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Review Article

Pachychoroid Spectrum Disorders: A Review of Clinical Features and Management

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Abstract

Pachychoroid disorders are an entity distinct from age-related macular degeneration and constitute four major variants along a continuum- pachychoroid pigment epitheliopathy, central serous chorioretinopathy (CSCR), pachychoroid neovasculopathy (PNV), and polypoidal choroidal vasculopathy (PCV). The common characteristics include presence of dilated outer choroidal vessels (pachyvessels), choriocapillaris and retinal pigment epithelium (RPE) attenuation with or without increased choroidal thickness in a focal area or diffuse in topography. Whether choroidal congestion and hyperpermeability is the primary event with consequent choriocapillaris atrophy or choriocapillaris attenuation occurs primarily with resultant compensatory outer choroidal vascular dilatation, remains poorly understood. Chronic choroidal inflammation and ischemia predispose to angiogenic factor release which together with overlying RPE-Bruch's disruption leads to type 1 choroidal neovascular membrane (CNV) formation. Pachychoroid disorders occur in younger population, does not have multiple soft drusen, and have distinct genetic polymorphisms and favourable treatment response when compared to the age-related macular degeneration. Systemic associations are known to occur with pachychoroid disorders. The treatment is required in cases of CSCR with chronic subretinal fluid and PNV or PCV with CNV and macular exudation. While acute cases of CSCR resolves spontaneously, diffuse epitheliopathy often requires photodynamic therapy or focal laser photocoagulation depending upon the site of RPE leakage. Pachychoroid disorders with exudation from CNV respond to three monthly intravitreal anti-vascular endothelial growth factor (anti-VEGF) injections followed by pro-re-nata treatment. The presence of polyps and branched vascular network in PCV often requires photodynamic therapy instead or in addition to anti-VEGF therapy. Significant advances have occurred in the understanding of this novel spectrum with the help of indocyanine green angiography and optical coherence tomography angiography. However, there remain several areas of uncertainty including the pathogenesis and superiority of the various treatment approaches. Specific therapies aimed at the pathological changes occurring in the pachychoroid disease are the need of future.

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Introduction

The word 'pachy' in Greek refers to 'thick' and therefore 'pachychoroid' literally means thick choroid. The choroid is the multifunctional layer of eye and is believed to play an important role in the pathophysiology of numerous ocular disorders. Pachychoroid is not a disease but a phenotype characterized by certain specific choroidal changes. The choroid is often thick but is not the quintessential criteria.[1] The typical features include focal or diffuse areas of choriocapillaris and Sattler's layer attenuation, dilated outer choroidal vessels (Haller's layer), and overlying retinal pigment epithelium (RPE) dysfunction.[1]

Types

The pachychoroid group of diseases includes conditions with overlapping features and representing different presentations of a common underlying pathology. The following entities are included in pachychoroid spectrum-

1. Pachychoroid pigment epitheliopathy (PPE)
2. Central serous chorioretinopathy (CSCR)
3. Pachychoroid neovasculopathy (PNV)
4. Polypoidal choroidal vasculopathy (PCV)
5. Peripapillary pachychoroid syndrome (PPS)
6. Focal choroidal excavation (FCE)

Clinical Features

There are certain common clinical features of the pachychoroid disorders. These are as follows-

1. Fundus appearance

The normal fundus tessellations are decreased with or without additional pigmentary alteration.

2. Optical coherence tomography

Choroidal morphology and the sclero-choroidal junction may be studied either using spectral domain optical coherence tomography with enhanced depth imaging (EDI) or swept-source optical coherence tomography (SS-OCT).[2]

Cross-sectional imaging

The choroidal thickening may be focal or diffuse, and foveal or extrafoveal. Although there occurs a variation due to difference in imaging systems, the normal subfoveal choroidal thickness in Indian population is reported to be 299.1± 131.2µm.[3] There is no particular threshold value of SFCT for thick choroid. Still most researchers consider SFCT >300um as suggestive of a thick choroid.[1,4] In case of extrafoveal thickening, the SFCT may be normal but the CT at the extrafoveal area of interest may be at least greater by 50um as compared to SFCT.[4]

The outer choroidal vessels in the Haller's layer are pathologically dilated (pachyvessels).[1] These are seen as hyporeflective lumen with large diameter on cross-sectional OCT. Often these are present in the area of choroidal thickening and tend to be displaced inward towards the RPE. Another important characteristic is focal or diffuse attenuation of the choriocapillaris and intermediate size choroidal vessel layer (Sattler's layer).[4] This occurs overlying the pachyvessels. The inner layers may be sometime so attenuated that the overall CT may be near normal. This highlights the importance of altered morphology rather than the mere increase in CT in making a diagnosis of pachychoroid.[5] Newer automated softwares aim to quantify the luminal areas in choroid as compared to the total area and provide with a more accurate picture of the disease.[6]

Apart from the choroidal changes, outer nuclear layer thinning and RPE layer attenuation have also been reported in pachychoroid diseases.[7]

En-face imaging

The pachyvessels are seen as abnormally dilated channels that do not taper but terminates abruptly.[4] These may be seen in the superficial en-face planes if the disease is advanced with inward displacement of the pachyvessels.

3. Indocyanine green angiography (ICGA)

The pachyvessels are better delineated on ICGA.[8] In addition, there may be presence of choroidal filling defects and hyperfluorescence.[8,9] Early phase shows delayed arterial filling while mid-late phase shows punctuate hyperfluorescence i.e choroidal vascular hyperpermeability (CVH).[8,9] CVH occurs due to leakage from the dysfunctional outer choroidal vessels or choriocapillaris. The apparently normal fellow eyes may also have such ICGA findings. CVH generally occurs in areas with increased CT; however, the opposite may not always be true.[10]

Specific Features

Pachychoroid pigment epitheliopathy

Warrow et al. first described this entity as characteristic RPE changes occurring over the areas with choroidal thickening at the posterior pole.[11]

The patients are often young. PPE is often detected incidentally in the fellow eyes of CSCR or PNV and is not visually significant.[11] Earlier such cases were mislabeled as age-related macular degeneration or acute retinal pigment epitheliitis.[12]

Fundus shows focal foveal/ extrafoveal areas of RPE mottling along with decreased fundus tessellation (Figure 1a).

OCT shows focal RPE alterations such as attenuation or thickening along with pachyvessels and choriocapillaris attenuation (Figure 1b). There is no evidence of subretinal fluid, choroidal neovascular membrane (CNV) or outer retinal changes on OCT.

The subtle RPE changes are better detected with short-

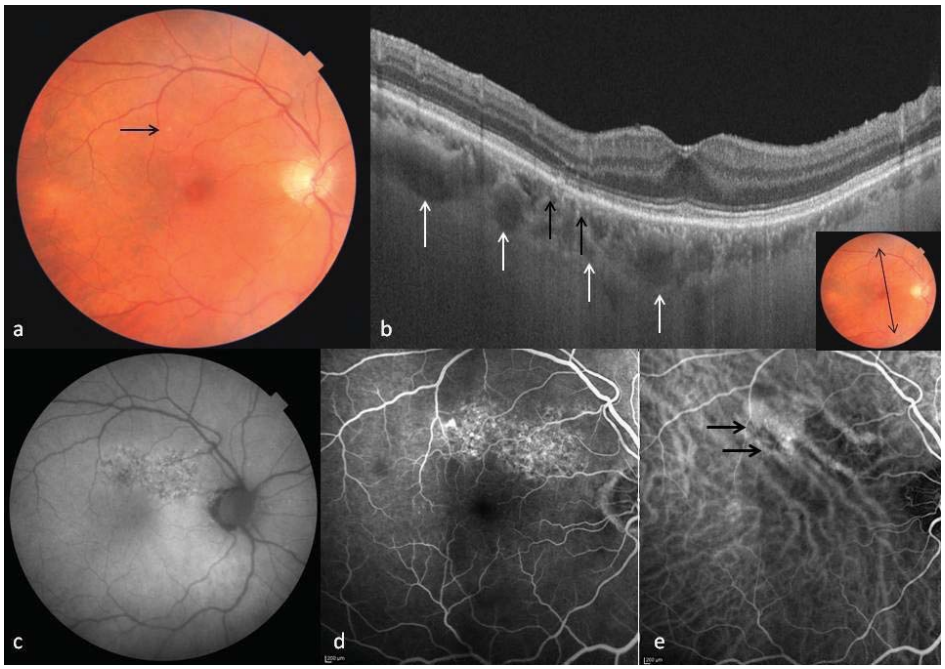

Figure 1: *Multimodal imaging in a case of pachychoroid pigment epitheliopathy. (a) Color fundus photo shows focal area of RPE mottling in the superior macula (black arrow) along with decreased fundus tessellation. (b) Macular OCT shows focal RPE and choriocapillaris attenuation (black arrows) and pachyvessels (white arrows). (c) Short-wave FAF stippled hyper-autofluorescence in the superior macula. (d) FFA shows a granular pattern. (e) ICGA shows large choroidal vessels and hyperfluorescence (black arrows) in the area corresponding to RPE mottling.*

wave autofluorescence (AF) (Figure 1c). The pattern may be either stippled hyper-autofluorescence or granular hypo-autofluorescence depending upon the health of RPE.
FFA shows mixed granular pattern due to local RPE changes (Figure 1d).
The ICGA shows CVH in areas corresponding to RPE mottling on color fundus imaging (Figure 1e).

Central serous chorioretinopathy
Von Graefe first coined the term "central recurrent retinitis" for cases with recurrent serous macular detachments.[13] It was Gass who gave the name "central serous choroidopathy" in 1967 after studying the clinical features and pathophysiology in detail.[14]
CSCR is characterized by serous exudation at the posterior pole with associated RPE leakage and choroidal hyperpermeability. The disease typically presents as acute onset of blurring of vision with distortion of image (metamorphopsia) and central field defect (scotoma) in young adults.
The disease occurs in two phases depending upon the duration- acute (≤3 months) and chronic (>3 months). Acute cases have NSD at the posterior pole, which appears as an elevated transparent area with well defined margins. Pigment epithelium detachment (PED) may also be present, which appear as a smaller well-defined orange elevation deeper to the NSD (figure 2a). Acute cases may have subretinal fibrin. The site of involvement may be foveal or extrafoveal, and uni-centric or multi-centric. Chronic cases have diffuse RPE mottling with shallow NSD. Classic feature is the presence of gravitational tract, which is an area of RPE hypo-pigmentation occurring at the macula and extending inferiorly across the inferior arcade.
OCT confirms the NSD and PED, both of which are serous and usually optically clear (Figure 2b). Sometimes, in acute cases, subretinal fibrin may be seen as heterogeneous reflectivity within the NS elevation. While the NSD and PED are steep in acute cases, these become shallow and broad in chronic cases. Outer retinal changes such as elongated outer segments, disruption of ellipsoid zone, and atrophy of outer nuclear layer are seen in chronic cases. Rarely cystoid degeneration may also occur.[15]
AF shows vertical gravitational tracts of hypoauto-fluorescence due to underlying RPE atrophy in chronic cases (Figure 2c).[16]
FFA shows single or multifocal leaks at the level of RPE in the form of ink-blot in acute cases (Figure 2d).[1] The dye pools in the NSD from the site of RPE leak in the superior direction giving appearance of a smoke-stack. Chronic cases have granular window defect in areas of RPE atrophy.[1] The RPE leaks are often indistinct.
ICGA shows the common clinical findings (Figure 2e).
OCTA rules out the presence of CNV.

Pachychoroid neovasculopathy-
PNV is a pachychoroid disease with type 1 or sub-RPE CNV in the absence of other identifiable entities such as myopic degeneration, drusen and posterior segment inflammation. Pang and Freund were the first to describe this entity in eyes developing type 1 CNV over background changes of PPE.[17] PNV cases were earlier misdiagnosed as neovascular AMD or labeled as idiopathic CNV. Current literature shows that PNV is distinct form neovascular AMD.[18,19]
PNV mostly occurs in young adult males. The fellow eyes may have features of other pachychoroid disorders.
CNV is the primary fundus feature of PNV, which may

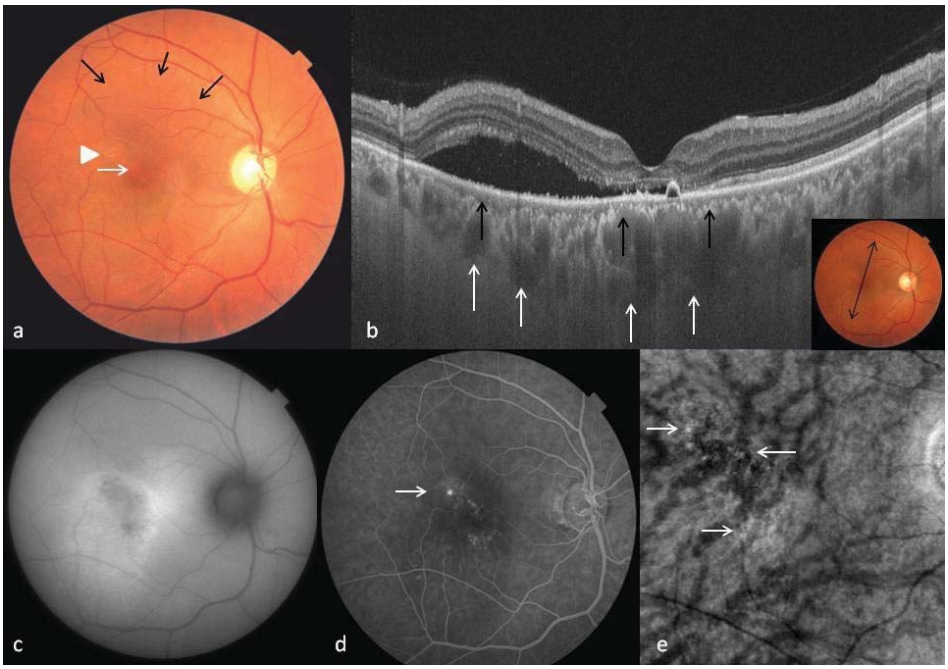

Figure 2: *Multimodal imaging in a case of central serous chorioretinopathy. (a) Color fundus photo shows decreased fundus tessellation, focal area of RPE mottling (white arrowhead), foveal PED (white arrow), and NSD involving the superior macula (black arrows). (b) Macular OCT shows focal RPE and choriocapillaris attenuation (black arrows), pachyvessels (white arrows), serous NSD and a foveal small serous PED. (c) FAF shows hypoautofluorescence due to RPE attenuation. (d) FFA shows an ink bloat leak (white arrow). (e) ICGA shows large choroidal vessels and stippled hyperfluorescence (white arrows) in the area corresponding to RPE mottling.*

be foveal or extrafoveal in location. A dirty grey membrane is usually seen with minimal exudation and retinal hemorrhages (Figure 3a).

OCT shows a shallow irregular PED with internal reflectivity suggestive of sub-RPE or type 1 CNV (Figure 3b).17 A 'double layer sign' may be seen with hyperreflective gap signifying a separation of RPE form Bruch's membrane by the CNV (Figure 3b).[20] Subretinal or intraretinal fluid is usually scant.

Since the CNV lies external to RPE, PNV is seen as occult membrane on FFA.17 Stippled hyperfluorescence is noted in the late phase (Figure 3d). ICGA (Figure 3e) and AF (Figure 3c) findings are non-specific with no evidence of polypoidal lesions and branched vascular network on ICGA.[1,17]

OCTA shows a tangled vascular meshwork corresponding to the sub-RPE CNV.[21]

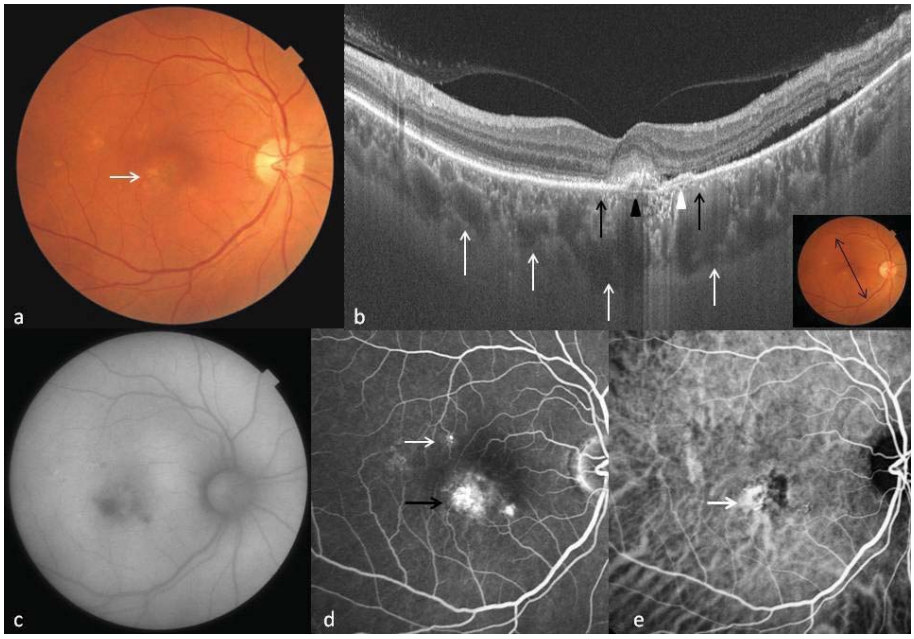

Figure 3: *Multimodal imaging in a case of pachychoroid neovasculopathy. (a) Color fundus photo shows decreased fundus tessellation, RPE mottling and a foveal dirty-grey CNV membrane (white arrowhead). (b) Macular OCT shows focal RPE and choriocapillaris attenuation (black arrows), pachyvessels (white arrows), fibrovascular PED (black arrowhead) and a double layer sign (white arrowhead). (c) FAF shows hypoautofluorescence due to RPE attenuation and blockage from subretinal exudation. (d) FFA shows an ink bloat leak (white arrow) and stippled hyperfluorescence form CNV (black arrow). (e) ICGA shows stippled hyperfluorescence (white arrow) in the area corresponding to CNV.*

Polypoidal choroidal vasculopathy-

PCV is a pachychoroid disease characterized by multiple recurrent serosanguineous bilateral PEDs. It is also known as aneurysmal type 1 CNV as there occurs sub-RPE or type 1 CNV with polypoidal vascular changes at the level of choriocapillaris.[22] PCV was first described by Yannuzzi et al. in 1990.[23] The classical ICGA features were later given by Spaide et al. in 1995.[24]

Clinically polyps are seen as orange bulging lesion in the macular and peripapillary area. Often serosanguineous PEDs are present (Figure 4a). Intraretinal or subretinal hard exudates suggest chronicity of disease (Figure 4a). Sometimes massive subretinal and subRPE bleed results from the abnormal vasculature. Characteristically there is absence of features of AMD such as multiple or extensive soft drusen and geographic atrophy and reticular pseudodrusen.

OCT shows a sub-RPE CNV with aneurysmal lesions/ polypoidal lesions between the RPE and Bruch's membrane (Figure 4b).[22] Other OCT features include tall peaked PED (Figure 4b), notched PED, and double layer sign.[20,25] AF features are non-specific (Figure 4c).

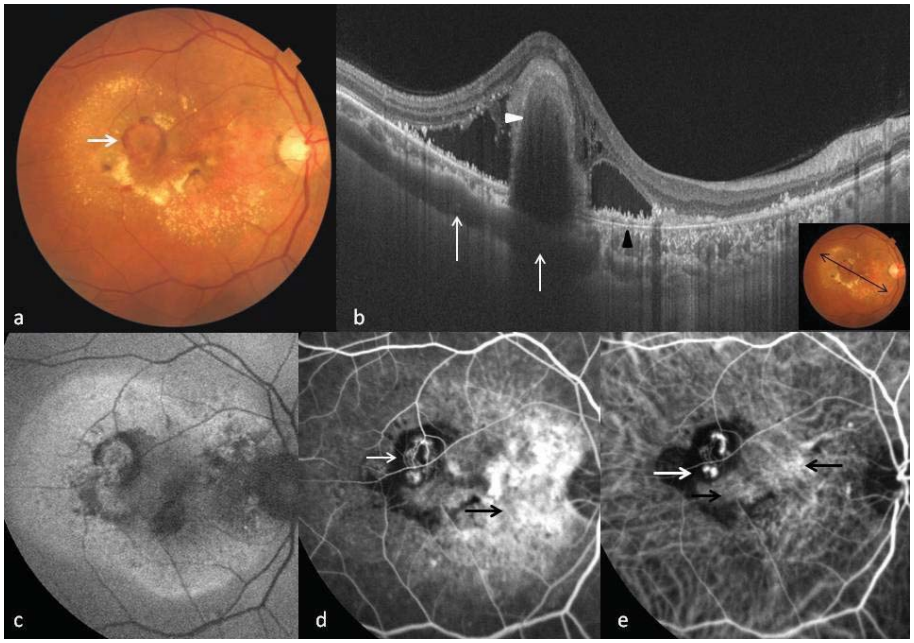

Figure 4: *Multimodal imaging in a case of polypoidal choroidal vasculopathy. (a) Color fundus photo shows a large juxtafoveal hemorrhagic PED (white arrow) and diffuse RPE changes and retinal hard exudates. (b) Macular OCT shows pachyvessels (white arrows), tall peaked fibrovascular PED (white arrowhead) and a double layer sign (black arrowhead). (c) FAF shows hypoautofluorescence due to RPE attenuation and blockage from retinal exudation. (d) FFA shows window defect in nasal macula (black arrow) and stippled hyperfluorescence in the area of PED (white arrow). (e) ICGA shows a polyp in the form of hot-spot (white arrow) and stippled hyperfluorescence (black arrow) in the area of BVN.*

FFA shows ill-defined stippled leakage from the polyps and BVN suggestive of occult CNV (Figure 4d).[26] With significant RPE erosion, a classic CNV may be uncommonly seen. Cases with subretinal bleed shows blocked fluorescence in the area of bleed and fails to highlight the choroidal vasculature.

ICGA delineates the BVN clearly (Figure 4e).[26] It is the investigation of choice for PCV as the penetration is possible through the subretinal bleed and exudation and inner choroid is imaged very well. Leakage from the polyp appears as early hyperfluorescent nodule at the ends of BVN with a halo of hypofluorescence usually appearing within the first minute of injection (Figure 4e).[27]

On OCTA, BVN appears as a hyperflow complex at the level of Bruch's membrane.[28,29] The flow level in the polyps may be below the threshold for OCTA. Polyps may appear as hypoflow round structures or hyperflow structures with hypo halo. A choroidal stalk may be seen connecting the BVN complex to the underlying large choroidal vessels. The limitation of OCTA is inability to visualise the pathology in the presence of subretinal bleed or exudation.[28,29]

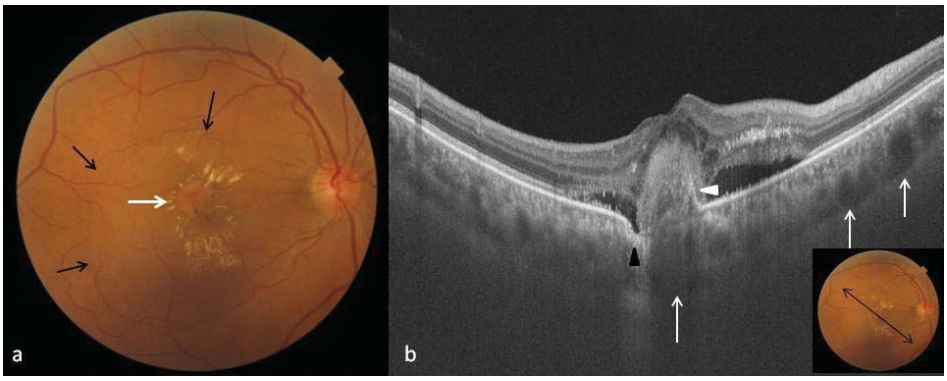

Figure 5: *Fundus imaging in a case of focal choroidal excavation. (a) Color fundus photo shows a large NSD (black arrows) and a foveal CNV (white arrow) with retinal hard exudates and hemorrhage. (b) Macular OCT shows pachyvessels (white arrows), focal excavation (black arrowhead), a fibrovascular PED (white arrowhead) adjacent to excavation, NSD and intraretinal edema.*

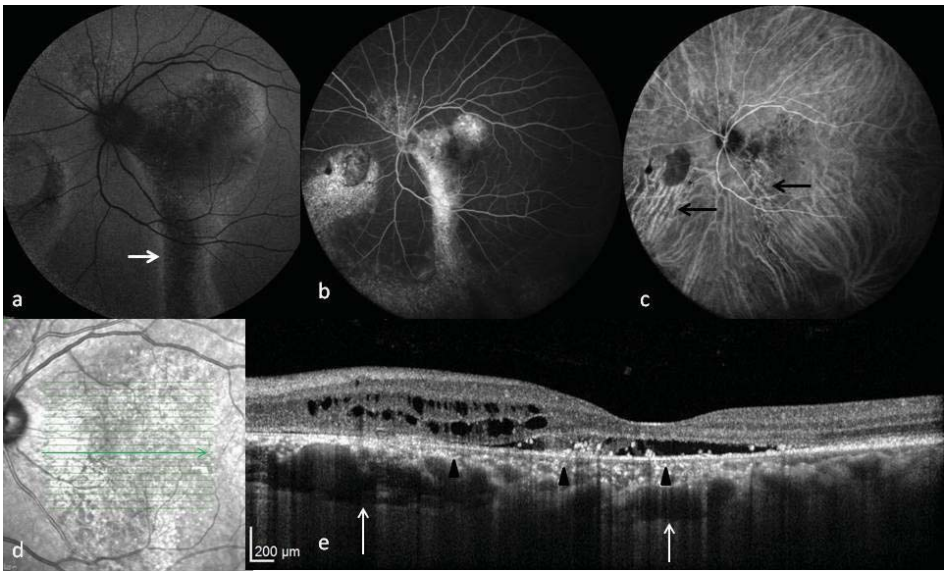

Figure 6: *Fundus imaging in a case of peripapillary pachychoroid syndrome. (a) FAF shows patches of hypoautofluorescence primarily involving the papillo-macular bundle area and extending inferiorly as gravitational tracts (white arrow). A small patch of hypoautofluorescence may also be seen nasally. (b) FFA shows window defect in the areas seen as hypoautofluorescent in FAF. (c) ICGA shows a pachyvessels and CVH (black arrows). (d) Infra-red image shows the axis (green arrow) of line scan OCT shown in 'e'. (e) Macular OCT shows RPE and choriocapillaris attenuation (black arrowheads), pachyvessels (white arrows), a serous NSD, intraretinal fluid in the nasal half of macula and a relatively normal architecture in the temporal half.*

Pathophysiology

The mechanism for development of the pachychoroid disorders is poorly understood. One school of thought is that the primary event is the dilatation and hyperpermeability of the large choroidal vessels that precedes the clinical features.[30] Thereafter the overlying choriocapillaris and Sattler's layer atrophy ensues due to increased choroidal hydrostatic pressure. The alternate opinion is that the increased sympathetic tone and arteriosclerosis leads to primary choriocapillaris obliteration and ischemia.[1,31] With persistent sympathetic activation, the luminal areas expand due to increase in the blood flow to the choroidal veins.[31]

PPE appears to be an incipient form of pachychoroid disease.[11]

CSC occurs when the hydrostatic pressure overcomes the Bruch's- RPE complex and results in focal or diffuse leakage into the sub-RPE and subretinal space. Alternatively, the primary RPE-choriocapillaris dysfunction from aberrant steroid metabolism leads to NSD and PED formation. Mineralocorticoid receptors in the choroid upon stimulation may lead to choroidal hyperpermeability and congestion.[32,33]

Choriocapillaris attenuation leads to an ischemic milieu and vascular endothelial growth factor expression. Breach in the Bruch's membrane in such an angiogenic state leads to CNV formation in the sub-RPE space as seen in PNV.[34] Some believe that chronic inflammation of the choriocapillaris may also be involved in CNV formation.

PCV develops when there occurs aneurysmal dilatation of the terminal ends of the vascular network between RPE and Bruch's membrane.[1] Alternatively, the polyps may develop in the absence of CNV due to chronic choroidal venous hypertension.[1] Hyalinization of the inner choroidal vessels is seen on histopathology.[35]

Newer Pachychoroid Entities

Focal choroidal excavation

Focal choroidal excavation (FCE) is a distinct focal area of choroidal excavation in the absence of diseases known to cause choroidal thinning and without any evidence of scleral ectasia or staphyloma.[1] It was first described by Jampol et al. in 2006[36] and the term "focal choroidal excavation" was coined by Margolis et al. in 2011.[37]

Generally seen in 4th and 5th decades, with no gender predilection and myopes being more involved, it causes diminution of vision and metamorphopsia. It is usually unilateral and not associated with any systemic abnormality. Fundus examination shows non-specific RPE changes in an area of decreased fundus tessellation with or without CNV (Figure 5a). On OCT, it is visible as a localized area of choroidal excavation (Figure 5b). FCE is described as "confirming" if the photoreceptor layer is in direct contact with the RPE and "non-conforming" if the photoreceptor layer is detached from the RPE with a hyporeflective cleft in between.1,38 The choroido-scleral interface is smooth and there is no evidence of scleral involvement. The SFCT is usually increased. FA shows window defects due to overlying RPE atrophy. Leakage signifies the presence of secondary CNV. ICGA shows filling defect in early phase (choriocapillaris loss) and punctuate hyperfluorescence (CVH) in the late phase.

FCE is believed to be a congenital choroidal defect hypothesized to arise from RPE retraction due to local scarring of choroidal stroma from previous inflammation.[1,38] The association of FCE with other pachychoroid disorders such as CSC and PCV is well known.[38–40] FCE can occur either in the same eyes with pachychoroid disorders or in the fellow eyes. The proposed mechanisms behind this association include focal RPE-Bruch's damage/dysfunction and choroidal ischemia in the area of anatomical abnormality.[39] CNV may develop in eyes with FCE, which may be type 1 (Figure 5a) or type 2.[41] Since the CNV develops close to the FCE, it is believed that the RPE-Bruch's damage from FCE is responsible for CNV growth.

FCE is generally a stable lesion.[42] Treatment is required for secondary CNV, which may be intravitreal anti-VEGF therapy with or without additional PDT. The cleft in non-confirming type usually disappears on treatment.

Peripapillary pachychoroid syndrome

Peripapillary pachychoroid syndrome is a novel pachychoroid spectrum disorder described by Phasukkijwatana et al. where the morphological pachychoroid features are found in the peripapillary area and nasal macula rather than the fovea.[43] It is often associated with hyperopia, crowded disc and choroidal folds.

The disease may be misunderstood as uveal effusion syndrome due to its association with short axial length and serous retinal detachment in the posterior pole, but the absence of choroidal detachment rules out the same.[1,43] While uveal effusion occurs due to a poorly permeable sclera, in PPS the primary pathology is a thicker and hyperpermeable choroid. Peripapillary choroidal congestion causes overlying RPE dysfunction and leakage into the subretinal space. A compartment syndrome-like situation arises in the peripapillary area which leads to optic disc edema and crowded disk appearance.

The common clinical features include intraretinal and/or subretinal fluid in the peripapillary area and optic nerve head edema in some eyes. FAF shows mottled hypofluorescence and gravitational tracks in the peripapillary area (Figure 6a). FA shows window defects in the corresponding areas without focal leakages (Figure 6b). Mild late disc leakage may be seen in majority of the cases. ICGA shows CVH and pachyvessels in the peripapillary area (Figure 6c). OCT shows intraretinal fluid and NSD in the peripapillary and papillo-macular bundle area with pachyvessels and choriocapillaris attenuation (Figure 6d-e) The characteristic clinical and imaging features help differentiate this entity from posterior uveitis and neuro-ophthalmological condition with similar presentation.[43]

Management

CSC- Spontaneous resolution of the disease occurs in 90% of the cases. However, recurrence occurs in around 50% of the cases after resolution of subretinal fluid.

In patients with exogenous steroid intake, the steroids should be stopped or tapered as needed.[44]

Treatment is required in cases with duration greater than 3 months (chronic), highly symptomatic patients, or patient with poor vision in the fellow eye.[45]

The treatment type is governed by the phase of disease and the site of leakage on FFA.[45]

Laser photocoagulation is considered for the treatment of extrafoveal leakage points in acute cases.[45] Focal thermal coagulation seals the RPE defects and prevents further accumulation of subretinal fluid. However, focal laser photocoagulation causes permanent damage to the RPE and overlying photoreceptors and also carries the risk of iatrogenic CNV formation especially if the laser spot size is less than 100micron.[45] To overcome these shortcomings of conventional laser system, sub-threshold micropulse (STM) laser was introduced.[46] STM laser does not cause thermal damage to the RPE. Instead, it stimulates the proliferation of RPE cells. Since it is not destructive and does not produce visible burns/scars, STM laser may be used for even juxtafoveal leaks.[47] Yellow wavelength (577nm) is often used for STM laser in CSC.[47] The limitation of STM laser is reduced efficacy in chronic cases with diffuse retinal pigment epitheliopathy.[47] This is because STM acts at the level of RPE and does not alter the dysfunctional hyperpermeable choroidal vasculature.

Verteporfin photodynamic therapy (PDT) is the preferred treatment for chronic cases.[45] PDT targets the choroidal hyperpermeability, reduces the dilated choroidal vasculature, reduces the CT, and leads to resolution of subretinal fluid.[48] PDT significantly decreases the thickness of Haller's layer without alteration of the choriocapillaris and Sattler's layer, thereby restores the normal choroidal morphology.[49] Conventional full dose and full laser fluence PDT may have certain adverse effects such as transient visual disturbances, unexplained visual loss, diffuse RPE atrophy, CNV formation, and choroidal ischemia.[48] To improve the safety, half dose and/ or half fluence PDT have been advocated, but the efficacy remains questionable.[48] However, half dose PDT has shown promise in attaining better final visual acuity and lesser recurrence than conventional PDT in a few studies.[50,51] Since aberrant steroid metabolism is thought to the underlying cause for CSCR, numerous systemic drugs have been tried with equivocal results. Mineralocorticoid receptors in the choroidal vasculature increase the congestion upon

stimulation, therefore antagonists such as spironolactone and eplerenone may have a role in treatment.[33] Rifampicin, a mineralocorticoid antagonist, potentiates the catabolism of endogenous steroids and has been reported to accelerate the resolution of subretinal fluid.[52] However, the majorities of the studies reporting the benefits of systemic therapy in chronic CSC lacks a control group or have small sample size. There is no level 1 evidence to support the use of anti-VEGF agents in the treatment of persistent fluid in chronic CSC cases in the absence of underlying CNV.

PNV

The treatment of PNV involves intravitreal anti-VEGF injections and/or PDT.[53] PNV responds to anti-VEGF therapy better than AMD in term of number of injections, re-treatment free interval, and resolution of exudation.[53] Repeated injections are often less required in PNV as compared to AMD. Perhaps this occurs due to relatively lower intraocular VEGF levels in PNV as compared to AMD. The choroidal structural changes after anti-VEGF treatment correlate with the visual outcomes.[54] PDT is required in cases resistant to anti-VEGF therapy.

PCV

Direct thermal photocoagulation (argon laser) may be considered for extrafoveal symptomatic PCV lesions.[55] For symptomatic juxtafoveal or subfoveal lesions, full fluence or reduced fluence PDT and intravitreal anti-VEGF injection are the options.

With PDT, there occurs selective endothelial uptake of photo activated verteporfin in the abnormal choroidal vasculature.[56,57] The thrombosis is higher in smaller calibre choroidal vessels which may be the reason for better resolution of polyps than BVN with PDT.[56] The area of interest i.e greatest linear diameter should include the polyps as well as BVN. New or recurrent lesions may develop which needs repeat PDT. Apart from the usual adverse effects of PDT, subretinal hemorrhage and RPE rips/tear are the feared complications of treatment in PCV.[58]

Anti-VEGF therapy causes resolution of the exudation from the polyps and BVN. However, the polyps and BVN persist in the majority of cases. Therefore, anti-VEGF therapy is often used in conjunction with PDT and monotherapy is considered only in cases of predominant exudation with minimal polyp activity or cases where polyps and BVN are not clearly visible on ICGA due to subretinal haemorrhage.[57,59] The superiority of a particular anti-VEGF agent is not proven in PCV. For refractory exudative lesions, a switch to a different anti-VEGF agent may be effective.[59]

The EVEREST study compared PDT with Ranibizumab therapy in PCV and found significantly better polyp regression with PDT.[27] However, the visual outcomes were marginally better with anti-VEGF therapy. Similarly, LAPTOP study reported better final visual outcomes following three monthly injections followed by as-needed injections of ranibizumab than PDT alone.[60] Therefore, PDT monotherapy induces effective regression of polypoidal lesions, but the same does not apply to the visual outcome.

The combination treatment carries the advantage of simultaneous regression of the polypoidal lesions and resolution of subretinal exudation.[61] Regardless of the treatment type, patients should be monitored regularly with OCT, FFA and ICGA to assess the activity of polyps, amount of subretinal exudation and to determine the need for re-treatment.

For PCV with subretinal hemorrhage larger than 4 disc area and presenting within 10-14 days of onset, pneumatic displacement with intravitreal gas (sulphur hexafluoride or perfluoropropane) and tissue plasminogen activator can be performed.[62] The bleed gets displaced in 1 or 2 weeks and angiography can then be performed. Vitrectomy with subretinal injection of tissue plasminogen activator may be considered as alternative in cases with massive subretinal hemorrhage or breakthrough vitreous hemorrhage.[59] Subsequently PDT with or without anti-VEGF therapy can be performed in cases with active disease on angiography.[59]

Conclusion

Although our understanding of the pachychoroid disorders has expanded, there are still many uncertainties regarding the pathophysiology and appropriate management of the disorders. The primary pathological site in these disorders remains an enigma. The heterogeneity in the presentation and transition from one type to another type needs to be understood. The current treatment relies solely on decreasing the exudation from the abnormal vasculature. In future, improved imaging systems with greater resolution will provide useful information about the morphology of the choroid, its vasculature and blood flow. Only then, newer therapies may be directed to modulate the pathological changes occurring in the disease.

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