Interpreting posterior uveitis by integrating indocyanine green angiography, optical coherence tomography, and optical coherence tomography angiography data: A narrative review

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Abstract:

Posterior uveitis is sight-threatening disease entity that can be caused by infectious and non-infectious entities. Vision loss in posterior uveitis can be following complications such as cystoid macular edema, epiretinal membrane, artery and vein occlusions, vasculitis, papillitis, choroidal neovascular membrane, retinal neovascularization, tractional retinal detachment, vitreous hemorrhage, glaucoma, cataract, among others. Diagnosis of posterior uveitic entities have been revolutionized following introduction of choroidal imaging with techniques such as indocyanine green angiography (ICGA), optical coherence tomography (OCT) and optical coherence tomography angiography (OCTA). Med Line search and PubMed search was performed pertaining to causes of posterior uveitis, ICGA in posterior uveitis, OCT in posterior uveitis, OCTA in posterior uveitis, retinal and choroidal vascular changes in posterior uveitis, quantification of choriocapillaris lesion area in posterior uveitis, subfoveal choroidal thickness in posterior uveitis, quantification of choriocapillaris in posterior uveitis, vascular indices for quantification of choriocapillaris. This review article highlights various changes in the choroid and the quantification of choroid using various parameters in ICGA, OCT and OCTA.

Keywords:

Indocyanine green angiography, optical coherence tomography, optical coherence tomography angiography, posterior uveitis

Introduction

Posterior uveitis in isolation or as a part of panuveitis can be caused by infectious and noninfectious entities. The pathological process associated with uveitis includes inflammation, vascular leakage and occlusion, local ischemia, and release of cellular and inflammatory mediators that can potentially lead to cystoid macular edema (CME), epiretinal membrane formation, artery and vein occlusions, retinal and choroidal neovascularization, vitreous hemorrhage, tractional retinal detachment, cataract, glaucoma, and so on.[1,2]

Fluorescein angiography (FA) is an invasive procedure that can cause localized and generalized adverse reactions. It is useful to detect vascular leakage in vasculitis, macular ischemia, CME, optic nerve head leakage, inflammatory choroidal neovascular membrane (CNVM), patterns of fluorescence, and response to treatment. However, deep choroidal vasculature and CNVM with an associated subretinal hemorrhage may not be clearly delineated with FA.[3] Indocyanine green angiography (ICGA) is preferred for choroidal lesions and to study choroidal vasculature that are not clearly delineated with FA. Choroidal granulomas in Vogt–Koyanagi–Harada disease (VKH), inflammatory CNVM, and CC hypoperfusion are better highlighted using ICGA. ICGA still plays a very pivotal role in choroidal inflammatory disorders. FA and ICGA are invasive procedures.[3] Optical coherence tomography (OCT) is extremely useful in studying retinal layers and highlights retinal pathology by the technique of low

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coherence interferometry. However, conventional OCT does not penetrate RPE, while newer modalities such as enhanced depth imaging-OCT (EDI-OCT) are able to penetrate better and give details about choroid by displacing the zero-delay point. This, in turn, is useful in the visualization of choroid and helps in quantitative measurement of the thickness of choroid with high reliability and reproducibility.[4]

OCT angiography (OCTA) is a noninvasive technique that outlines the retinochoroidal vasculature, particularly in uveitis. These vascular changes can get obscured by conventional angiography. OCTA can show recurrences at a very early stage by revealing changes in CC circulation. It is extremely useful to monitor changes in CNVM following response to treatment. Measurements of retinal vascularity index, choroidal vascularity index (CVI), and foveal avascular zone (FAZ) are areas of research interest that would possibly shed light on blood flow in the retina, choroid, optic nerve head, and macular area.[3,5]

This review article aims at highlighting choroid and choriocapillaris (CC) changes and its imaging using ICGA, OCT, and OCTA.

Method of Literature Search

MedLine search and PubMed search were performed pertaining to causes of posterior uveitis, ICGA in posterior uveitis, OCT in posterior uveitis, OCTA in posterior uveitis, retinal and choroidal vascular changes in posterior uveitis, quantification of CC lesion area in posterior uveitis, subfoveal choroidal thickness in posterior uveitis, quantification of CC in posterior uveitis, and vascular indices for quantification of CC.

Indocyanine green angiography in posterior uveitis

The advantage of ICGA is that it is more protein bound and reduces the amount of leakage through the fenestrations of CC, thereby enabling clear view of the choroidal circulation. Gradual impregnation of choroid takes place with time, which helps us to delineate better in the mid and late phases of the angiogram in chorioretinal inflammatory diseases. This impregnation is affected by choroidal inflammatory diseases, leading to decreased or increased fluorescence. The early phase is extremely useful as it clearly shows the choroidal filling pattern. ICGA can penetrate pigmented layers, lipid deposits, hemorrhages, and serous exudation much better than FA as it fluoresces in the near-infrared spectrum (830 nm). ICGA shows occult vessels and feeder vessels in those with uveitis CNVM that are not seen on FA.[6-9]

The early phase occurs 1 min after the injection of ICG, wherein large choroidal arteries and choroidal veins along with retinal vasculature can be visualized. The middle phase is between 5 and 15 min after the dye injection, wherein hyperfluorescence from choroidal veins and retinal vasculature diminishes. The late phase which starts approximately after 15 min (18–22 min) after dye injection has optic disk showing dark and large choroidal vessels becoming hyperfluorescent highlighting choroidal abnormalities against the dark background.[6-9]

Table 1: Details of hyperfluorescence on indocyanine green angiography in various conditions

Hyperfluorescence	Pathology
Pseudo-fluorescence	Fibrosis, hemorrhage
Retinal	Leakage - Extensive vascular damage breaking blood-retinal barrier as in Behcet's disease
Optic disk	Uveitis or posterior scleritis (VKH, Behcet's disease)
Subretinal	Abnormal and new vessels - Inflammatory CNVM
	Pooling - VKH
	Tissue staining - Pinpoint hyperfluorescent leakage from choroid to retina (VKH)
Choroid	Leakage - Choroidal inflammatory disease leading to leakage from stromal vessels - Diffuse hyperfluorescence in the late phase
	Vessel staining - In acute stage of severe VKH from choroidal stromal vessels in the early phase
	Tissue staining - Late focal hyperfluorescence as seen in VKH

VKH: Vogt–Koyanagi–Harada, CNVM: Choroidal neovascular membrane

Hyperfluorescence in ICGA is always due to choroidal hyperfluorescence due to leakage from CC or large choroidal vessels or due to staining and never due to window defects. They must be looked for in the intermediate and late phases of ICGA [Table 1].[6-9]

Hypofluorescence should be looked for in the intermediate and late phases of angiogram and during follow-up or after treatment in the angiogram.[6-9] Hypofluorescence in various phases of ICGA and its correlation with FA, fundus lesion, and choroidal diseases are given in Table 2.[6-9]

Choroidal involvement in uveitis can occur as the following:

Choriocapillaritis[9]

a. Primary: Multiple evanescent white dot syndrome (MEWDS), acute posterior multifocal placoid pigment epitheliopathy (APMPPE), acute zonal occult outer retinopathy (AZOOR), idiopathic multifocal choroiditis (MC), and serpiginous choroiditis (SC) (predominantly white dot syndromes)
b. Secondary: Acute syphilitic posterior placoid chorioretinitis.

ICGA shows patchy or geographic hypofluorescent areas of variable sizes in the early, intermediate, and late phases of angiography, predominantly in the late phases suggestive of CC nonperfusion or hypoperfusion. There can be complete or incomplete regression or no regression at all in the convalescent phase. Areas of chorioretinal atrophy show hypofluorescence during the convalescent phase that correspond to window defect and masking effect on FFA. In those with progressive lesions as in SC, there will be hyperfluorescence at the edges of the lesions.[9]

Stromal choroiditis[9]

a. Primary obligatory stromal choroiditis: VKH, SO, and BC.
b. Stromal choroiditis seen at a random location as a part

of systemic disease: Sarcoidosis, TB, syphilis, and other infectious stromal choroiditis.

ICGA shows hypofluorescent lesions corresponding to the granulomatous inflammatory foci at the level of stroma associated with inflammation of the nonfenestrated stromal vessels that appear as fuzzy in the intermediate phase and followed by diffuse late hyperfluorescence. The hypofluorescent spots are regular and uniform in size in primary choroiditis, whereas they are random in secondary choroiditis.[9] ICGA findings in various posterior uveitis are given in Table 3.

Optical coherence tomography features in posterior uveitis

Choroid consists of three vascular layers: outer Haller's layer that includes large vessels, middle Sattler's layer that includes medium sized vessels in choroidal stroma, and innermost CC layer that is in close association with Bruch's membrane. The outer two-third of the retina is supplied by these vessels.[5,12]

The different types of OCT include spectral-domain OCT (SD-OCT), swept source OCT (SS-OCT), and EDI-OCT. SD-OCT visualizes details of vitreous and retina but not

Table 2: Details regarding hypofluorescence on indocyanine green angiography imaging

Early phase	Intermediate phase	Late phase	Persistent on successive ICGA	Fundus lesions	Fluorescein angiogram	Diagnosis
Hypo	Hypo	Hypo	Hypo	Hypopigmented	Hyperfluorescent	Chorioretinal atrophy or scars
Hypo	Hypo	Hypo	Hypo	No visible lesions	No visible lesions	Selective chorioretinal stromal atrophy with intact RPE after choroidal inflammation, after treatment in SO and VKH
Hypo	Hypo	Hypo	Resolving	Faint lesions	Moderate hyperfluorescence	Involvement of inner choroid with obliteration or hypoperfusion of choriocapillaris as in MEWDS and APMPPE
-	Hypo	Hypo	Resolving	Visible lesions	-	Full-thickness choroidal lesions that had responded to steroidal therapy
-	Hypo	Iso or hyper	Resolving	Visible lesions	Visible lesions	Partial thickness resolved choroidal lesions as seen in BC, VKH, sarcoidosis, SO, TB lesions

SO: Sympathetic ophthalmia, TB: Tuberculosis, MEWDS: Multiple evanescent white dot syndrome, APMPPE: Acute posterior multifocal placoid pigment epitheliopathy, RPE: Retinal pigment epithelium, BC: Birdshot choroidopathy, VKH: Vogt–Koyanagi–Harada, ICGA: Indocyanine green angiography

Table 3: Indocyanine green angiography findings in various posterior uveitic entities

Diseases	ICGA findings	Involvement of structures
Birdshot chorioretinopathy[10]	Early - Visible hypofluorescent dark spots	Retina and choroid
	Intermediate - Sharply defined hypofluorescent lesions	Partial-thickness lesion in choroidal stroma (can respond to treatment)
	Late	
	Isofluorescent	Persistent scarred full-thickness granulomas, CC nonperfusion (can respond to treatment)
	Persistent hypofluorescent (cream color)	Chorioretinal atrophy (no response to treatment)
	Persistent hypofluorescent (depigmented or atrophic areas)	Untreated disease replacing hypofluorescent area in the intermediate phase by diffuse hyperfluorescence
	Diffuse hyperfluorescence	Leakage from large choroidal vessels (responds to treatment)
SC[6,11]	Active - Persistent areas of hypofluorescence in all phases	Due to choriocapillaris nonperfusion or blocked fluorescence due to inflamed RPE cells and outer retina in the active stage
	Healed - Heterogenous hypofluorescent areas in all phases	In progressive stage, diffuse hyperfluorescence at the edges of the progressing lesions
Acute posterior multifocal pigmented placoid epitheliopathy[6]	Marked hypofluorescence in all phases which persists in the late phase	Nonperfusion or hypoperfusion of choriocapillaris with early phases showing large choroidal vessels at the level of choriocapillaris beneath areas of hypofluorescence
Multifocal choroiditis[6]	Hypofluorescence at the posterior pole which persisted in all phases and homogenous background fluorescence in late phases	Hypofluorescence of choriocapillaris or blocked fluorescence due to inflammatory debris at the level of choriocapillaris
Multiple evanescent white dot syndrome[6]	Multiple well-defined hypofluorescent spots in the intermediate and late phases. Involvement of macular area could be picked up only in ICGA	Level of RPE or inner choroid
Ocular toxoplasmosis[3]	Hypofluorescence of the main lesion. Satellite lesions around the main retinochoroiditis lesion appear hypofluorescent	
	Progressive increasing hyperfluorescence in areas of CNVM	
VKHs disease[6]	Hypofluorescence in the early phase	Hypoperfusion of small vessels and perfusion delay of choriocapillaris. Diffuse leakage from inflamed vessels which are seen as fuzzy and indistinct choroidal vessels
	Diffuse late hyperfluorescence	
	Hypofluorescent dots which remained isofluorescent in late phases	Partial-thickness granulomas
	Hypofluorescent dots which remained hypofluorescent in late phases	Full-thickness granulomas

VKH: Vogt–Koyanagi–Harada, ICGA: Indocyanine green angiography, CC: Choroid and choriocapillaris, RPE: Retinal pigment epithelium, CNVM: Choroidal neovascular membrane, SC: Serpiginous choroiditis

choroid or sclera. EDI-OCT is a form of SD-OCT which penetrates deep enough to study choroid and sclera but unable to visualize the superficial vitreous. SS-OCT that employs a wide field scan visualizes both the vitreous and deeper structures with ease.[13]

The vitreous signs in posterior uveitis as picked up by OCT include vitritis, posterior hyaloid face precipitates as in acute retinal necrosis and toxoplasmosis, and superficial retinal precipitates as in syphilis and preretinal lesions as in fungal diseases. The peripapillary signs include fluid tracking from swollen optic nerve and optic nerve granulomas, and the inner retinal OCT signs include retinal nerve fiber layer thickening, foveolitis as seen in dengue fever, CME, diffuse retinal thickening, and perivascular thickening in posterior uveitis. The outer retinal signs in posterior uveitis include subretinal fluid (SRF) in VKH, retinal pigment epithelitis, acute macular neuroretinopathy lesions, ellipsoid layer inflammation or loss, dots, and spots in MEWDS, trizonal changes in AZOOR, RPE nodularities and ellipsoid layer loss in syphilis with placoid lesions, inflammatory CNVM, subretinal deposits in primary vitreoretinal lymphoma, varied presentations in necrotizing retinitis, and finally thinning or atrophy.[14]

The choroidal changes in OCT in posterior uveitis include inflammatory changes in CC, diffuse or localized thickening of choroid, changes specific for toxoplasmosis and BC, and presence of suprachoroidal fluid that may indicate BC lesion or a chorioretinal atrophic lesion.[14]

Table 4 gives the details of various OCT features in posterior uveitis disorders.

Table 4: Optical coherence tomography features of various uveitic entities

Diseases	OCT features
Ocular toxoplasmosis[15]	Full thickness hyperreflectivity and disruption of the retinal areas in the necrotic areas, shadowing, and choroidal thickening beneath the lesion
	Hyperreflective deposits on the inner retinal surface, posterior hyaloid and hyperreflective spots on the retro-hyaloid area
Tubercular choroidal granuloma[16]	Intraretinal fluid formed like a cystic space. ELM courses anterior to the cystic space while the myoid zone is split forming bacillary layer detachment. EZ is irregular with photoreceptor remnants at the floor of the cystic space. The outer segments and IZ remain intact with the entire granuloma seen as homogenous hyporeflective area in the stroma on SD-OCT
VKH disease[5,15]	Increased subfoveal choroidal thickness in acute and rebound increase in recurrence on EDI-OCT
	Acute VKH shows multi-lobar serous detachment with undulations or subretinal septae in the RPE
	Decreased subfoveal choroidal thickness or choroidal atrophy in chronic disease on EDI-OCT. Subfoveal choroidal thickness decreased more with severe depigmentation of fundus than with mild depigmentation of fundus
Behcet's disease[5]	Nonnecrotizing partial thickness retinitis lesions
	Increased subfoveal choroidal thickness in acute and quiescent stage that might indicate persistent subclinical inflammation on EDI-OCT
	Thinning in the subfoveal area was due to choroidal ischemia from recurrent inflammation leading to progressive fibrosis and thinning of the choroid on EDI-OCT
Sarcoidosis[5]	Granuloma seen as a homogenous hyporeflective area well demarcated from the surroundings. Subretinal fluid in the adjacent peripapillary area and healthy choroid in between the lesions on EDI-OCT
Birdshot chorioretinopathy[5,14]	ERM, a symmetric central CME along with thinning of retina and choroid and loss of inner - outer segment hyperreflective bands, subfoveal choroidal thinning, thinning of Sattler's layer with extramacular choroidal thinning. Presence of hyporeflective line corresponding to suprachoroidal fluid as a sign of disease activity on OCT

ELM: External limiting membrane, EZ: Ellipsoid zone, IZ: Interdigitation zone, ERM: Epiretinal membrane, OCT: Optical coherence tomography, SD-OCT: Spectral-domain OCT, EDI-OCT: Enhanced depth imaging-OCT, VKH: Vogt–Koyanagi–Harada, RPE: Retinal pigment epithelium, CME: Cystoid macular edema

Optical coherence tomography angiography in posterior uveitis

OCTA is a noninvasive technique that uses amplitude (intensity) decorrelation and phase variance to detect retinal and choroidal blood flow without detecting vascular leakage. It gives details of microvasculature without getting interference or obscuration from vascular leakage. OCTA is used to assess the vascular changes in iris, choroid, and retina, which are the major areas of involvement in the pathogenesis of ocular inflammation. The retinal vascular changes in those with retinal vasculitis includes areas of retinal capillary hypoperfusion, perifoveal capillary changes (dilated, rarefied, and shunting vessels), perifoveal capillary arcade disruption, enlargement of FAZ, disorganization of capillary network, and decreased capillary vessel density. The choroidal changes can be CC flow voids either due to ischemia of CC or due to space-occupying granulomas.[15,17,18]

OCTA not only detects vascular flow but also neovascularization and may aid in detecting inflammatory biomarkers qualitatively, quantitatively, and objectively. Depth-resolved capability aims at evaluating deep retinal capillary plexus that is specific target in retinal vasculitis and inflammatory disorders. Spectral-domain OCTA uses short wavelength (near 800 nm) that penetrates less and causes more scatter from media opacities, while SS-OCTA uses longer wavelength (near 1050 nm) that penetrates deeper but with lower axial resolution. The newer ultra-high-resolution wide-field OCTA has deeper penetration with higher resolution that allows fine discrimination of structural and microvascular components of retinal and choroidal anatomy.[15,18]

Table 5 gives OCTA findings in various posterior uveitis disorders.

Choroidal analysis on indocyanine green angiography

In both FA and ICGA, choroidal impregnation by ICGA fluorescence occurs during the intermediate and late phase of ICGA and this gets primarily disturbed in inflammatory

Table 5: Optical coherence tomography angiography findings in various posterior uveitic entities

Conditions	OCTA findings	Pathology
Birdshot chorioretinopathy[3]	Focal dilatations of the lumen of capillaries and focal areas with end-on capillary loops	Microvascular alterations (inner and outer retinal vascular plexus)
	Focal areas with abnormal tortuous vessels	Vascular telangiectasia
	Generalized or focal increase in intercapillary space in the perifoveal region	Inner retinal ischemia
	Decreased or absent flow in choriocapillaris in the area of lesions. Larger choroidal vessels bordering or traversing the hypofluorescent spots	Inner choroidal ischemia
VKH disease [Figure 1][18,19]	Hypoperfusion of choriocapillaris seen as dark foci and loss of choriocapillaris with flow void in acute stage	Hypoperfusion of choriocapillaris
	Choroidal granulomas compress the choroidal vasculature and show as flow void in choriocapillaris	
	Reduction in size and number of choriocapillaris flow void areas in the convalescent phase	
	Absence of choriocapillaris flow void areas in healed phase and reappearance of these areas in the recurrent phase	
Multifocal choroiditis and punctate inner choroidopathy[3,20]	Lacy tangled vessels extending from choriocapillaris to the outer retinal layers	CNVM (choriocapillaris and deep retina)
	PED with hyperreflective material under the RPE - mature vessels	
	PED with hyperreflective material in the subretinal space or outer retina - immature or fine vessels	
Ocular toxoplasmosis[1,3]	Termination of choriocapillaris and RPE in the region of CNVM and abnormal tangled retinal vessels	Only retinal vascular plexus and deep retina, no contribution from choroid
	Neovascular network from retinal vasculature only	
Multiple evanescent white dot syndrome[1,4,18]	Choriocapillaris and capillary retinal blood flow are normal	Disease of the RPE-photoreceptor complex
Acute posterior multifocal pigmented placoid epitheliopathy[1,4,18]	Flow reduction on choriocapillaris and inner choroid	
SC [Figure 2][1,4]	Flow reduction in choriocapillaris in active areas	In choroid
	In inactive areas, there is some detectable flow from medium to large choroidal vessels	
	Intact retinal vasculature	
Sarcoidosis [Figure 3][1,4]	Capillary dilatation, perifoveal telangiectasia and shunting of vessels -perifoveal capillary abnormalities	Full thickness of the choroid
	Capillary nonperfused or hypoperfused areas	
	Disorganized capillary network and cystoid spaces seen as well-defined black round areas in DCP, FAZ enlargement and reduced CVD in choriocapillaris and DCP	
	Flow void areas in areas of granulomas that blocks choriocapillaris flow	
Tubercular choroiditis [Figure 4][1]	Flow void areas due to hypoperfusion of choriocapillaris by the granulomas	
	Few preserved areas of choriocapillaris seen among hypoperfused areas	
	Healing shows medium-large vessels following atrophy of choriocapillaris	
	Tangled blood vessels from choriocapillaris	
Behcet's uveitis[4,21]	Capillary dilatation, perifoveal telangiectasia and shunting of vessels -perifoveal capillary abnormalities	SCP, DCP and FAZ
	Capillary nonperfused or hypo-perfused areas	
	Disorganized capillary network and cystoid spaces seen as well-defined black round areas in DCP, FAZ enlargement and reduced CVD in choriocapillaris and DCP	
	Resolved retinal infiltrate seen as irregular hypointense greyish areas	

PED: Pigment epithelial detachment, SCP: Superficial capillary plexus, DCP: Deep capillary plexus, CVD: Capillary vessel density, RPE: Retinal pigment epithelium, CNVM: Choroidal neovascular membrane, FAZ: Foveal avascular zone, OCTA: Optical coherence tomography angiography, SC: Serpiginous choroiditis

lesions showing as hypo- or hyperfluorescence. Herbort *et al*. determined the features of ICGA in posterior uveitis and proposed a schematic approach for the interpretation of ICGA findings in patients diagnosed with posterior uveitis. They proposed that hyperfluorescence is caused by leakage (CC leakage or from large choroidal vessels) or staining and not by window defects. They showed retinal ICG hyperfluorescence in Behcet's disease, diffuse zonal hyperfluorescence around hypofluorescent lesions in cases of toxoplasma retinochoroiditis and posterior scleritis, hyperfluorescence in CNVM, leakage from large choroidal vessels in the intermediate phase in cases of VKH and tissue staining at the subretinal level in posterior scleritis and VKH and tissue staining at the choroidal level in granulomatous lesions as in sarcoidosis, TB, syphilis, and MC. They proposed that hypofluorescence was seen in majority of cases of posterior uveitis and described five different patterns as described in Table 2. They proposed that the impregnation of choroid in the recirculation phase can be enhanced due to leakage from CC or from large choroidal vessels or impaired due to hypoperfusion of CC or space-occupying lesions causing impairment of filling.[7-9]

Howe *et al*. demonstrated that ICGA leakage did not occur in those with retinal vasculitis, whereas in those diagnosed with

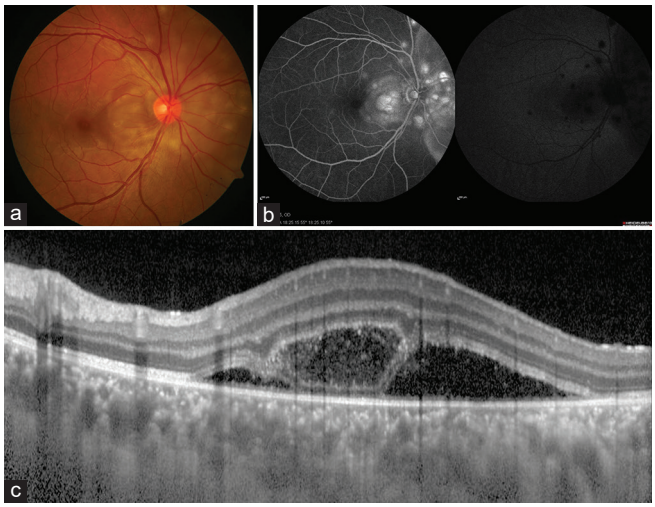

Figure 1: Multimodal imaging of a 29-year-old girl with sudden loss of vision in both eyes (right eye shown). The fundus photograph reveals deep yellow choroidal lesions suggestive of choroidal granulomas (a). The combined FA and ICGA (b) shows multiple hypofluorescent lesions corresponding to the choroidal stromal granulomas, and the FA shows hyperfluorescence in the late phase due to leakage and pooling of the dye. The optical coherence tomography shows subretinal fluid accumulation and compartmentalization of fluid in the inner retina (c). FA: Fluorescein angiography, ICGA: Indocyanine green angiography

active chorioretinitis (toxoplasma retinochoroiditis, APMPPE, MEWDS, SC, and VKH), they observed hypofluorescence either due to masking by inflammatory infiltrate (TB granuloma) or CC hypoperfusion (focal as in APMPPE or generalized as in VKH), hyperfluorescence in late phases in case of inflammatory CNVM, ill-defined areas of late hyperfluorescence as seen in active cases of BC and SC due to choroidal leakage and pooling in late stages as seen in VKH and no leakage from large choroidal vessels at any stage of ICGA. They concluded that ICGA was an adjunct in picking up choroidal pathology in inflammatory uveitis and that all lesions correlated with corresponding hypofluorescence in the early stage or hyperfluorescence in the late stage in active choroiditis on FA.[22]

Bouchenaki *et al*. classified choroidal vasculitis in posterior uveitis into primary inflammatory choriocapillaropathies, secondary inflammatory choriocapillaropathies, and choroidal stromal vasculopathies using ICGA. The primary inflammatory choriocapillaropathies include MEWDS, APMPPE, SC, MC, punctate inner choroidopathy, acute pigment epitheliitis, ampiginous choroidopathy, wherein the primary pathology is CC nonperfusion and the lesions were at the posterior pole as in APMPPE, SC, MC and ampiginous choroidopathy while peripapillary and midperiphery distribution as in MEWDS. All these lesions showed hypofluorescence on ICGA and during the convalescent phase and either disappeared completely indicating CC reperfusion as in APMPPE or MEWDS or, partial or complete chorioretinal atrophy following partially resolved or completely unresolved indicating irreversible CC nonperfusion. In the secondary choriocapillaropathies, the CC nonperfusion was in association with severe retinitis or

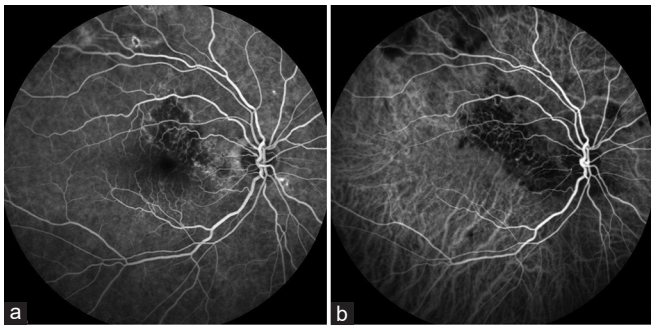

Figure 2: The combined FA (a) and ICGA (b) of a patient with TB SLC shows early hypofluorescence on FA due to the active choroiditis lesion, which appears prominently hypofluorescent on ICGA. This appearance is due to the choriocapillaritis due to the TB SLC. FA: Fluorescein angiography, ICGA: Indocyanine green angiography, TB SLC: Tubercular serpiginous-like choroiditis

severe choroiditis (toxoplasma retinochoroiditis, tubercular, and sarcoid chorioretinitis) with lesions showing as hypofluorescent dark areas on ICGA. In the choroidal stromal inflammatory vasculopathies (VKH, SO, and BC – primary) and TB, sarcoid and Behcet's disease– secondary), there is loss of stromal choroidal vessels that appeared fuzzy and indistinct in the intermediate phase followed by diffuse choroidal hyperfluorescence in the late phase indicating inflammation and leakage from stromal choroidal vessels. These respond to anti-inflammatory or immunosuppressive therapy.[23]

Choroidal analysis on optical coherence tomography

Enhanced vitreous imaging was introduced by Pang *et al*. for better visualization of vitreous and structures anterior to retina. SS-OCT allowed clear delineation of premacular bursa and Martegnani space on the scans.[24] Specific patterns of vitreous inflammation such as "nebulous pattern" and "volcanic pattern" as in cytomegalovirus (CMV) retinitis,[25] hyperreflective oval deposits between vitreoretinal interface and detached posterior hyaloid as in toxoplasma retinochoroiditis,[26,27] and "rain cloud sign" as in candida endophthalmitis have been described.[28] OCT in retinal lesions has shown nerve fiber layer infarct, diffuse retinal thickening with disruption of retinal architecture as in retinal ischemia, large empty spaces in outer nuclear layer as in CMV associated with retinal detachment, full-thickness increase in retinal thickness and hyperreflectivity along with disruption of all layers as seen in toxoplasma retinochoroiditis and so on. OCT of the outer retina has a prognostic implication as it can determine the visual outcome. Photoreceptors can get damaged by the inflammatory process itself or as a part of RPE or CC dysfunction. Disruption of the EZ and IZ as in placoid syphilitic chorioretinopathy, focal disruption of the junction between RPE and photoreceptors as in MEWDS, and interruption of RPE as in MC have been described. The presence of SRF though not specific for any uveitis entity can show presence of hyperreflective septa with pockets of fluid within the subretinal space specific for VKH. Similarly, hyporeflective focal thickenings with loss of physiological hyperreflective dots are specific for APMPPE and SC.[13]

Choroidal thickness increases in the acute stage of the disease due to increased blood flow due to inflammation and this can be used as a tool to monitor during treatment and recurrence. Specific patterns of hyporeflective area with homogenous content in the choroidal stroma and showing increased transmission through the underlying structures were seen in choroidal granulomas as seen in TB, sarcoidosis, and VKH. Massive choroidal thickening was seen in VKH, and focal choroidal thickening with disruption of choroidal architecture overlying an area of focal retinitis was seen in toxoplasma retinochoroiditis. Selective enlargement of Sattler's layer was seen in sarcoid uveitis.[13] OCT shows specific features for inflammatory CNVM (as in MC, APMPPE, BC, MEWDS, and AZOOR), in the form of "pitchfork sign" (multiple hyperreflective, vertical projections from CNVM area to the outer retinal space), located above the RPE in the subretinal space, presenting between disrupted RPE and outer retinal layers and presence of subretinal or intraretinal fluid in active stages.[29]

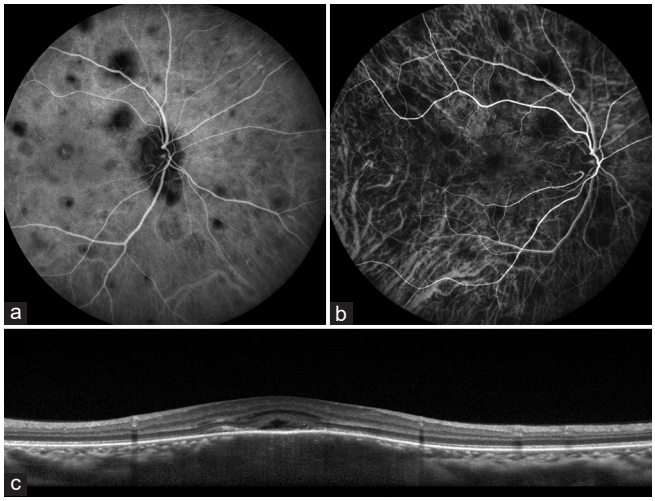

Figure 3: The figure shows a patient with multiple sarcoidosis-related choroidal granulomas. The ICGA reveals multiple round-to-oval lesions suggestive of stromal choroidal granulomas (more prominent in the late phase – (a). The early phase also shows hypofluorescent lesions suggestive of choroidal granulomas (b). The OCT (c) shows large choroidal granuloma in the subfoveal region causing an elevation and subretinal fluid accumulation. ICGA: Indocyanine green angiography, OCT: Optical coherence tomography

Mahendradas *et al*. used a combined capillary density index (CDI-OCT), SD-OCT, and EDI-OCT) to assess the posterior vitreous, vitreoretinal interface and inner and outer choroid. It helps in assessing the area of interest with much depth. Increased choroidal thickness as seen in choroidal granulomas, acute choroiditis, and outer choroidal border was picked up well with CDI-OCT and EDI-OCT (sarcoid and VKH). There was a major impact on the visualization of posterior vitreous and outer choroid. However, in patients who had poor fixation and increased retinal thickness, CDI-OCT was not very helpful.[30] Mehta *et al*. showed that enlargement of Sattler's layer was significant in sarcoid uveitis (48.3%) than TB uveitis (40.5%), increased choroidal thickness was found in acute granulomatous uveitis cases, choroidal thinning whether generalized or focal in chronic granulomatous uveitis was associated with decreased visual acuity, thicker choroid in active stages of VKH and Behcet's due to spongiform choroidal vasculature being reactive in the inflammatory state rather than in the quiescent state.[31]

OCT recognizes three types of patterns of fluid accumulation in uveitis as per Markomichelakis *et al*.: diffuse macular edema, CME, and concomitant serous detachment.[32] OCT also detects vitreomacular interface abnormalities such as epiretinal membrane or vitreomacular traction. A 20% change in retinal thickness affects the visual acuity to a greater extent. Inner retinal infiltrates are seen as focal hyperreflective retinal thickening with smudging of inner retinal layers and shadowing beneath in Behcet's disease. Toxoplasma lesions show full-thickness hyperreflectivity with disruption of the retinal layers in the necrotic area and hyporeflectivity of the choroid beneath the necrotic area. Hyperreflective oval deposits are seen on the inner retinal surface, posterior hyaloid, and along the retrohyaloid area. Intraretinal edema with hyperreflective vertical stripes within the outer nuclear layers is seen in viral retinitis. Involvement of outer retina is seen in MEWDS, APMPPE, SC, AZOOR, and MC, and loss of outer retinal

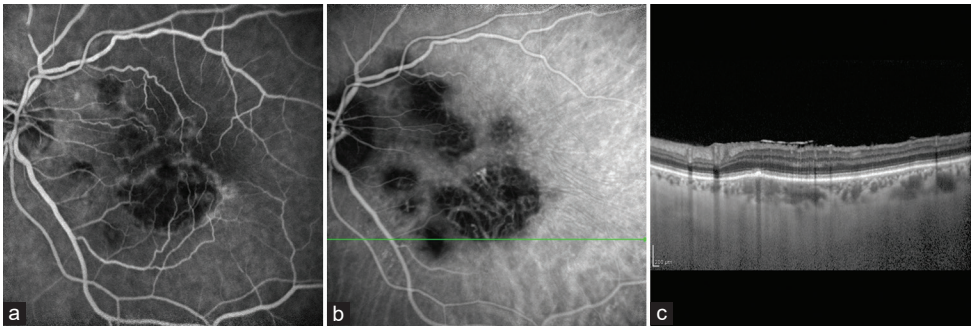

Figure 4: The combined FA and ICGA (a and b), and OCT (c) of a patient with SC shows hypofluorescence with leakage of the dye from the active edges on FA, and hypofluorescence of the choroiditis lesion suggestive of choriocapillaris ischemia due to the active choroiditis. The OCT shows an epiretinal membrane, thickening of the choriocapillaris suggestive of ischemia, and focal choroidal thickening (c). SC: Serpiginous choroiditis, ICGA: Indocyanine green angiography, OCT: Optical coherence tomography, FA: Fluorescein angiography

layers and increased transmission defect is seen in the late stage of SC. Evolution from early edematous stage to the late atrophic stage is observed in BC. Evolution of five stages of choroidal infiltration, formation of sub-RPE nodules, formation of chorioretinal nodules, their regression, and herniation of the retina is observed in punctate inner choroiditis. While VKH and SO showed diffuse choroidal inflammation with serous retinal detachments, acute stage of VKH showed multilobar serous retinal detachments with subretinal septae or undulations of RPE.[15]

EDI-OCT has gained importance not only in primary choroiditis such as VKH, SO, and BC but also in secondary choroiditis such as sarcoid and TB choroiditis. EDI-OCT shows diffuse choroidal thickening in acute VKH and choroidal atrophy in chronic cases of VKH. Choroidal thickening mixed with atrophic areas indicates recurrence. In BC, there was thickening of choroid that reduced with treatment. In both cases of VKH and BC, ICGA was much more sensitive during follow-up than EDI-OCT.[15]

SS-OCT has been comparable in studying choroidal diseases as much as EDI-OCT more so in studying CVI.[15] Pichi *et al*. when describing various EDI-OCT signs of posterior uveitis have shown hypoperfusion of CC in active stages of APMPPE, active edges of SC, active serpiginous-like choroiditis and VKH, and that OCT helps in predicting the evolution of these disease entities over time. OCT also shows diffuse choroidal thickening as seen in acute VKH because of inflammatory infiltrates and in addition choroidal granulomas can cause compression of precapillary arterioles and venules in Sattler's layer. Focal choroidal thickening with elevation of RPE in the area under the lesion has been seen in SC with poor response to treatment and complicated by CNVM formation. EDI-OCT helps in assessing granulomas over time when compared to ICGA and limits the differentials to sarcoid, TB uveitis, and VKH disease. OCT helps in monitoring the response to treatment and in assessing choroidal thickness with response to treatment. Healing shows thinning of choroid with chorioretinal scar formation. OCT and OCTA have been helpful in birdshot choroidopathy in assessing the progression from the acute stage to the atrophic stage when compared to conventional ICGA and FA.[14,15,17]

Choroidal analysis in optical coherence tomography angiography

Retinal vasculitis changes in OCTA have been shown to be areas of retinal capillary hypoperfusion, perifoveal capillary changes, including dilated, rarefied, and shunting vessels, perifoveal capillary arcade disruption, enlargement of FAZ, disorganization of capillary network, and decreased capillary vessel density. Eyes with retinal vasculitis have shown changes in both SCP-decreased flow density, capillary remodeling, enlargement, or irregularity of FAZ and DCP– greyish hypo or nonperfused areas, elevated, dilated, or shunting perifoveal vessels and well delineated flow void areas. OCTA showed flow voids in CC in APMPPE and flow void due to granuloma (VKH, sarcoidosis) and focal arteriolitis as in BC.[15,33,34]

OCTA shows dilatation of vessels in acute inflammation and increase in vessel density in the disk area during inflammation. OCTA can help in studying new vessels growing in the preretinal space in response to inflammation and using vitreous as a scaffold. Reduced vascular density with complex branching patterns in the superficial and deep retinal vascular plexus and heterogenous flow signal have been observed in CC in OCTA in intermediate uveitis. It allows in the visualization and quantification of retinal hypoperfusion in occlusive vasculitis. In areas of retinitis, OCTA has shown disruption of normal retinal capillary plexus, neovascular network within the lesion as in Bartonella and chorioretinal anastomosis following resolution of retinal lesion in candida endogenous endophthalmitis. In BC, acute lesions do not show any changes in OCTA; however, if not treated, the atrophic lesions with impairment of CC blood flow are observed as reduced areas of blood flow. OCTA helps in differentiating inflammatory CNVM from inflammatory lesions of MC by showing blood flow in the neovascular network. OCTA demonstrates diminished and discrete areas of blood flow as CC nonperfusion in VKH, APMPPE, and SC. OCTA helps in differentiating inflammatory CNVM from inflammatory nonneovascular lesions by showing the presence of neovascular network that are seen only in the CNVM. These lesions are located at the level of outer retinal layers and disrupted RPE and seen as accumulation of hyperreflective material. Blood flow on b-scan and coronal section will help us diagnose the lesion precisely without projection artifacts.[13]

OCTA provides useful information in diseases affecting RPE/CC such as white dot syndromes, choroidal stromal diseases, VKH, and ocular toxoplasmosis. In MEWDS, there was no CC involvement as it was primarily a disease of the RPE or photoreceptors. OCTA shows dark areas of flow deficit in *en face* OCTA in areas of activity in SC, APMPPE, and MC that is useful in follow-up of patients and assessment of CC flow deficit areas as the lesions heal. OCTA categorizes type 1 CNVM predominantly in tubercular serpiginous like choroiditis, type 2 CNVM in choroidal granulomas and toxoplasma retinochoroiditis. OCTA shows hyporeflective dark dots in the CC layer that differentiates it from central serous retinopathy and helps in assessing the response to treatment.[35]

Agarwal *et al* quantified retinochoroidal vascular parameters in patients with quiescent posterior uveitis and panuveitis using SS-OCTA. In this cross-sectional study, the parameters studied were fractal dimension (FD – a geometric measure of the complexity of the retinal microvasculature tissue and is calculated as a ratio using mathematical models), FAZ (area in SCP measured in pixels and converted to millimeters and squared for analysis), retinal vascularity index (RVI) and choroidal vascularity index (CVI – Luminal area / Total choroidal area – LA/TCA). RVI was measured in terms of capillary density index (CaDI) that is defined as the percentage

of capillary density over stromal area in the macular region in each quadrant. It measured both the SCP and DCP and the global CaDI is the average CaDI value within 1.5 mm radius circle centered on the subfoveal region. The retinal parameters – Decreased FD compared to controls in both SCP and DCP with $p < 0.001$, enlarged FAZ than controls with $p < 0.001$, Lower CaDI than controls in SCP with $p = 0.019$, reduced central macular thickness than controls with $p < 0.001$ with no changes in DCP. The choroidal parameters – choroidal thickness in the foveal center was lower than controls with $p = 0.025$, CVI was lower than control with $p < 0.001$. Lower FD in DCP was predominantly present in those with Behcet's, sarcoid and healed choroiditis when compared to controls and Lower CVI was present predominantly with TB, sarcoidosis, healed choroiditis and retinal vasculitis when compared to controls. This study was performed to know the etiology behind improvement in suboptimal vision in healed patients without macular scars or fibrosis. The authors hypothesized that reduction in FD may have contributed to the suboptimal vision gain in these patients. All the diseases caused damage to both retinal and choroidal vasculature except retinal vasculitis which affected the retinal vasculature.[36]

Table 6 gives the pathology behind reduction of various parameters in those with quiescent posterior uveitis and panuveitis when compared to controls.[36]

McKay *et al*. advocated a custom-made algorithm using *en face* SS-OCTA for identification and quantification of inflammatory CC in posterior uveitis entities. The algorithm delineated the boundary of the lesion and quantification of area. This was comparable and reproducible to identification of lesions by masked human graders using Sorensen–Dice coefficient and intraclass correlation coefficient. The algorithm showed good special overlap except in cases of CNVM and lesions with low contrast boundaries. This quantitative metrics using CC flow deficit will act as an imaging biomarker of disease activity in patients with posterior uveitis and their response to treatment.[36]

Chu *et al*. analyzed CC flow deficit (FLD) in patients with uveitis using flow deficit number (FDN), mean FLD size (MFDS), and FLD density (FDD) with *en face* SS-OCTA. The images were obtained from 3 mm × 3 mm and 6 mm × 6 mm scans. Numerous, small, and evenly spaced FLD were seen in the entire macula in the controls. The coefficient of variation (CV) ranged from 1.29% to 6.65% and MFDS having the lowest CV among all the three. There was no significant difference between the controls and uveitis patients in FDN. However, the MFDS was 751.7 μm^2 per 3 mm × 3 mm area and 802.0 μm^2 per 6 mm × 6 mm area in controls and 838.4 μm^2 per 3 mm × 3 mm area and 870.9 μm^2 per 6 mm × 6 mm area in uveitis eyes confirming significantly larger FLD areas in uveitis eyes. FDD was also higher in uveitis patients than in controls ($P = 0.0002$ in 3 mm × 3 mm area to $P = 0.0076$ in 6 mm × 6 mm area). MFDS and FDD were greater in those with choroidal involvement than in those without choroidal involvement and controls. Posterior uveitis patients had larger FD metrics than other uveitis entities and control group.[37]

Table 6: Reduction in retinochoroidal vascular parameters and their pathological causes

Parameters	Pathology
Decreased CaDI and CVI with reduced CMT and SFT	Healing leads to atrophy that causes reduction of retinal and choroidal thickness that leads to decreased vascular density as a secondary phenomenon
Reduced FD in SCP and DCP	Actual reduction in branching with in the retinal layers and rarefaction of blood vessels in both SCP and DCP
Enlargement of FAZ	Inflammation leads to long-standing damage to retinal microvasculature and permanent reduction of parafoveal vascularity

CMT: Central macular thickness, SFT: Subfoveal choroidal thickness, CDI: Combined depth imaging, CVI: Choroidal vascularity index, FD: Fractal dimension, DCP: Deep capillary plexus, FAZ: Foveal avascular zone, SCP: Superficial capillary plexus

Discussion

Both FA and ICGA are comparable during the initial phases in posterior inflammatory diseases, but the significant difference lies during the recirculation time when ICG leaks from the fenestrated choroidal capillaries that slowly impregnates the entire choroidal thickness. This can be enhanced by increased leakage from the CC or from the large choroidal vessels. ICGA is able to give a clear understanding of the choroidal vasculature in the active and healed stage (SC-generalized hypofluorescence in all phases in active stage and stippled heterogeneous hyperfluorescence in the healed stage, delayed choroidal filling not seen with FA were related to the active lesions). ICGA would also show whether macula is involved as it would warrant immediate intervention. ICGA helps in differentiating various inflammatory conditions that have similar clinical appearance MC shows hypofluorescent lesions at the posterior pole compared to resumed ocular histoplasmosis syndrome (POHS), which shows hyperfluorescent lesions at the posterior pole during periods of activity. ICGA also helps in the diagnosis of inflammatory conditions like MEWDS, which shows posterior pole hypofluorescence at the intermediate phase with peripapillary hypofluorescence with a punctate outer margin, compared to BC which shows hypofluorescent lesions in the early and late phases. MC shows peripapillary hypofluorescence which has a discrete line of abnormal fluorescence. Choroidal involvement is evidenced by the involvement of large and small choroidal vessels in those with active disease in VKH. Thus, ICGA is extremely helpful in delineating choroidal inflammatory conditions that present with multiple spots. It may help in follow-up of patients in response to therapy.[6]

Pichi *et al*. have described choroidal biomarkers in acute and inactive stages of few uveitis entities. In APMPPE, EDI-OCT in the acute stage shows focal areas of CC thickening and hyporeflectivity beneath with increase in subfoveal choroidal thickness that resolve in the inactive stage and seen earlier in EDI-OCT than on ICGA. In SC, EDI-OCT shows increased

CC thickness and hyporeflectance that transforms to decreased CC thickness, choroidal thinning and CC thinning and atrophy in the healed stage. In VKH, both SS-OCT and EDI-OCT have been able to quantify subfoveal choroidal thickness before (increased choroidal thickness in acute stage) and after treatment (decreased choroidal thickness) with steroids. Similarly, choroidal granulomas in VKH are seen as hyporeflective, homogenous round lesions with well-defined margins with increased choroidal transmission effect beneath the granulomas.[38] Ciulla *et al*. assessed OCT features and BCVA in macular edema in noninfectious uveitis. Pretreatment EZ integrity and presence of central subfield cystoid spaces or SRF were taken into consideration to predict the therapeutic response in those eyes. 24-week change in BCVA in those with disrupted central subfield EZ was less than those with normal EZ (9.4 letters vs. 11.9 letters, $P = 0.006$), and 24-week change in BCVA in those with central subfield cystoid spaces or SRF was better than those without such changes (13.7 letters and 17.2 letters vs. 5.5 letters and 9.5 letters, respectively).[39]

Bittencourt evaluated choroidal thickness and choroidal vessel diameter (CVD) in normal, myopic, and noninfectious uveitis (MC, BC, VKH, AZOOR, SC, and PIC) using SD-OCT. Patients in the noninfectious uveitis group were in disease remission and had decreased choroidal thickness (194.6 ± 54.6 μm vs. 261.6 ± 41.6 μm in normal vs. 260.2 ± 50.6 μm in myopic group) and that was seen more in BC, SC, and MC than in other nonuveitis entities. Decreased VD (123.6 ± 37.4 μm in the uveitis group vs. 159.8 ± 32.2 μm in the normal group vs. 163.2 ± 33.2 μm in the myopic group) was seen in the uveitis group than in the normal or myopic groups. This is hypothesized to be due to inflammation and ischemia, leading to atrophy of choroidal layers. This is consistent with the findings of Bittencourt *et al*. in MEWDS,[40] Karampelas *et al*. (thinning of choroid and Haler's layer) in panuveitis,[41] and Keane *et al*. (thinning of Sattler's layer and choroid) in BC.[42] Thus, this study paved the way to future research with choroidal thickness and CVD as potential parameters to monitor patients with noninfectious uveitis.

Agrawal *et al*. studied CVI using EDI-OCT in patients with panuveitis and posterior uveitis at baseline and at 3 months and compared that with normal subjects. The results showed that CVI had decreased in the uveitis eyes at baseline and at 3-month follow-up (74.1 ± 4.7% vs. 69.4 ± 4.8%), and the percentage change of CVI was 6.2 ± 3.8 (4.3–8.0) in uveitis eyes that was significantly higher than that in the control group (0.7 ± 1.1 [0.2–1.3], $P < 0.001$). This percentage gives the vascularity of the choroid that can affect the thickness of the choroid and hence the disease progression. Thus, it can be used as a biomarker to assess disease activity, disease progression, and the choroidal perfusion status. CVI was able to demonstrate the activity of chorioretinal diseases in VKH, BC, and SO through structural alterations in choroid. CVI demonstrated choroidal ischemia, which was proposed as one of the mechanisms for poor vision in specific patients.[43]

SD-OCT classifies uveitis macular edema into CME, diffuse macular edema, and SRF. Abnormalities of the outer retina particularly disruption of the photoreceptor IS/OS segment junction and cystoid changes in the outer plexiform and inner nuclear layer and the presence of epiretinal membrane are associated with poor visual outcome. Both increased foveal thickness and foveal thinning have prognostic implications in uveitis. Foveal atrophy (as a result of atrophy of RPE and choroid), macular edema, macular ischemia (due to occlusive retinal vasculitis), CNVM, and damage to photoreceptors can lead to permanent visual impairment in posterior uveitis. The coronal or C-section in *en face* OCT helps in assessing the location and extent of inflammation in retina and choroid. The C-section images between outer plexiform layer and ganglion cell layer correlates with visual outcome much better than macular thickness or volume measurements in uveitic macular edema as per Cohen *et al*.[44] Though Keane *et al*. reported SD-OCT measurement of vitreous signal intensity for quantifying vitreous inflammatory activity to prognosticate the visual outcome in patients with intermediate, posterior and panuveitis, more clinical trials using automated vitreous measurements in commercial OCT are required. Though EDI-OCT can assess deeper choroidal structures qualitatively and choroidal thickness quantitatively, it cannot examine fundus as a whole as in stromal choroiditis like VKH and BC. It is also less sensitive and reactive in detecting subtle short-term changes in choroiditis unlike ICGA, which is still the gold standard for close monitoring in such cases. EDI-OCT can then be used as an additional modality for long-term follow-up.[5,12-16,44-46]

OCTA gives us details about the retinal and choroidal vessels by imaging retinal and choroidal vascular layers in multiple *en face* images in contrast to single *en face* image in FA or ICGA. It is noninvasive and involves three techniques: speckle variance, amplitude decorrelation, and phase variance. OCTA detects early peripapillary neovascular proliferation or telangiectasia or neovascularization obscured by retinal hemorrhage earlier than in FA. The problem in OCTA is artifacts that can be due to head or eye movements. Several studies have shown that retinal hypoperfusion was more in DCP than SCP in the inferior macular area and parafoveal capillary telangiectasia in DCP in Behcet's disease. Similarly, OCTA findings have been described above in various posterior uveitis entities and white dot syndromes.[47]

Levison *et al*. showed that OCTA was able to identify CNVM in 11/12 patients who were suspected to have CNVM following PIC or MC. OCTA was able to pick up better than FA in some patients. However, FA was important in showing associated features such as retinal vascular leakage, peripheral nonperfusion, and peripheral retinal evaluation. Inflammatory CNVM may not have the classical intraretinal and SRF in OCT as in other CNVM and pigmentation of the retina following inflammation and previous CNVM can make the diagnosis difficult with FA. OCTA identifies early CNVM and CNVM growth that might otherwise be missed with other modalities.

OCTA showed response to anti-VEGF therapy and appearance of vascular structure in active and treated stage.[20]

The recent consensus using the modified Delphi process recommended OCTA images measuring more than 70° field of view as wide-field OCTA, 90° or 120° field of view to be considered as ultrawide field OCTA, nondetectable flow signal as absent OCTA flow signal due to displacement of vessels due to fluid or solid lesions (SCP, DCP, CC and choroid), flow deficit as absent blood flow such as SCP or DCP due to occlusive vasculitis or ischemia of the CC, inflammatory CNVM as "loose" for large diameter network of vessels with small number of branches and "dense" for network of vessels with dense capillary branching resembling a fine net pattern. A threshold ≥30% of the absolute area to be considered as a large area of decreased wide-field flow signal.[48]

Conclusion

Although ICGA is the gold standard for diagnosing and following up of patients with posterior uveitis, OCT and OCTA have been exclusive in quantifying choroid through measurement of various parameters such as choroidal inflammation, choroidal thickness, FLD, RVI, and CVI. Thus, multimodal investigations using ICGA, OCT, and OCTA are upcoming and challenging areas where there is a tremendous scope for future research.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initial s will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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