Pachychoroid Spectrum of Diseases

Andreea Moraru, D. Costin

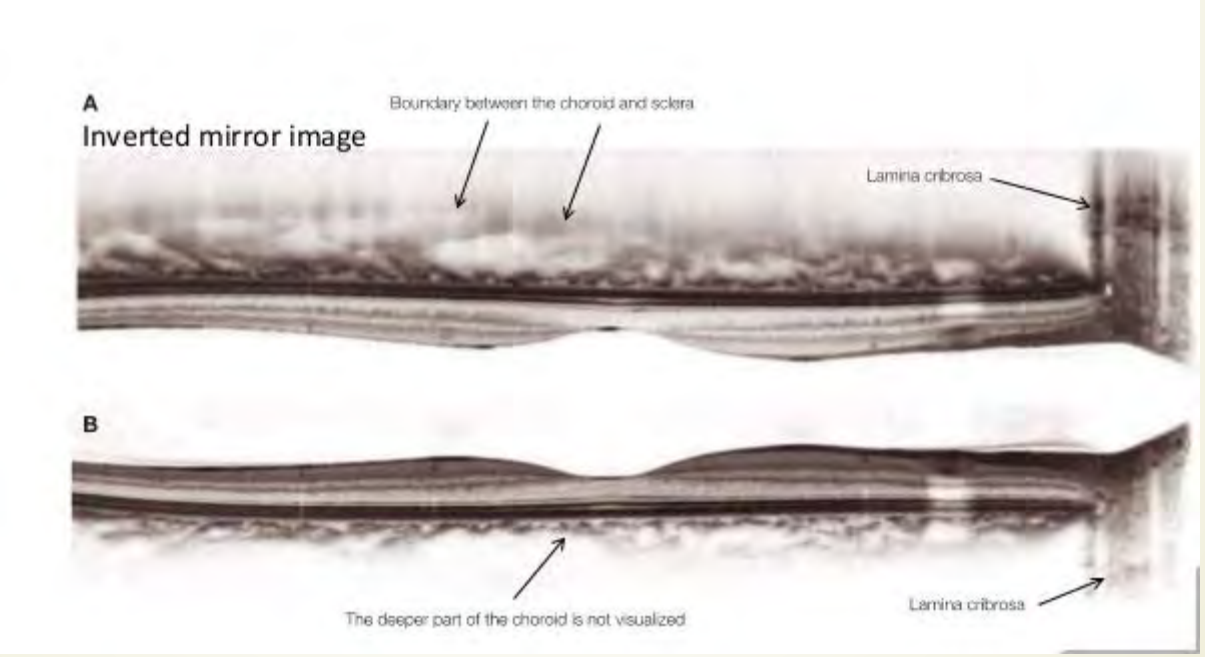
UMF "Gr. T. Popa" Iasi

- Pachy – the term derives from greek – παχύ – thick.
- Pachychoroid diseases started to be discussed in 2013, when Freund and colleagues described pachychoroid pigment epitheliopathy [1].
- The study specified a group of conditions characterized by choroidal thickening and retinal pigment epithelial changes, with or without corresponding retinal abnormalities.

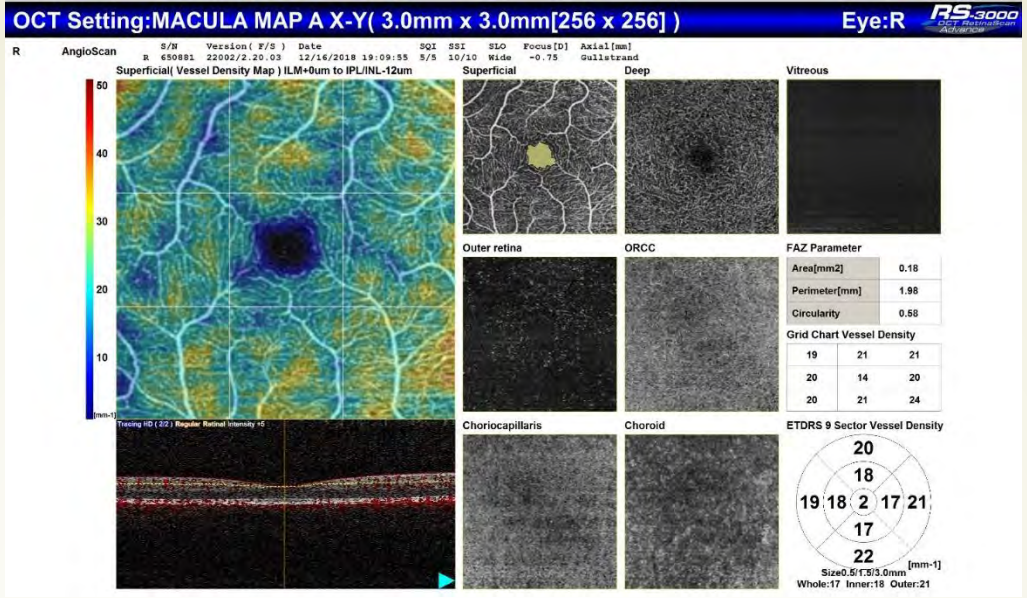
1. Warrow DJ, Hoang QV, Freund KB. Pachychoroid pigment epitheliopathy. Retina. 2013;33:1659-1672.

- Spaide et al.- 2008 -presented the OCT module EDI (Enhanced Depth Imaging), with improved display of the depth, which enabled more precise structural and functional analysis of the retina and choroid [2].

2. **Spaide, RF., Koizumi, H., Pozzoni, MC.:** Enhanced depth imaging spectral-domain optical coherence tomography .Am J Ophthalmol ,



Spaide et all, Am J Ophthalmol 2008

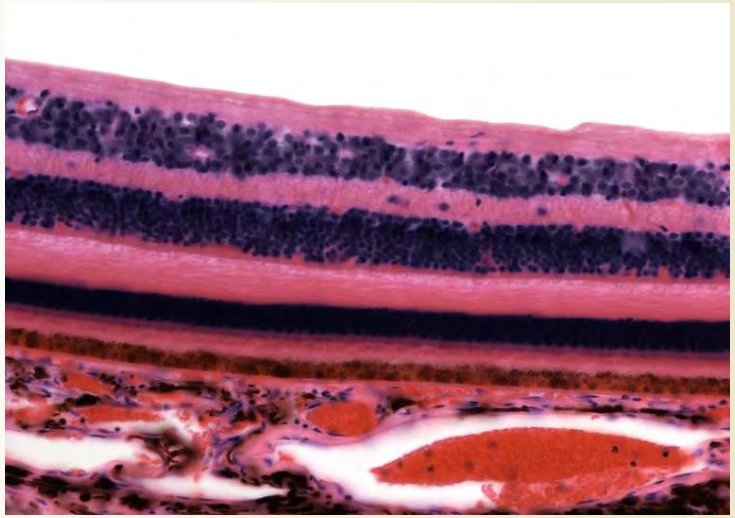


- A current modern examination method is optical coherence tomographic angiography (OCTA), which enables imaging of both retinal and choroidal vascularisation without the use of a contrast substance, with the aid of non-invasive 3D imaging of blood flow [3].
- Unlike EDI-OCT, which gives a cross-sectional view, OCT-A is usually viewed en face.
- It uses fast scanning to visualize blood flow, and it can focus at different levels to provide information on both retinal and choroidal vessels.

3. **Bonini Filho, MA., de Carlo, TE., Ferrara, D. et al.:** Association of Choroidal Neovascularization and Central Serous Chorioretinopathy with Optical Coherence Tomography Angiography. JAMA Ophthalmol, 133; 2015: 899–906.

Choroid Anatomy

- Bruch Membrane
- Choriocapillaris
- Sattler Layer - medium diameter blood vessels
- Haller´s Layer - large diameter blood vessels
- Suprachoroid Lamina - transitional zone between choroid and sclera

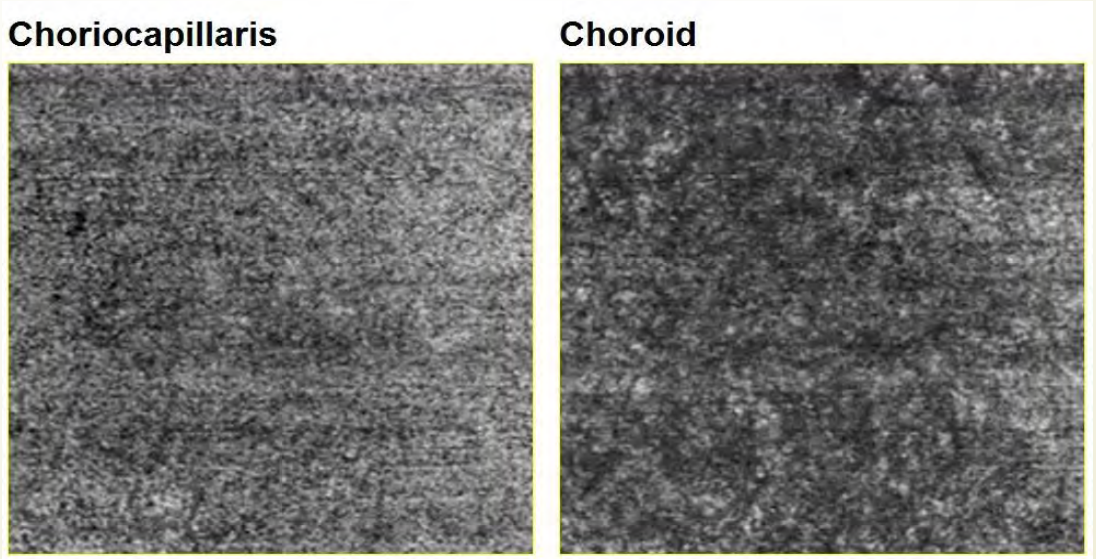


Choroid Anatomy - OCT

- Choroid is thickest in subfoveal region, thinner in nasal region and has a progressive thinning through temporal region.
- Subfoveal choroidal thickness (SFCT) is ~190 - 300 µm and the median choroidal thickness is approximate 260 µm.
- Thickness varies based on characteristics such as age, gender, ethnicity

- The choroid has the highest blood flow per unit weight of any tissue in the body, about 20 times to 30 times greater than that of the retina. [4]
- The vasculature of the choroid supplies nutrients and oxygen to the retinal pigment epithelium, the outer retina, the avascular fovea and the prelaminar portion of the optic nerve.

4. Mrejen S, Spaide RF. Optical coherence tomography: imaging of the choroid and beyond. Surv Ophthalmol. 2013;58(5):387-429



Normal aspect is dense and homogenoous

- Choroidal thickness decreases with an increase in the age of the patient and the axial length of the eye [5,6].
- Temporary increase in choroidal thickness is generally linked with acute stages of severe posterior uveitis (Vogt-Koyanagi-Harada syndrome, multifocal choroiditis, multiple white dot syndrome)
- In the case of pachychoroid disease there is a sustained increase in choroidal thickness >300 µm.
- Increase in thickness is mainly due to dilated choroidal vessels in the Haller's layer, with subsequent hyperpermeability.

5. **Goldenberg, D., Moisseiev, E., Goldstein,M. et al.:** Enhanced depth imaging optical coherence tomography: choroidal thickness and correlations with age, refractive error, and axial length. Ophthalmic Surg Lasers Imaging, 43(4); 2012: 296–301.

6. **Margolis, R., Spaide, RF.:** A pilot study of enhanced depth imaging optical coherence tomography of the choroid in normal eyes. Am J Ophthalmol, 147(5); 2009: 811–5.

- It is assumed that "pachychoroid" disease has an autosomally dominant type of heredity [7]. Depending on the further effect of various exogenous and/or endogenous factors, pachychoroid may occur.

- Although clinical manifestations of pachychoroid spectrum disorders vary considerably, OCT has shown that they share similar morphological findings in the choroid - increased thickness and dilated outer choroidal vessels.

- Eyes with pachychoroid disease may have a normal subfoveal choroidal thickness, but increased in the extrafoveal area → defined as > 50 µm difference compared to subfoveal thickness

7. **Yoneyama, S., Sakurada, Y., Kikushima, W. et al.:** Genetic factors associated with choroidal vascular hyperpermeability and subfoveal choroidal thickness polypoidal choroidal vasculopathy. Retina, 36(8); 2016: 1535-41.

Pachychoroid disease spectrum:

- Pachychoroid pigment epitheliopathy (PPE);
- Central serous chorioretinopathy (CSCR);
- Pachychoroid neovasculopathy (PNV);
- Polypoidal choroidal vasculopathy (PCV)
- Focal choroidal excavation (FCE)
- Peripapillary pachychoroid syndrome (PPS).

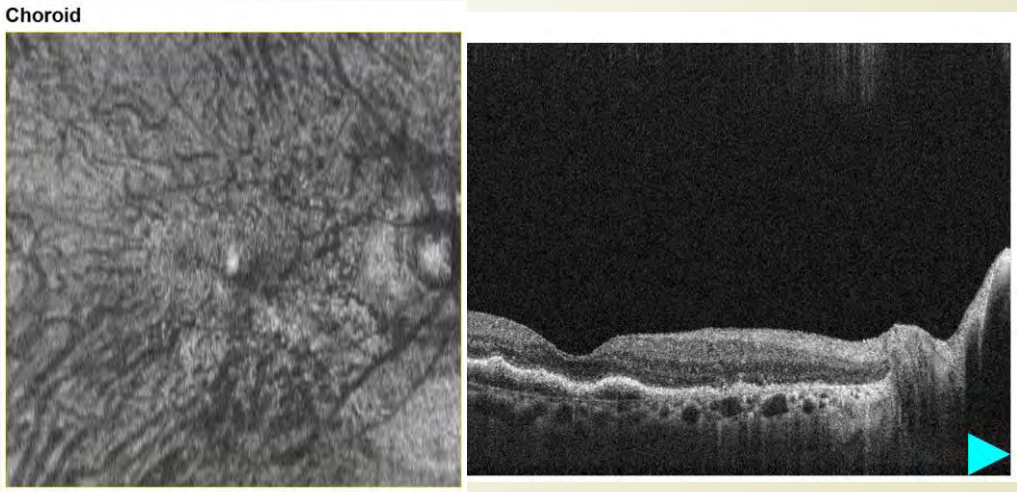
- All exhibit characteristic choroidal alterations and are believed to represent different manifestations of a *common pathogenic process*.

- With the progression of the pathology, a *gradual transition* to a further stage of the disorder takes place [8].

- Their fundamental common features are:
  - Increase in thickness of the choroid,
  - Pachyvessels - dilated vessels of the Haller's layer,
  - Thinning of the Sattler's layer and the layer of the choriocapillaris [8]

8. **Dansingani, KK., Balaratnasingam, C.,Naysan, J. et al.:** En face imaging of pachychoroid spectrum disorders with swept-source optical coherence tomography. Retina, 36(3); 2016: 499–516.

- **Pachyvessels** can be identified as a choroidal vessels with enlarged caliber, which can occupy almost the entire thickness of the choroid.
- Pachyvessels can also be seen as dilated submacular vessels which do not taper toward the posterior pole en face OCT, but retain a large caliber and terminate abruptly.
- The pachyvessels may be distributed in a diffuse or focal manner.
- Pachyvessels usually exhibit choroidal vascular hyperpermeability which may suggest choriocapillaris ischemia.
- Their location is correlated with the areas of maximum choroidal thickness and choriocapillaris thinning.



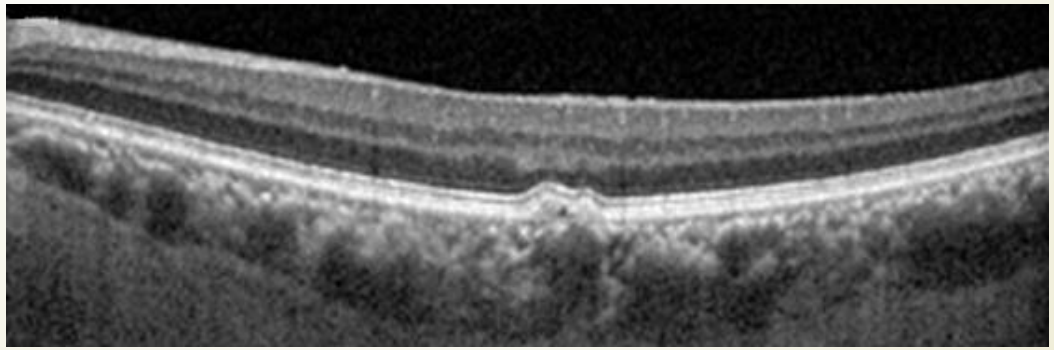
Pachychoroid pigment epitheliopathy

- PPE was described by Warrow et al. in 2013 [9].
- Considered a pre-stage of CSC - 61% of the CSC cases present signs of PPE, which are also present in the fellow eye [10].
- The choroid is typically thickened in association with RPE abnormalities, including small RPE detachments.
- Subretinal fluid and drusens are not evident.

9. **Warrow, DJ., Hoang, QV., Freund, KB.:** Pachychoroid pigment epitheliopathy. Retina, 33(8): 2013: 1659–1672.

10. Ersoz MG, Karacorlu M, Arf S, *et al* Pachychoroid pigment epitheliopathy in fellow eyes of patients with unilateral central serous chorioretinopathy *British Journal of Ophthalmology* 2018;**102**:473-478.

- Pachyvessels are located in close proximity to the complex of the RPE – Bruch's membrane, and thus mechanically contribute to the onset of pigment epitheliopathy.
- Usually confused with AMD, pattern dystrophia, pigment epithelitis.
- OCTA showes increased choroidal thickness, pachy-veins in Haller’s layer, thinning in Sattler’s layer and choriocapillaris



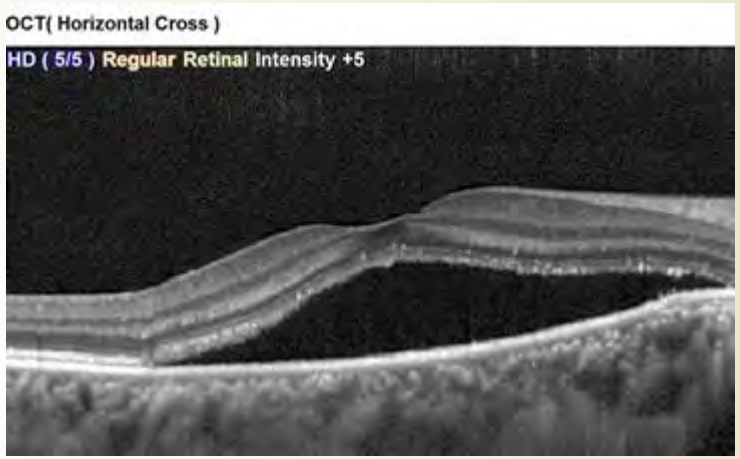
Central serous chorioretinopathy

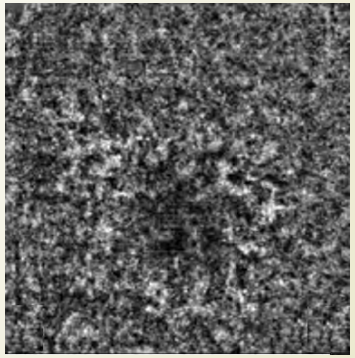
- Recurring disorder of the macula - serous detachment of the neuroretina +/-detachment of the RPE.
- The second stage of pachychoroid disease of the macula [11].
- Predisposing factors include type A personality, hypochondria, hysteria, use of corticoids (Cushing's syndrome), pregnancy, systemic hypertension, Japanese or South Asian race, SLE and psychopharmacological medication. Men are affected in 72-88% of cases.

11. Dansingani, KK., Balaratnasingam, C.,Naysan, J. et al.: En face imaging of pachychoroid spectrum disorders with swept-source optical coherence tomography. Retina, 36(3); 2016: 499–516.

Central serous chorioretinopathy

- SRF - serous , hyporeflective
- PED – within/outside the SRF, pachychoroid
- Exudation beneath the retina occurs as a result of increased hydrostatic pressure and permeability of the choroid, disorder of the Bruch's membrane and abnormalities of the RPE.



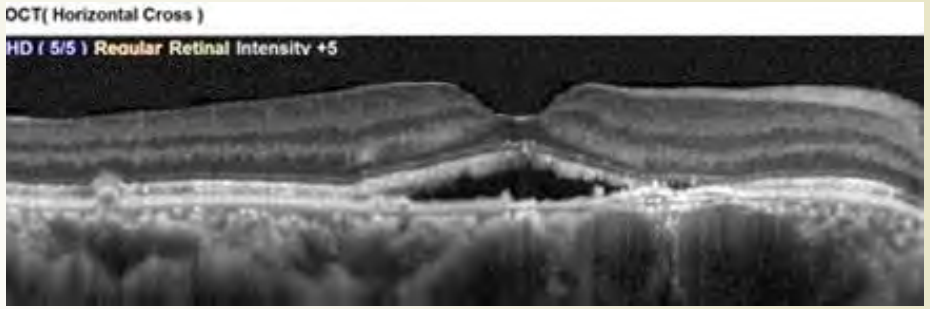


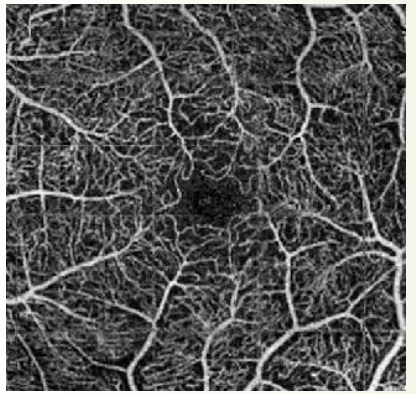
Choriochapilaris

Chronic CSC

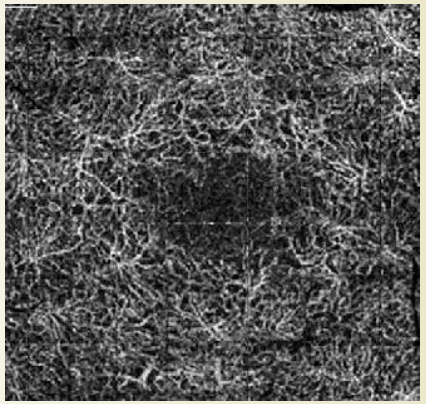
- shallow persistent SRF
- RPE degeneration
- cystoid retinal edema
- elongated photoreceptor outer segment

- OCTA - choriocapillary hypoperfusion with hyperperfusion in the surrounding area.

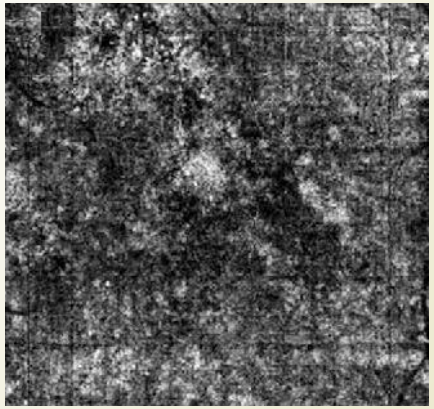




Superficial vascular plexus



Deep vascular plexus



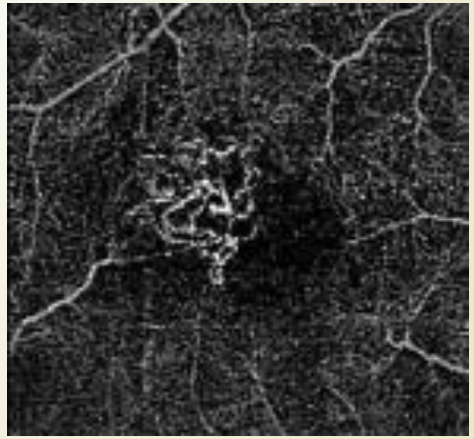
Choriochapilaris

Pachychoroid neovasculopathy

- Late complication of PPE and CSC - may linked to genetic risk of CNV [12].
- Cases of the occurrence of PNV are documented in patients with PPE, as well as without previous signs of CSC
- Younger age at onset of neovascularization, and a thick choroid
- Typically occult CNV
- Increased thickness of the choroid with pachyvessels
- Absence of drusens

12. Pang CE, Freund KB. Pachychoroid pigment epitheliopathy may masquerade as acute retinal pigment epitheliitis. Invest Ophthalmol Vis Sci. 2014 Aug 22;55(8):5252.

- A common secondary finding is focal dilation of the vessels of the choroid directly beneath CNV.
- According to current opinion, the cause of occurrence of CNV is long-term pressure on the Bruch's membrane and subsequent ischaemia of the choriocapillaris and Sattler's layer, which stimulates the proliferation of vessels of the Haller's layer.
- OCT- irregular RPE detachment – double-layer sign
- OCTA – network of vessels corresponding to tipe I neovascularization



Polypoid choroidal vasculopathy (PCV/AT1)

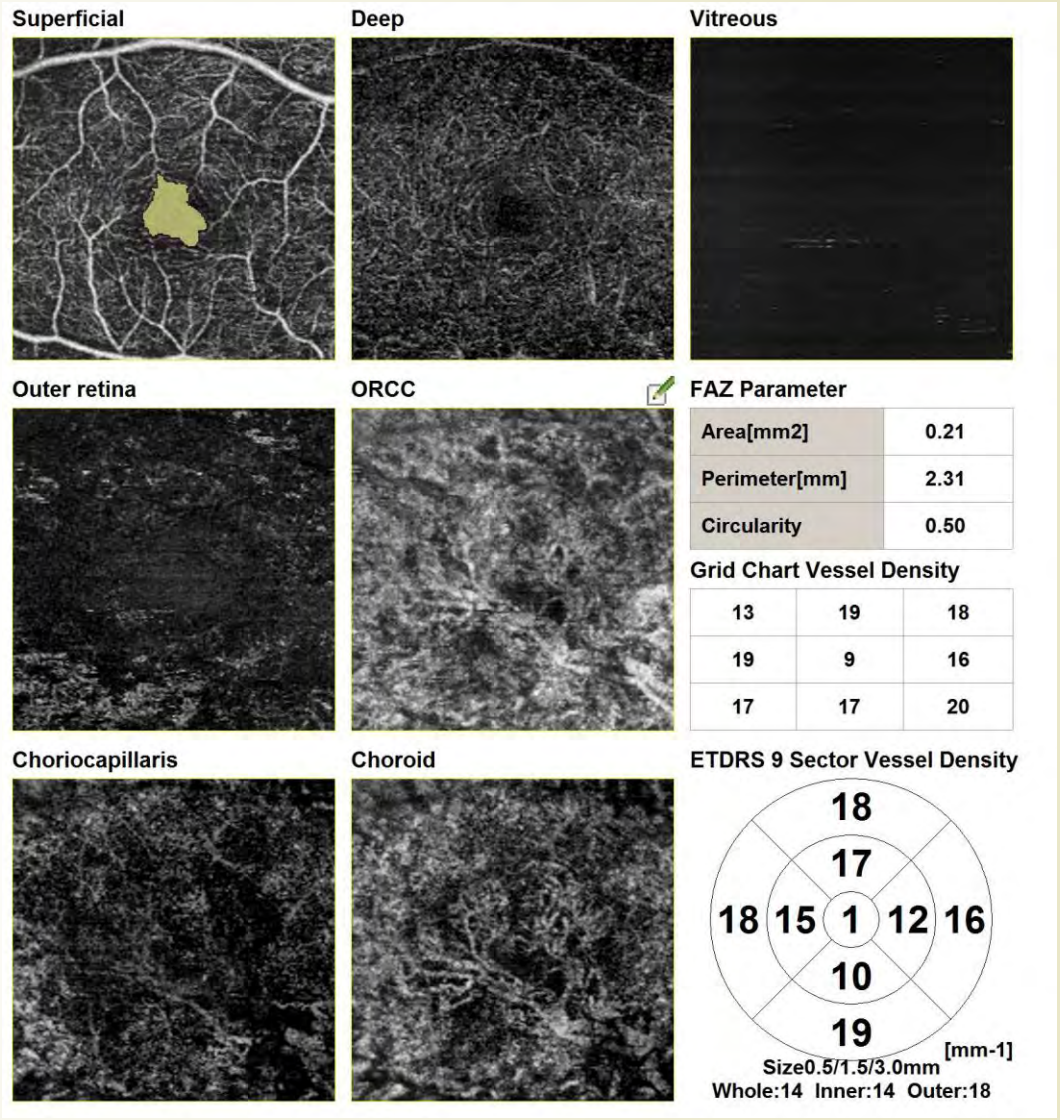
- Polypoid choroidal vasculopathy/ aneurysmal tipe 1 neovascularization was described by Yannuzzi et al. as a proliferation of the choroidal capillaries beneath the RPE and the development of aneurysms in the form of polyps on the tip of the capillary proliferation, with subsequent serous infiltration and hemorrhage beneath the RPE and neuroretina [13].
- This represents the most advanced stage of the spectrum of pachychoroid disease.
- 4-12% of nAMD [14]
- Patients with atherosclerosis and other vascular wall alterations- hyalinization within vessel walls

13. Imamura Y, Engelbert M, Iida T, Freund KB, Yannuzzi LA. Polypoidal choroidal vasculopathy: a review. Surv Ophthalmol. 2010 Nov-Dec;55(6):501–15.

14. Freund KB, Zweifel SA, Engelbert M. Do we need a new classification for choroidal neovascularization in age-related macular degeneration? Retina. 2010 Oct;30(9):1333–49

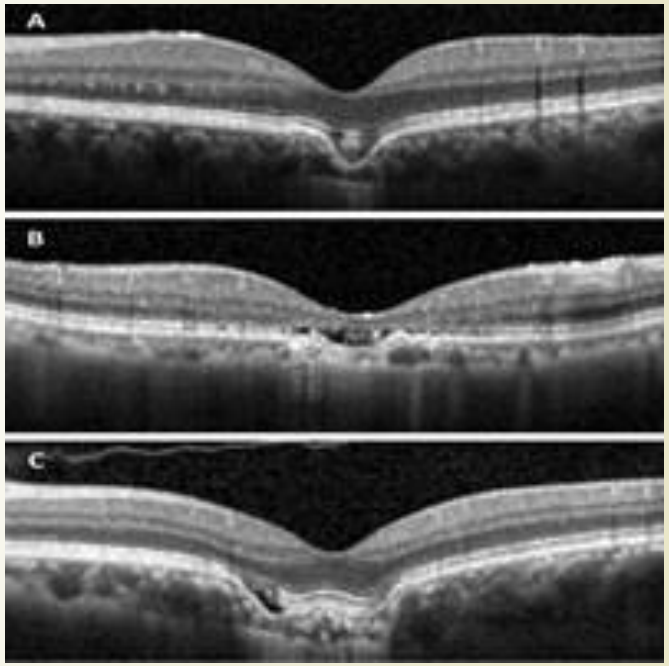
- Better visual prognosis than typical nAMD – slow progression + subretinal fibrosis is unsual
- Soft drusen, cuticular drusen, reticular pseudodrusen (subretinal drusenoid deposits) can be present
- Thick choroid in contrast to choroidal thinning in nAMD and the greatest increse in thickness is nasally - particularity

- Aneurysmal dilatations may occur from type 1 lesions in eyes with PNV or other pachychoroid spectrum diseases.
- The exudation can partially resolve spontaneously due to thrombosis of the aneurysmal dilatation, but the neovascular network grows continously for years, forming new aneurysms at the margins of the original lesion associated with chronic, multiple, recurrent exudative changes.
- OCTA - hyper-reflective filamentous neovessels in the ORCC



Focal Choroidal Excavation

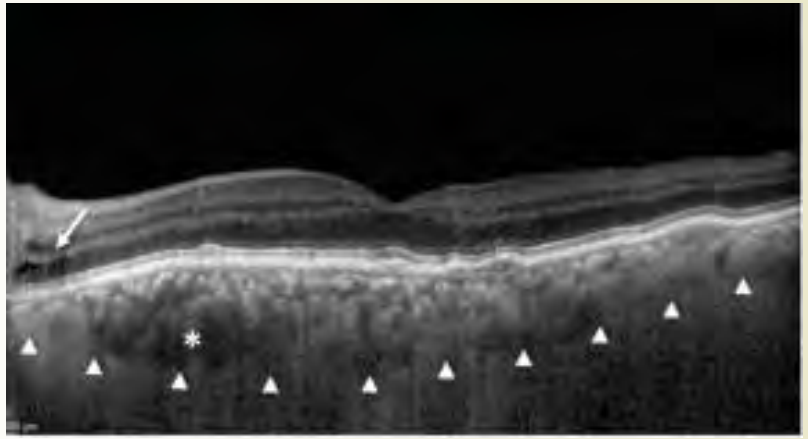
- Localized areas of choroidal excavation without history of posterior staphyloma
- Focal scarring of choroid connective tissue (inflammatory?) ➡ compression of choriocapillaris
- Usually myopic patients with metamorphopsia and non-specific pigmentary changes at posterior segment examination
- 2 patterns of excavation in FCE – with/without direct contact between photoreceptors tips and RPE
- Limited reports regarding long term evolution of FCE, most lesions are stationary



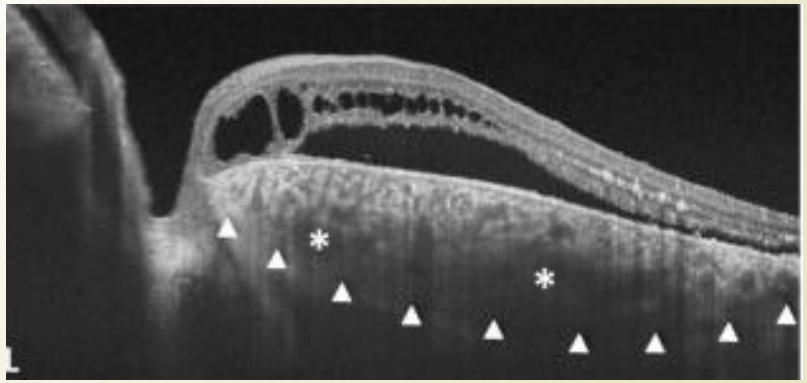
15. Shinojima, Ari MD, PhD; Kawamura, Akiyuki MD, PhD; Mori, Ryusaburo MD; Yuzawa, Mitsuko MD- MORPHOLOGIC FEATURES OF FOCAL CHOROIDAL EXCAVATION ON SPECTRAL DOMAIN OPTICAL COHERENCE TOMOGRAPHY WITH SIMULTANEOUS ANGIOGRAPHY. Retina: July 2014 - Volume 34 - Issue 7 - p 1407–1414

Peripapillary Pachychoroid Syndrome

- Maximal choroidal thickness close to the optic nerve, not subfoveal
- SRF and/or intraretinal fluid nasally +/- optic disc edema
- No association wiyh inflammatory sndromes
- 80% have hyperopic refraction+/- choroidal folds [16]



16. Phasukkijwatana N, Freund KB, Dolz-Marco R, Al-Sheikh M, Keane PA, Egan CA, Randhawa S, Stewart JM, Liu Q, Hunyor AP, Kreiger A, Nagiel A, Lalane R, Rahimi M, Lee WK, Jampol LM, Sarraf D- PERIPAPILLARY PACHYCHOROID SYNDROME. Retina. 2018 Sep;38(9):1652-1667



Therapeutic Options ?

- Asymptomatic pachychoroid disease – monitorization
- CSC with persistent SRF – subthreshold micropulsated laser

  - anti –VEGF – resolution of SRF, but not of subfoveal choroidal thickness (PROMETHEUS)

- PCN, PCV/ATI, CNV secondary to CSC/ FCE – anti-VEGF
- PCV/ATI – reccurrent exudation – may evolve to more typical CNV

Conclusions

Use of the EDI module on classic OCT and modern methods of OCTA have provided a better understanding of the role of pathological changes of the choroid and have helped define the term "pachychoroid".

The spectrum of pachychoroid diseases is characterised by three common features:

- increase in choroidal thickness ≥ 300 μm,

- dilation of the vessels of the Haller's layer

- thinning of the layer of the choriocapillaris and the Sattler's layer.

These pathologies include

- CSC - choroidal congestion and hyperpermeability

- PPE – pre-stage of CSC;

- PNV&PCV - occult CNV, the most advanced form of pachychoroid disease.

-FCE- asymptomatic; +/- CNV

- PPS- nasal SRF+/- disc edema