seen both at the surface and within the tumor. In 5 eyes these hyper reflective dots were seen in vitreous cavity. The normal retina-tumor interface at the boundary of the lesion was well defined in 8 of 11 eyes. On the basis of the OCT the exact location of tumor extending into surrounding structures was noted as follows: limited to inner retinal layers in 4 eyes, extending into outer retinal layers in 6 eyes and in 1 case it was difficult to recognize. In 4 eyes with choroidal involvement, there was increased choroidal reflectance at the choriocapillarie level with intact outer retinal layers [Table 2].

OCT-A in the RPC slab showed presence of surface tumor vascularization in a honeycomb pattern in 7 of 8 eyes with hypo reflective areas adjacent to the tumor. The corresponding B scan also showed presence of increase retinal vascularity in the superficial layers. In the choroidal slab, fine intrinsic vascularity was seen within the tumor in all eyes with surrounding hypo reflective areas. The mean flow rate percentage calculated in the RPC slab over the entire tumour surface area (8 eyes) was 65.1 ± 3.77% (CI: 61.9-68.2) higher as compared to mean flow rate of 60.4 ± 1.06% (CI: 59.5-61.2) in the fellow unaffected eye; this was statistically significant (p = 0.01, Paired t- test). In the patients where tumor extended into the retina-choroidal layers (n = 3), the choroidal slab showed an iso to hyper reflective central lesion with hypo reflective areas at the boundary [Table 3].

At the last follow-up (mean 6.3 months; range 3-10 months), the BCVA, and the size and color of the tumor were unchanged. SRF, retinal hemorrhages or vascular occlusion was not present in any of the affected eye.

To differentiate from juxtapapillary choroidal nevus and choroidal melanoma, we compared the SD OCT and OCT-A features as reported in the literature with our series. SD OCT in a case of nevus showed a highly reflective choroidal layer underneath the RPE-Bruch membrane with well-organized and intact outer retinal layers;[9,10] OCT-A in RPC slab showed normal peripapillary capillary network over the optic disc; the nevus part in the choroidal slab showed a well-defined hypo reflective central lesion with hyper reflective areas at the boundary. The mean flow rate percentage over the lesion was comparable with unaffected normal eye.[8,9]

In case of melanoma, the SD OCT showed a highly reflective choroidal layer with thickening of RPE-Bruch membrane and presence of intraretinal fluid and shaggy photoreceptor

Table 1: Demographic details of patients diagnosed with optic nerve head melanocytoma

Case no	Age (years)	Sex	Laterality	BCVA	Size in DD	Colour	Tissue involvement	Margins	Disc Edema	Follow up (months)
1	66	F	LE	20/20, N6	3/4 DD	Dark brown	Retina	Irregular	No	3
2	46	F	LE	20/40, N8	3/4 DD	Dark brown	Retina + choroid	Well defined	No	6
3	62	M	RE	20/80, N12	1/2 DD	Faint brown	Limited to disc	Well defined	No	5
4	58	M	RE	20/20, N6	1/3 DD	Faint brown	Limited to disc	Well defined	No	4
5	69	M	RE	20/20, N6	1 DD	Dark brown	Retina	Irregular	No	9
6	42	F	LE	20/20, N6	1DD	Faint brown	Retina	Irregular	Yes	10
7	57	M	RE	20/25, N8	1/2 DD	Dark brown	Retina	Irregular	No	9
8	57	F	RE	20/40, N8	2 DD	Dark brown	Retina + choroid	Irregular	No	6
9	45	F	RE	20/20, N6	2 DD	Dark brown	Retina + choroid	Irregular	No	4
10	44	F	LE	20/20, N6	1/2 DD	Faint brown	Retina	Well defined	No	8
11	35	F	LE	20/20, N6	2 DD	Dark brown	Retina + choroid	Irregular	Yes	6

BCVA - Best corrected visual acuity; DD - Disc diameter; LE - Left eye; RE - Right eye

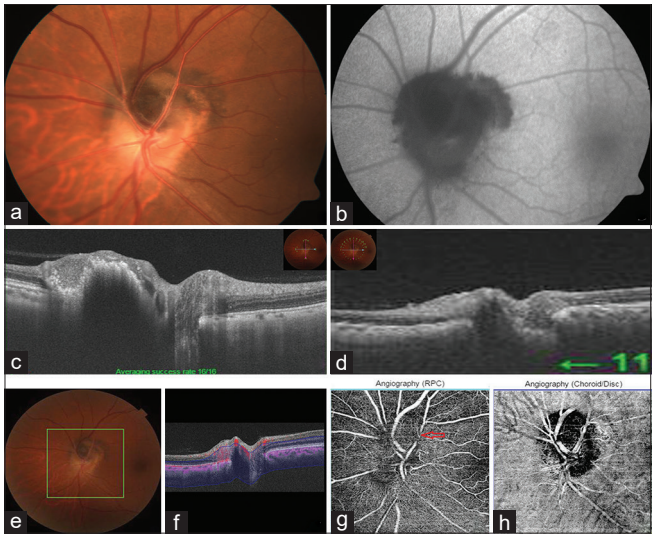

Figure 1: (a) Fundus photograph showed a dark brown tumor extending into retina-choroidal layers. (b) AF showed hypo autofluorescence. (c and d) SD OCT showed elevated hyper reflective lesion with posterior shadowing and overlying disorganized retina. A hyper reflective choroidal layer with intact outer retinal layer noted in area invading the choroid (d). (e-h) OCT-A, a 6 × 6 mm scan (e) showed increased flow signals (f). The RPC slab showed surface vascularity (arrow) with few hypo reflective signals adjacent to tumor (g). In choroidal slab, intrinsic vascularity along with hypo reflective boundary was seen (h)

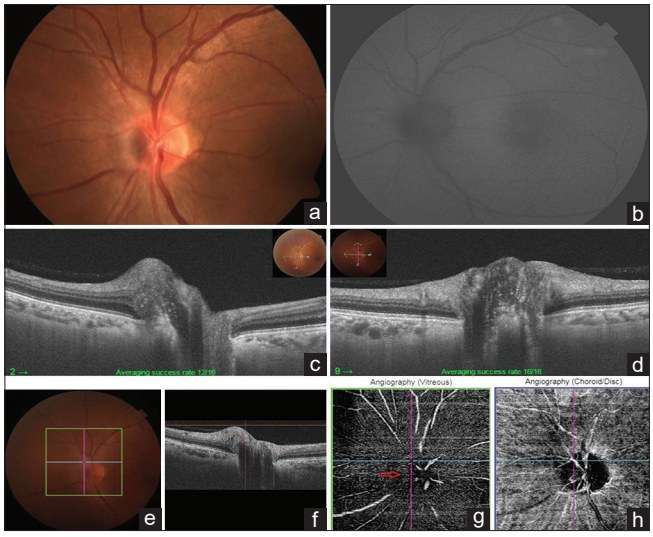

Figure 2: (a) Fundus photograph showed a faint brown pigmented tumor. (b) AF showed hypo autofluorescence. (c and d) SD OCT showed elevated hyper reflective lesion with incomplete posterior tumor shadowing. The overlying retina was organized with visible retina layers and presence of multiple hyper reflective dot-like lesions. (e-h) OCT-A, a 6 × 6 mm scan (e) with corresponding OCT B scan (f). The RPC slab showed surface vascularity (arrow) with few hypo reflective signals adjacent to the tumor (g). In the choroidal slab, intrinsic vascularity with hypo reflective boundary was seen (h)

layer;[9,10] OCT-A in the choroidal slab showed iso reflective areas at the center with hyper reflective ring surrounding the lesion. The vasculature within the lesion showed thinning of choroidal vessels with decreased flow rates as compared to unaffected normal eye and choroidal nevus.[8,9] Table 4 shows the comparison of clinical presentation and different imaging features of ONH-MCT, juxtapapillary choroidal nevus and choroidal melanoma.

Discussion

Tumor vascularity is one of the important features of any intraocular malignancy and could be an important marker of malignancy. ONH-MCT has been always considered an avascular tumor; based on the AF and FFA that do not show surface or intra lesion vascularity, perhaps due to dense tumor pigmentation.[2,3] We therefore used (OCT-A) to unravel the structural and microvascular characteristics as well as flow rates within the tumor and the surrounding retina and choroid. OCT-A showed presence of surface tumor vascularization in the RPC slab (7 out of 8 eyes) as well as intrinsic vascularity in the choroidal slab (all eyes). Other investigators have also reported similar surface and intrinsic vascularity in ONH-MCT.[11,12]

Quantification of the microvascular flow rate is considered the morphological gold standard for assessing the neovasculature in human tumors. This has both prognostic and predictive value.[13] The microvascular flow rate varies within and at the boundary of the lesion depending on

Table 2: OCT and OCT angiography features

Case no	Tumor location	Overlying retina	Posterior hyporeflective shadow	Normal retina-tumour Interface	Hyper-reflective dots	OCT-A	RPC slab Surface vascularity	Choroidal slab intrinsic Vascularity
1	Not recognised	Disorganised	Present, complete	Ill-defined	Yes	Yes	Present	Yes
2	Outer retina, choroid	Disorganised	Present, complete	Well defined	Yes	No	-	-
3	Inner retina	Disorganised	Present, incomplete	Ill-defined	Yes	Yes	Present	Yes
4	Inner retina	Disorganised	Present, incomplete	Well defined	Yes	No	-	-
5	Outer retina	Disorganised	Present, complete	Well defined	Yes	Yes	Present	Yes
6	Outer retina	Disorganised	Present, incomplete	Well defined	Yes	Yes	Present	Yes
7	Inner retina	Disorganised	Present, complete	Ill-defined	Yes	No	-	-
8	Outer retina, choroid	Disorganised	Present, complete	Well defined	Yes	Yes	Present	Yes
9	Outer retina, choroid	Organised	Present, complete	Well defined	Yes	Yes	Absent	Yes
10	Inner retina	Organised	Present, incomplete	Well defined	Yes	Yes	Present	Yes
11	Outer retina, choroid	Disorganised	Present, complete	Well defined	Yes	Yes	Present	Yes

OCT-A- Optical coherence tomography- angiography; RPC- Retinal peripapillary capillary

Table 3: OCT-A showing microvascular flow rate over the tumor in choroidal slab

Case no	OCT-A	Size (mm^2)	Flow rate (mean)	area 1	area 2	area 3	area 4	area 5	Flow rate other eye (mean)	area 1	area 2	area 3	area 4	area 5
1	yes	2.02	60.95	60.35	61.56	-	-	-	60.99	60.88	61.1	-	-	-
3	yes	1.35	64.15	64.15	-	-	-	-	58.55	58.55	-	-	-	-
5	yes	2.7	68.95	68.75	69.1	-	-	-	59.71	59.31	60.11	-	-	-
6	yes	2.5	60.9	61.25	60.55	-	-	-	61.49	61	61.99	-	-	-
8	yes	5.4	67.69	69.02	68.85	65.29	66.23	69.1	59.66	60.8	59.51	58.11	59.69	60.23
9	yes	5.2	70.36	69.87	71.51	69.33	70.12	71	61.53	63.71	61.28	61	60.11	61.57
10	yes	1.42	66.45	66.45	-	-	-	-	61.25	61.25	-	-	-	-
11	yes	5	61.49	60.88	62	62.15	61.47	60.98	60.43	60.14	59.47	60.22	60.98	61.35

Table 4: Differentiating features of ONH- melanocytoma, Juxtapapillary choroidal nevus and Choroidal melanoma

Features	ONH-melanocytoma	Juxtapapillary Choroidal Nevus	Choroidal Melanoma
Location	Optic disc, with/without retinal or choroidal component	Around or adjacent to optic disc	Optic disc or juxtapapillary
Colour	Dark brown, pigmented	Brown	Brown, amelanotic rare
Margins	Irregular	Well demarcated	Irregular
SRF	rarely	rarely	Yes
Orange surface pigmentation	No	rarely	Yes
FFA	Hypofluorescent through all phases	Hypo with few hyperfluorescent pin point lesions	Hyperfluorescent with late leakage from vessels
AF	Hypo AF	Hypo AF, Hyper if associated with orange pigment	Bright hyper AF
SD OCT: Structural	Intact RPE Bruch layers, overlying retina disorganised with post shadowing, clear interface seen between tumor and normal retina, hyper reflective dots within the tumor and in vitreous	A high reflective band within choriocapillarie layer associated with intact outer retinal layers	A high reflective band associated with intraretinal fluid and shaggy photoreceptors
OCT-A			
Microvascular patterns	Surface tumor vascularization in RPC slab Intrinsic vascularity in choroidal slab with surrounding hypo reflective areas	Central hypo reflective area with surrounding hyper reflective areas	Central hypo to iso reflective areas with surrounding hyper reflective areas
Flow rate over the lesion	Higher flow rate as compared to normal fellow eye	Comparable to normal fellow eye	Low flow rate as compared to normal fellow eye

the tumor vascularity. At the boundary of the lesion the microvascular flow is high in both nevus and melanoma; whereas at the center of the lesion, the flow rate is high in nevus, but low in melanoma. This is explained by the vertical growth of melanoma towards least resistance retina rather than rigid sclera underneath and thereby causing compressive effect on choriocapillaries and its blood supply leading to low flow noted at apex of tumor.[9]

The microvascular flow rate percentage in our series for ONH-MCT (65.1 ± 3.77%) was higher as compared to unaffected fellow eye (60.4 ± 1.06%) and case of melanoma (55.73 ± 4.3%) whereas it was comparable to the flow rate of choroidal nevi (63.6 ± 3.18%).[9] This has not been described earlier and could be one of the important findings to predict transformation of ONH-MCT or choroidal nevus into melanoma. Additional and newer imaging techniques such as phase-based and speckle-variance OCT-A could improve the microvascular flow rate quantification in ONH-MCT.

The limitations of our study include small number of cases, retrospective nature and shorter longitudinal follow-up. Most of our analysis of SD OCT and OCT-A were qualitative except flow rate calculation over the lesion (quantitative).

Conclusion

To conclude, SD OCT and OCT-A in ONH-MCT helps in better understanding of structural, microvascular and flow rate characteristics, which may help in distinguishing it from other pigmented lesions.

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Statement of ethics

This study was approved by the Institutional Review board at L V Prasad Eye Institute, and it conformed to tenets of Declaration of Helsinki.

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Conflicts of interest

There are no conflicts of interest.

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