Central Serous Chorioretinopathy (CSC) and the Pachychoroidal Disease Spectrum

Ramana S. Moorthy, MD FACS
Founding Partner – Associated Vitreoretinal and Uveitis Consultants
Associate Clinical Professor of Ophthalmology
Indiana University Medical Center
Indianapolis, Indiana
Poll Question 1

• What is the average thickness of normal subfoveal choroid measured using SD-OCT?

A. 150 microns
B. 250 microns
C. 320 microns
D. 400 microns
Anatomy

Anatomy
Poll Question 2

• In pachychoroidal diseases, which OCT layer is effaced or absent?
  A. Sattler layer
  B. Haller layer
  C. Nerve fiber layer
  D. Bruchs membrane / RPE complex
Pachychoroidal Diseases

- Abnormal and permanent increase in choroidal thickness
  - Larger Haller layer vessels apposed to Bruchs membrane complex and medium vessels of Sattler layer absent or effaced

- Why does this happen?
  - Choroidal vascular congestion?
    - Thickened sclera
    - Lengthened intrascleral course of vortex veins
  - Physiologic Factors
    - Excess choroidal interstitial fluid
      - Precapillary arteriolar hypertension
      - Altered intravascular osmolality (serum proteins (albumin))
      - Pharmacologic agents: Corticosteroids, PDE inhibitors
  - Alterations in interstitial tissues in the choroid

Poll Question 3

• Pachychoroid disease spectrum includes which of the following diseases?

A. Central Serous Chorioretinopathy
B. Polypoidal Choroidal Vasculopathy
C. Pachychoroid Pigment Epitheliopathy
D. All of the Above
Pachychoroidal Diseases

• Spectrum of Disease
  – Pachychoroid Pigment epitheliopathy
  – Central Serous Chorioretinopathy (CSC)
    • Acute
    • Chronic
  – Pachychoroid Neovasculopathy
    • Polypoidal Choroidal Vasculopathy
    • Other entities?

Pachychoroid Pigment Epitheliopathy (PPE)

- Variable appearance from Forme Fruste of CSC to Chronic CSC
- Orange red fundus appearance
  - Absence of normal fundus tessellation
  - RPE changes mistaken for ARMD or pattern dystrophy
- OCT scattered RPE elevations, small serous PEDs, thick choroid
- ICG shows mid-phase hyperfluorescence suggestive of hyperpermeability
- Fundus Autofluorescence shows granular hypoautofluorescence and stippled mixed areas of hyper and hypoautofluorescence

PPE
CSC

• Demographics
  – 3rd to 6th decades
  – M>F
  – Personality ?, Exogenous corticosteroid exposure

• Symptoms
  – Metamorphopsia, micropsia, scotoma

• Signs
  – Serous PED(s)
  – Localized serous retinal detachment in posterior pole
  – RPE disruption
CSC

• What’s new?
  – Ideas about pathogenesis
    • Imaging – OCT, FAF, ICG
  – Treatment
CSC Pathophysiology

Choriodal exudate  PED
CSC

• Pathogenesis
  – Role of Choroid
    • Hyperpermeable in CSC
      – Stasis, Ischemia, Inflammation (Wyman GJ, AJO. 1963;55:1265)
      – Evidence
        » Staining of inner choroid on ICG (Spaide et al, Retina. 1996 16:203-213 and others)
      – Increased tissue hydrostatic pressure → RPED → SRF
CSC – Choroidal Hyperpermeability
CSC

• Pathogenesis
  – Role of Choroid
    • Thickened – EDI OCT (Imamura et al., Retina. 2009:29:1469-1473)
      – Normal thickness of subfoveal choroid – 250 microns
      – In CSC – thickness of subfoveal choroid – 320 microns
      – Does not correspond to the areas of staining on ICG
      – May be the result of corticosteroid induced increased vascular permeability and secondary sympathomimetic induced impaired choroidal autoregulation
CSC

• Pathogenesis
  – Role of Choroid
    • Choroidal lobular ischemia on ICG (Okushiba et al., NGGZ. 1997;101:74-82.)
    • Increased amplitudes of pulsatile choroidal blood flow.(Tittle et al. Arch Ophthalmol, 2003; 121:975-8)
CSC

• Pathogenesis
  – RPE
    • Probably secondary to choroidal changes
    • RPE abnormalities present in asymptomatic fellow eyes on OCT (Gupta et al. Int Ophthalmol. 2010;30:175-181)
    • Focal RPE defects – which way is flow of fluid
      – Response to focal laser in active cases
      – Still not well understood
CSC

• Pathogenesis
  – Hormonal factors
    • Endogenous cortisol elevated in CSC (Garg et al. BJO. 1997; 81: 962-4)
    • Exogenous corticosteroids
      – Exacerbate CSC – recognized since 1966
      – Haimovici et al – definitively established relationship as risk factor for CSR exacerbation (Ophthalmology. 2004; 111: 244-9)
      – Affect choroid
        » Increased adrenergic receptor transcription
        • Impaired vascular autoregulation
      – Affect Bruch’s Membrane
        » Inhibit collagen synthesis
      – Affect RPE
        » Altered water and ionic transport
        » Impair barrier function
      – Interestingly local corticosteroids (topicals, regional) appear not to make CSR worse
CSC

• Pathogenesis
  – *Helicobacter pylori* Infection
    • Associated with thrombotic disease
    • Molecular mimicry – immune mediated damage to choroidal endothelial cells
    • French study found 40% of CSC patients vs. 25% of the general population had *H. pylori* infection in gut (Ahnoux-Zabsonre et al. J. Fr. Ophthalmol. 2004;27:1129-1133)
      – Not confirmed in other studies
    • Treatment did reduce time for SRF resorption but no effect on visual outcomes (Rahbani-Nobar et al. Mol Vis. 2011;17:99-103)
CSC

• Pathogenesis
  – Genetics
    • Weenink et al. 52% of families of chronic CSC patients had CSC like pathology (Ophthalmologica. 2001;215:183-7)
    • Higher prevalence in whites, Hispanics, and Asians than in African Americans
  – Cytokine analysis (Shin et al. Retina. 2011;31:1937-43)
    • VEGF not elevated in CSR
    • IL-6, IL-8, others not elevated
CSC

• Insights from Imaging

  – OCT

    • EDI – Choroidal thickening

      – CSC – 368 microns vs Normal – 242 microns


      – Reduced by 20% after PDT

CSC

• Insights from Imaging
  – OCT
    • Outer nuclear layer thinning correlates with VA
      – 74 microns Va<20/20; 105 microns Va>20/20
      – 125 microns for age matched controls
    • Elongation of photoreceptor outer segments
CSC

- **Insights from Imaging**
  - **OCT**
    - White precipitates – hyperreflective deposits in the retina and in subretinal space with subretinal fluid
      - Etiology unknown – macrophages with OS?
    - RPED near areas of leak on FA with detectable RPE breach
CSC

OCT

• All areas of leak have hyperreflective material “spewing out” into subretinal space
CSC
CSC

OCT Image

Scanned Image
CSC
CSC

- Insights from Imaging
  - OCT
    - Foveal thinning even after subretinal fluid resolution in chronic CSC and correlates with Va
CSC

• Fundus Autofluorescence (FAF)
  – Acute CSC – can be normal
  – Hyperautofluorescence
    • In area of subretinal fluid over months
    • Accumulates at margins of subretinal fluid
    • White retinal precipitates - Macrophages with OS?
    • Accumulation of shed OS from serous retinal detachment
CSC

- Fundus Autofluorescence
  - Hypoautofluorescence
    - Diffuse retinal pigment epitheliopathy (DRPE)
    - Granular, confluent, and descending tracts
      - Can be dramatic: large flask shaped areas extending from disc and or macula to the dependent inferior retina
      - RPE atrophy and outer retinal atrophy
  - Chronic CSC
CSC

• Multifocal ERG
  – Corresponds to local disease activity but can also demonstrate more widespread retinal dysfunction

• Microperimetry
  – Reduced retinal sensitivity in areas of RPE irregularity and Ellipsoid Zone disruption

CSC

- Adaptive Optics
  - Cone density decreased in CSC even if Ellipsoid Zone intact and Va≥20/20.
  - 42380 in CSC vs 67900 in controls
  - Underscores the subclinical functional loss after each episode of CSC
Poll Question 4

• The quality of evidence for therapeutic efficacy is best for which method of therapy for recurrent CSC?

A. Diode micropulse laser
B. Systemic eplerenone
C. Photodynamic therapy
D. Systemic anti-glucocorticosteroids
CSC

• Treatment
  – Observation – (Quality of Evidence (QOE) – Fair)
    • Most cases of acute CSC resolve in 1-4 months
    • Longer duration more permanent loss of cones
CSC

• Treatment
  – Risk Factor Modification
    • Discontinue corticosteroids (QOE – Good)
      – Topical cutaneous creams, nasal sprays, systemic, regional injections
    • Reduce stress levels – Type A personalities (QOE – Fair)
      – 8 studies –
      – Physical exercise, mindfulness meditation, etc
    • Avoid 5-phosphodiesterase inhibitors (sildenafil, tadalafil)
      – Conflicting evidence of role in CSC
    • Avoid MDMA (Ecstasy) – can exacerbate CSR
CSC

- Helicobacter pylori treatment (QOE – Poor)
- Anti-glucocorticosteroids (QOE- Poor to Fair)
  - Ketoconazole - interferes with endogenous steroid production – Ineffective
  - Mifepristone – abortifacient and glucocorticoid receptor antagonist – mixed results
  - Finasteride – 5- alpha- reductase inhibitor reduces conversion of testosterone to DHT – used for BPH
    - Retrospective study of 23 patients (29 eyes) – after 3 months of use over 75% of patients had complete resolution of SRF and Va improved. 37.5% had recurrence of SRF with discontinuation of drug.
    - Clinical trial ?
  - Adrenergic blockade – beta blockers - ineffective
CSC

• Carbonic anhydrase inhibitors (QOE – poor)
  – 1 study showed more rapid resolution of SRF compared to controls in acute CSR

• Anti-VEGF agents (QOE – Poor)
  – Paucity of clinical trials, clinical heterogeneity, small sample sizes, short follow up
  – Hard to demonstrate positive clinical effect
  – PDT superior to ranibizumab in prospective clinical
CSC

• Laser Photocoagulation (QOE – Good)
  – 2 RCTs - Focal argon laser directly to leak site
    • Faster SRF resolution 6 weeks vs 16 weeks
    • No visual benefit
    • No reduction of recurrence
  – Many other case series with similar results for acute and recurrent CSC. No benefit in chronic CSC.
  – Rate of late CNV – around 10%
  – Best for well-defined extrafoveal foci of leakage
CSC

• Photodynamic therapy (QOE – Good)
  – Promotes resolution of SRF and prevents recurrences
    • RCT – half dose PDT vs Placebo
      – 37 of 39 (94%) eyes had no SRF at one year compared to 58% of controls
      – Va – improved or stable in 79% of eyes
    • RCT – Half dose PDT vs. 30%dose PDT
      – 131 patients – 1 year follow up showed
        » Half dose was superior to 30% dose
        • Resolution of SRF, FA leakage, and recurrence of SRF
  • Other studies – showed similar improvements
  • Risks
    – Foveal RPE atrophy worsening after PDT
    – Choroidal thinning after PDT
CSC
CSC

• Micropulse Diode Laser (MDL) (QOE – poor)
  – Chronic CSC –
    • 5 patients: all patients had resolution of SRF at 1 month
      – Bandello et al. IOVS. 2003;44: Abstract 4858
  – Acute CSC
    • RCT – MDL vs standard argon laser (12 eyes vs 3 eyes)
      – Faster visual acuity recovery
      – Better contrast sensitivity
      – No scotoma at site of laser application
  – Other studies of heterogenous patient mix, inadequate follow up, and varied outcome measures
CSC

- Mineralocorticoid Antagonists (QOE – Fair)
  - Aldosterone and Mineralocorticoid receptor (MR) play a role in choroidal hyperpermeability
  - Spironolactone – higher binding affinity to MR than eplerenone
    - Prospective study of 25mg BID for 12 weeks for CSC >3 months duration
    - RCT with crossover after 30 days for another 30 day period with 50mg QD
    - Both showed reduced SRF and CST and improved Va
CSC

- Mineralocorticoid Antagonists (QOE – Fair)
  - Eplerenone for Chronic CSC
  - Only case series and several retrospective studies
    - Some improvement in SRF and Va
    - Overall underwhelming evidence of efficacy and concern over side effects – 10%
      - Fatigue/malaise, reduced libido, gynecomastia (spir), nausea, leg cramps, thirst and dehydration, orthostatic hypotension, vomiting,
    - Pilot Prospective study
      - Reduction in SRF, trend of reduced choroidal thickening
  - All the studies used different dosing regimen
    - 25mg po qd for 1 week, then 50mg qd for remainder of 3 month trial
Chronic CSC - FAF
Chronic CSC - FAF

52 year old Asian woman with chronic CSC with incidental chronic resolved inferior peripheral serous RD
Chronic CSC
Chronic CSC
Chronic CSC
Chronic CSC
Chronic CSC
Persistent detachment > 6 mo
Pachychoroid Neovascularopathy

- Late Complication of PPE and Chronic CSC

- Characteristics:
  - OCT Findings of CSC and/or PPE
  - Type 1 sub RPE CNV
    - With or without subretinal fluid
    - OCT shows broad shallow elevation of RPE suggestive of CNV within Bruchs membrane – Type 1 CNV
    - ICG shows plaque like hyperfluorescence of type 1 CNV and hyperpermeability lesions
  - Eventually polypoidal choroidal vasculopathy may develop

Pachychoroid Neovasculopathy
Pachychoroid Neovasculopathy
Pachychoroid Neovasculopatathy
Pachychoroid Neovasculopathy
Pachychoroid Neovasculopathy
Focal Choroidal Excavation
Focal Choroidal Excavation
Focal Choroidal Excavation
Focal Choroidal Excavation
Focal Choroidal Excavation
Focal Choroidal Excavation
Focal Choroidal Excavation
Focal Choroidal Excavation
Focal Choroidal Excavation

- Focal Choroidal Excavation
  - Conforming Focal Choroidal Excavation
  - Non-Conforming Focal Choroidal Excavation

- Etiology: Why excavations?
  - Collapse of choroidal polyps
  - Spectrum of long-standing pachychoroidal disease

- Therapy
  - If non-conforming and subretinal fluid: anti-VEGF

- Complications?


References


