Emergent Viral Infections

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- There has been increased awareness of the following viruses and their ophthalmologic comorbidities with the advent of recent elevation in worldwide exposure, including epidemics, after increases in global travel and enterprise
  - West Nile virus (WNV)
  - Dengue virus (DFV)
  - Chikungunya (CHK)
  - Zika virus (ZKV)

West Nile Virus (WNV)

Overview

- Definition
  - Single-stranded ribonucleic acid (RNA) arbovirus, family *Flaviviridae*
  - Most commonly spread by mosquitos; birds are usually primary host
  - Typically bilateral multifocal chorioretinitis, occurring in almost 80% of patients with acute WNV infection associated with neurologic illness
  - Originally found in Uganda; US origins in New York 1999, now throughout North and South America
- Symptoms
  - Most have no ocular symptoms
  - Mild blurring
  - Floaters
- Laterality
  - Typically bilateral
- Course
  - Typically self-limiting but may have permanent sequelae

C. S. Foster et al. (eds.), *Uveitis*, https://doi.org/10.1007/978-3-030-52974-1_39

- Age of onset
  - Any
- Gender/race
  - Any/more prevalent in endemic areas
- Systemic associations
  - West Nile fever

Exam: Ocular

Anterior Segment

- Anterior uveitis associated with vitritis
- Nystagmus
- Strabismus

Posterior Segment

- Chorioretinal lesions in the midzone and/or periphery in almost all eyes
  - May be congenital
- Prominent linear clustering of chorioretinal lesions
  - Related to course of retinal nerve fibers, suggesting a contiguous spread of CNS disease
- Retinal hemorrhages
- Focal or diffuse occlusive vasculitis
- Optic neuritis

Exam: Systemic

- Flu-like syndrome
- Neurologic involvement
  - Meningitis, encephalitis
  - Poliomyelitis-like disease
  - Cranial nerve palsies
- Also hepatitis, pancreatitis, myocarditis, cardiac dysrhythmia, nephritis

Imaging

- OCT – hyperreflective lesions from ONL to RPE with focal disruption; atrophic changes
- FAF – hypofluorescent or hyper autofluorescent lesions comparable to exam
- FA – early hypofluorescence and late staining of the chorioretinal lesions; inactive lesions appear with a typical "target like appearance" on FA with central hypofluorescence and peripheral hyperfluorescence
- ICG shows multiple well-delineated hypocyanescent lesions

Laboratory and Radiographic Testing

- Serology – WNV-specific IgG, IgM (most common)
  - Cross-reactions of flaviviruses common
- WNV PCR
- CSF – WNV IgM, pleocytosis
  - Essential with suspected neurologic involvement
- CBC with differential
  - Leukocytosis, lymphocytopenia, thrombocytopenia, anemia
- Plaque reduction neutralization test
- Magnetic resonance imaging (MRI) to detect neurologic involvement

Differential Diagnosis

- Syphilis
- Tuberculosis
- Sarcoidosis
- Idiopathic multifocal choroiditis
- Histoplasmosis
- Birdshot retinochoroiditis

Treatment

- No definitive treatment

Referral/Co-management

- Infectious Disease
- Neurology
- Report to CDC

Dengue Fever (DFV)

Overview

- Definition
  - Single-stranded RNA arbovirus, five types, family *Flaviviridae*
    Subsequent infection with a different type may increase risk of severe complications
  - Commonly spread by mosquitos in tropical climates
  - Typically macular or foveal retinitis +/− hemorrhage which may occur in up to 10% of patients

- Symptoms
  - Blurring
  - Scotomas
  - Floaters
  - Less commonly redness, pain
- Laterality
  - Bilateral asymmetric
- Course
  - Acute onset of symptoms
  - Self-limiting with permanent sequelae
- Age of onset
  - Any
- Gender/race
  - Any/more prevalent in endemic areas (tropical)
- Systemic associations
  - Dengue fever

Exam: Ocular

Anterior Segment

- Anterior uveitis
- Opsoclonus (with neurologic involvement)

Posterior Segment

- Yellow subretinal dots, RPE mottling, foveolitis
- Retinal hemorrhages, retinal vascular sheathing
  - CRAO or BRAO
- Vitritis
- Retinochoroiditis
- Less common
  - Choroidal effusion, choroidal neovascularization
  - Optic disc swelling, optic neuritis
  - May cause panophthalmitis (rare)

Exam: Systemic

- Asymptomatic
- Classic dengue fever (high fever, severe headache, myalgias, arthralgias, nausea, vomiting, maculopapular rash)
  - Less common
    - Dengue hemorrhagic fever – hemorrhage, low platelets
    - Dengue shock syndrome – severe hypotension
- Encephalopathy

Imaging

- OCT: focal outer neurosensory retina–RPE thickening corresponding to the round, foveal yellowish lesion seen clinically (foveolitis)
- FA: prominent retinal vascular leakage, blocked fluorescence due to retinal hemorrhages and retinal–venular occlusion
- ICG: hypofluorescent spots corresponding to the subretinal lesions; large choroidal vasculopathy with hypercyanescence and leakage also common

Laboratory and Radiographic Testing

- IgM antibody capture ELISA
- Dengue group-specific NS1 monoclonal antibody (ELISA)
- CBC with differential

Differential Diagnosis

- Sarcoidosis
- Diabetic retinopathy
- Acute retinal pigment epitheliitis
- Syphilis
- Tuberculosis

Treatment

- No specific therapy
- Supportive therapy for uveitis, corticosteroid
- Vaccination recommended for those previously infected
- Systemic involvement may require hospitalization, transfusion
- Avoid NSAIDs due to risk of hemorrhage

Referral/Co-management

- Infectious disease
- Neurology with suspected encephalopathy
- Report to CDC

Chikungunya (CHK)

Overview

- Definition
  - Single-stranded RNA arbovirus, family *Togaviridae*
  - Commonly spread by mosquitos in tropical climates
  - Can be both endemic and epidemic, has occurred in Western nations
    Risk of death 1:1000
  - Systemic viral infection that may lead to a variety of ocular manifestations, most commonly uveitis
- Symptoms
  - Blurring
  - Redness
  - Light sensitivity
  - Pain
  - Floaters
  - Diplopia
- Laterality
  - Bilateral more than unilateral
- Course
  - Ocular involvement in acute disease
  - Less commonly initially manifest during chronic infection
- Age of onset
  - Any
- Gender/race
  - Any/more prevalent in endemic areas (tropical)
- Systemic associations
  - Chikungunya fever

Exam: Ocular

Anterior Segment

- Acute anterior uveitis (mimic herpetic anterior uveitis) – most common
  - May have hypopyon
  - Elevated IOP
- Keratitis, stromal edema
- Episcleritis, scleritis
- Conjunctivitis
- Cranial nerve palsies

Posterior Segment

- Mild vitritis
- Multifocal retinitis, retinal and macular edema, retinal hemorrhages

- Neuroretinitis
- Optic neuritis
- Central retinal artery occlusion
- Exudative retinal detachment
- Panophthalmitis

Exam: Systemic

- Findings associated with Chikungunya fever
  - Acute fever, severe arthralgia, skin rash
  - May have myocarditis, hepatitis, neurologic involvement

Imaging

- OCT: areas of hyper-reflectivity with after-shadowing; CME; retinal detachment; atrophic changes
- FA: early hypofluorescence with late-phase widespread retinal vascular leakage, staining of retinal infiltrates, and optic disc hyperfluorescence; capillary non-perfusion
- VF: arcuate or central scotomas, may be multifocal, cross-midline

Laboratory and Radiographic Testing

- Real-time PCR
- IgM serology

Differential Diagnosis

- Herpetic keratouveitis
- ANCA vasculitis
- Sarcoidosis
- Syphilis
- Tuberculosis

Treatment

- No definitive treatment for systemic disease
- Topical corticosteroids and cycloplegia for anterior segment manifestations
- Systemic corticosteroid therapy for more severe cases, that is, panuveitis, optic neuritis

Referral/Co-management

- Infectious Disease
- Others depending on systemic involvement
- Report to CDC

Zika Virus (ZKV)

Overview

- *Definition:*
  - Single-stranded RNA arbovirus, family *Flaviviridae*
  - Transmitted via mosquitos, sexual contact, pregnancy, transfusion
    Contagious 1–2 weeks after infection (also shed in tears)
  - First seen in Zika Forest, Uganda, 1947; spread to the Americas around 2007
- *Symptoms:*
  - Blurring, mild to severe
- *Laterality*
  - Unilateral or bilateral
- *Course*
  - Sub-acute, self-limiting
- *Age of onset*
  - Any; may also be congenital
- *Gender/race*
  - Any/more prevalent in endemic areas
- *Systemic association:*
  - Zika fever

Exam: Ocular

Anterior Segment
- None typical

Posterior Segment
- Grey perifoveal bull's-eye maculopathy
- Congenital
  - Retinal hemorrhages
  - Optic disc hypoplasia
  - Chorioretinal scarring, "torpedo maculopathy"
  - Vascular attenuation

Exam: Systemic

- May be asymptomatic
- Mild fever, rash, joint pain
- Guillain-Barré syndrome (rare)
- Congenital ZKV with microcephaly, brain malformations

Imaging (Only the Relevant Ones)

- OCT: disruptions in outer retina, RPE which may resolve
- FA: early hypofluorescence, late hyperfluorescence of macular lesion

Laboratory and Radiographic Testing

- PCR of serum, urine, saliva, tears, CSF while acutely ill
  - May be unable to perform if symptoms more than 7 days
- Serologic testing for ZKV IgM if symptoms >7 days
- Plaque reduction neutralization test (PRNT)
  - Subject to cross-reactivity with flaviviruses

Differential Diagnosis

- Acute idiopathic maculopathy

Treatment

- No definitive treatment
- Vaccines are currently in clinical trials
- Avoid sexual contact for 6 months post infection

Referral/Co-management

- Infectious Disease
- Report to CDC