Title: Cotton Wool and Roth Spots as Ocular Complications of Cyclophosphamide Treatment for Renal Disease

Abstract: A patient returning for follow up shows a large increase in retinal cotton wool spots and a Roth spot after initiation of cyclophosphamide treatment for renal disease.

I. Case History

- Patient demographics: 61 year old Caucasian male.
- Chief complaint: 6 month follow up for RPE abnormalities and questionable cotton wool spot.
- Last eye exam: 6 months ago
  - Ocular History: RPE abnormalities, 1 cotton wool spot, refractive error
- Medical history:
  - Chronic rapidly progressive glomerulonephritis
  - Type 2 insulin dependent diabetes mellitus without complications
  - Hepatitis C
  - Obesity
  - Hyperlipidemia
  - Hypertension
  - Chronic obstructive pulmonary disease
- Medications: insulin, cyclophosphamide, furosemide, losartan, metoprolol tartrate, prednisolone
- Other salient information: not currently on treatment for hepatitis C

II. Pertinent findings

- Clinical:
  - VAOD 20/20, OS 20/20 at D, OD 20/25, OS 20/25 at N
  - OD plano+0.75x007 BCVA 20/20, OS -0.25+0.50x153 BCVA 20/20
  - Add +2.25 OD, OS, OU 20/20 at near
  - Pupils: equal, round, and reactive to light, no RAPD; all other entrance tests unremarkable
  - Anterior segment:
    - 1+ nuclear sclerotic cataracts OU
  - Posterior pole:
    - OD: flame shaped hemorrhage, 6 scattered CWS along arcades
    - OS: Roth spot, flame shaped hemorrhage, 7 scattered CWS along arcades
- Laboratory studies:
  - HbA1C: 5.7% 1 month ago
  - Blood pressure: 127/82mmHg 1 month ago
- Others:
Nephrologist: started patient on cyclophosphamide 5 months ago for progressive glomerulonephritis

III. Differential diagnosis

- Primary/leading:
  - Chemotherapy induced ocular complication
  - Diabetic retinopathy
  - Hypertensive retinopathy
- Others:
  - HIV retinopathy
  - Subacute bacterial endocarditis
  - Severe anemia

IV. Diagnosis and discussion

- Elaborate on the condition:
  - Cotton wool spots are thought to arise from an interruption of axoplasmic flow from focal ischemia associated with occlusion of precapillary arterioles\(^4\). They are not specific to any specific disease process and are associated with many common and rare diseases. Cotton wool spots are most commonly associated with diabetes and malignant hypertension, yet they may also be associated with numerous other disorders such as HIV disease, leukemia or the use of chemotherapy agents.
  - Roth spots are white centered retinal hemorrhages. Previously thought to be pathognomonic for subacute bacterial endocarditis, they have now been shown to be not specific to any disease entity\(^3\). Roth spots may be observed in several conditions including blood dyscrasia and severe anemia.
- Expound on unique features:
  - The patient has never been on interferon treatment and physical exams indicate a history of well controlled diabetes and blood pressure. The large increase in the cotton wool spots and the new appearance of a Roth spot was observed on follow up after the patient was started on the chemotherapy alkylating agent cyclophosphamide for worsening renal disease. The potential of chemotherapy agents to cause retinopathy has been previously described and the observation of retinopathy in this patient is presumed to arise from the effects of the chemotherapy drug\(^{1,2}\).

V. Treatment and Management

- Management:
  - Observation and follow up with dilated fundus exam every 4-8 weeks or sooner given any vision changes.
• Discontinuation of cyclophosphamide may be indicated if cotton wool spots threaten the macula.

VI. Conclusion

• Clinical pearls:
  • Cotton wool spots and Roth spots present a myriad of challenging differentials that can be narrowed down upon review of a patient’s medications and medical history.

• References: