Three Unusual Cases of Retinopathy
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Abstract
This case series presents three patients with a history of chronic Hepatitis C treated with Peginterferon α-2a and Ribavirin with different presentation of ocular complications. This report summarizes the ocular manifestations of interferon treatment.

Patient 1:
1. Case History
   a. Demographics: 60 year old Caucasian male
   b. Chief Complaint: No ocular complaints
   c. Ocular History: large cup-to-disc ratio OU without glaucoma
   d. Medical History: Diabetes, Hypertension, Hepatitis c, Osteoarthritis
   e. Medications: Asprin 325 mg, Atenolol, HCTZ, Peginterferon α-2a 180 mcg weekly, Ribavirin 1200 mg/day, Citalopram hydrobromide, Doxycycline hyclate, Glyburide.
   f. Initiation of interferon treatment: 30 weeks prior to ocular exam

2. Pertinent findings
   a. Clinical findings
      • Visual acuity without correction was 20/25-2 OD and 20/20 OS
      • Extraocular motilities were full and smooth OU
      • Pupils were equal, round and reactive to light OU with no APD
      • Confrontation fields were full OU
      • Slit-lamp examination was within normal limits OU
      • Intraocular pressures were 14 OD and 16 OS
      • Dilated fundus examination revealed scattered peripapillary splinter hemorrhages OD, a small intraretinal hemorrhage OS and also a cotton wool spot.
   b. Physical findings
      • Normal
   c. Laboratory studies
      • Glucose, HbA1c, PTT and INR findings were within normal limits.

Patient 2:
1. Case History
   a. Demographics: 57 year old African American male
   b. Chief Complaint: Blurry vision at near OU
   c. Ocular History: History of parafoveal hemorrhages OS from untreated hypertension, chorioretinal scar OD, cataracts OU.
   d. Medical History: Obstructive sleep apnea, Hyperlipidemia, Hypertension, Osteoarthritis, Hepatitis c, Hypothyroidism.
   e. Medications: HCTZ, Metoprolol, Omeprazole, Simvastatin, Asprin 325mg, Peginterferon α-2a 180 mcg/weekly and Ribavirin 1200 mg/day.
f. Initiation of interferon treatment: 19 weeks prior to ocular exam. Of note, Peginterferon dose was decreased to 90 mcg/weekly at 8 weeks after starting therapy due to mild thrombocytopenia. Dosage was then increased to 135 mcg/weekly at 20 weeks.

2. Pertinent Findings
   a. Clinical findings
      - Visual acuity with correction was 20/25+ OD and 20/20 OS
      - Extraocular muscles were full and smooth OU
      - Pupils were equal, round and reactive to light OU with no APD
      - Confrontation fields were full OU
      - Slit-lamp examination was within normal limits OU
      - Intraocular pressures were 14 OD and 14 OS
      - Dilated fundus examination revealed stable parafoveal hemes OS, and multiple cotton wool spots OS

   b. Physical findings
      - Normal

   c. Laboratory studies
      - Glucose and cholesterol levels were within normal limits
      - Blood pressure 140/76

Patient 3:

1. Case History
   a. Demographics: 54 year old Caucasian male
   b. Chief Complaint: Sudden decrease in vision OS
   c. Ocular History: Longstanding optic neuropathy OD from unknown etiology
   d. Medical History: Hepatitis c, Hyperlipidemia
   e. Medications: Verdenafil HCL, Ranitidine HCL, Cyclobenzaprine HCL, Hydroxyzine pamoate, Diphenhydramine HCL, Dicyclomine HCL, Peginterferon α-2a 180 mcg/weekly and Ribavirin 1000 mg/day.
   f. Initiation of interferon treatment: 14 weeks prior to ocular exam

2. Pertinent findings
   a. Clinical findings
      - Visual acuity without correction was 20/30 OD and 20/25 OS
      - Extraocular motilities were full and smooth OU
      - Pupils were equal, round and reactive to light OU with no APD
      - Confrontation fields were full OU
      - Slit lamp examination was within normal limits OU
      - Intraocular pressures were 18 OD and 18 OS
      - Dilated fundus examination revealed diffuse temporal pallor OD and three peripapillary splinter hemorrhages OS with optic disc edema
      - Humphrey visual field 24-2 SITA Standard showed generalized absolute defect OD and inferior altitudinal defect OS

   b. Physical
c. Laboratory studies
   - Blood work ruled out hypertension, diabetes, temporal arteritis, compressive lesion, lupus systemic erythematosus, hyperviscosity and hypercoagulable syndromes, HIV and carotid artery obstruction.

d. Radiology studies
   - MRI of the brain showed few nonspecific white matter hyperintense lesions due to microvascular ischemia.
   - MRA of the head was essentially normal.

e. Other studies
   - Carotid duplex revealed no stenosis of right or left carotid arteries.

Differential Diagnosis

Cotton wool spots (Patient 1 and 2)
   a. Diabetes mellitus
      - Patient 1 had history of Type II Diabetes with HbA1c of 6.3 and LBS 166. Patient had no history of diabetic retinopathy.
   b. Systemic hypertension
      - Both patients 1 and 2 had history of systemic hypertension but good control of blood pressure.
      - Considered most common cause of cotton wool spots.
   c. Purtscher’s retinopathy
      - No recent history of long bone fractures or severe compressive injuries.
   d. HIV
      - Patients were HIV negative.
   e. Radiation retinopathy
      - No history of radiation treatment.
   f. Anemia
      - No history of anemia.

Non-arteritis Ischemic optic neuropathy (Patient 3)
   a. Malignant hypertension
      - Patient had no history of elevated blood pressure.
   b. Diabetes
      - Recent HbA1c and glucose were normal.
   c. Temporal arteritis (Giant Cell Arteritis)
      - Patient does not fall in the typical age range for GCA.
      - ESR 12 mm/hr, CRP 0.2 mg/dL (Normal).
      - Patient denied any classic symptoms such as, temporal headache, jaw claudication, scalp tenderness, neck pain and polymyalgia rheumatica.
   d. Compressive lesion
      - MRI was clear of any lesions.
   e. Systemic Lupus Erythematosus
      - Lupus panel was normal
f. Retinal vascular occlusion
   • Patient did not have any other ocular findings consistent with vein occlusion.

Diagnosis and discussion
a. Patients 1 and 2 were both asymptomatic and retinopathy was noted incidentally during a routine eye exam. Both patients returned for follow up visits during the course of therapy and retinopathy resolved once therapy was complete. However, patient 3 reported a sudden decrease in vision in the left eye with deterioration in vision at follow up visit. Due to the fact that he was undergoing interferon therapy and had an inferior altitudinal visual field defect with no significant systemic history except hyperlipidemia, prompted us to order extensive blood work and imaging.
b. All three patients were suspected to have interferon related ocular complications.
c. Background information:
   • Hepatitis C
      o Hepatitis C is the most common blood-borne infectious disease in the United States.
      o High risk groups include: Low socio-economic groups, health-care workers, military veterans, Intravenous drug users (IDU) alcoholics and prisoners.
   • Treatment
      o Current treatment includes combination therapy with interferon-alpha and ribavirin for 24 to 48 weeks.
      o New treatment option consists of pegylated interferon alpha which has a longer half-life, requiring only weekly injections.
      o Incidence of retinopathy has been reported with wide variability from 15% to 80 % of patients.
   • Mechanism of interferon retinopathy
      o One hypothesis is that interferon cause deposition of immune complexes in small retinal vessels which leads to ischemia.
      o Purvin et al. suggested involvement of the posterior ciliary arteries as a possible cause of AION.
   • Ocular manifestations
      o Cotton wool spots, retinal hemorrhages, ischemic optic neuropathy, neovascular glaucoma, optic disc edema, retinal detachment, intraocular hemorrhage, retinal vein and artery occlusion, and cystoid macular edema.

Treatment/Management of Interferon Retinopathy
a. Treatment
   • Patients 1 and 2 did not require any medical intervention and retinopathy resolved once treatment was stopped.
   • Patient 3 was started on oral prednisone 80mg for ten days with no improvement in vision despite discontinuing interferon therapy.
   • In Willson’s case report is a review of the literature related to visual complications related to interferon therapy. In his review of the literature, 75% of the patients’ ocular complications had resolved following withdrawal of interferon therapy.
• No standard protocol for monitoring patients on peginterferon α-2a and ribavirin has been established.

b. Bibliography
• Rhoads, J. Natural History and Epidemiology of Hepatitis C. Journal of the Association of Nurses and Aids Care. 2003; 14, 5:18S-25S.

Conclusion
a. The most common retinal findings are cotton wool spots and/ or retinal hemorrhages.

b. Patients with diabetes, hypertension, dyslipidemia and hypercoagulable conditions are more apt to develop interferon retinopathy and therefore should be followed more frequently.

c. Interferon retinopathy has been documented with variable treatment regimen.

d. Interferon-associated retinopathy is generally asymptomatic and usually reversible and severe ocular complications are rare.