The case of a 63-year-old man with sub-acute bilateral red eyes, parotitis, uveitis, and trabeculitis evokes consideration for Heerfordt’s syndrome: a rare sarcoid precursor with any combination of parotitis, uveitis, facial nerve palsy, and fever.

I. Case History
   a. Patient demographics: 63 year-old black male
   b. Chief complaint: This patient presents on August 19th from the emergency room as a consult for bilateral red eyes of approximately 3-week duration OD and 2-week duration OS; devoid of photophobia, mucous discharge, or epiphora. He denied any associated fever or sore throat. The patient was seen one week prior at which time a diagnosis of viral conjunctivitis was conferred based on symptoms and clinical observations. An immunoassay was not conducted. The patient has developed recent concern because his eyes have increased in redness with the new association of a dull ache behind his eyes.
   c. Ocular, medical history:
      i. Ocular
         1. Recent diagnosis of viral conjunctivitis (August 12th visit): red eyes without pain, photophobia, mucous discharge or epiphora. He had been using Visine to relieve redness; the left eye became red first, then the right eye became red one week later. At this visit he was instructed to discontinue Visine and begin artificial tears four times a day in both eyes
         2. Last comprehensive eye examination—March 2010:
            a. unremarkable anterior segment
            b. IOP: 18/17 @ 0900
            c. physiological cupping: glaucoma suspect findings within normal limits, highest measured IOPs 18 OD, OS
         3. Medical: Non-insulin-dependent diabetes mellitus, hypertension, dyspnea, post-traumatic stress disorder, depression, elevate prostate specific antigen, benign prostate hypertrophy, anemia, sleep apnea, right inguinal hernia, gout, chronic sinusitis, allergic rhinitis, hearing loss
   d. Medications:
      i. Systemic: acetaminophen/oxycodone, amlodipine, buspirone (mood/anxiety symptoms), finasteride, gabapentin, indomethacin (for arthritic complaints), metformin, omeprazole, quetiapine fumarate (for PTSD/night time agitation), sertraline (for anxiety/depression), simvastatin, sodium chloride nasal spray, bactrim for urinary tract infection (dysuria and discharge), terazosin, valsartan, venlafaxine, metronidazole
      ii. Ocular: artificial tears qid OU, Visine bid OU
   e. Other salient information: wife had been diagnosed with trichimonous at the beginning of August and requested sexually transmitted disease testing for the patient
II. Pertinent Findings
   a. Clinical
      i. visual acuity: 20/25 OD, 20/20 OS (reduced from 20/20 at previous visit)
      ii. anterior segment
         1. bulbar conjunctiva: 3+ diffuse injection 360
         2. palpebral conjunctiva: 2+ papillae superior, 1+ papillae inferior, 1+ follicles inf OU
         3. anterior chamber: 1+ flare OU, trace cells OS (no anterior chamber reaction at previous visit)
         4. van Herrick angles: 4+ OU
         5. conjunctival injection blanched with 2.5% phenylephrine
      iii. Goldmann intraocular pressure with tonosafe tips: 40/36 @ 1156
      iv. dilated fundus examination: unremarkable
      v. Gonioscopy (to rule out plateau iris): open to ciliary body inferior and scleral spur nasal/temporal/superior, flat iris approach
      vi. post-dilation IOP c tonosafe tips: OD 47, OS 38 @ 1435
      vii. post-dilation IOP s/p iopidine and timolol c tonosafe tips:
           1. OD 34, OS 38 @ 1540
   b. Physical
      i. Parotid glands: tempromandibular area is noticeably enlarged/swollen, right side more than left side. Palpation of the gland revealed a non-rigid, elastic consistency with tenderness present on right side.
      ii. Thyroid gland: normal by palpation
      iii. Submandibular, sublingual, cervical and supraclavicular lymph nodes: no hardening, no swelling, no tenderness. Preauricular nodes could not be identified by palpation because of the extensive parotid gland swelling.
   c. Laboratory Studies
      i. RPR and MHA-TP: nonreactive and negative
      ii. Hepatitis C: negative
      iii. HIV antibodies: negative
      iv. Chlamydia by urethra swab: negative
      v. Lyme Titers: normal
      vi. Bartonella Titers: normal
      vii. Conjunctival scraping: negative for inclusion bodies and trichimonous
      viii. Conjunctival bacterial culture: negative of all organisms
      ix. ACE: normal
      x. Mumps IgG: elevated (5.24), IgM <0.80
   d. Radiological Studies: Chest X-ray normal
   e. Others:
      i. Follow-up Visits
         1. August 19th: ordered 2-500mg tablets of Azithromycin to cover ocular chlamydia as lab results were pending, ordered Cosopt twice a day OU for IOP lowering
2. August 23rd:
   a. visual acuity improved to baseline 20/20 OD, OS
   b. parotid gland presentation stable
   c. conjunctiva presentation stable
   d. anterior chamber: increased to 1+ cellular reaction, 1+ flare remains
   e. Goldmann IOP: 42/42 @ 0751
   f. Presumed trabeculitis diagnosed and he was started on Pred Forte 1gt q1h x 4 hours, q2h x 2 days, q4h x 3 days; Viroptic 1gt OU qid to cover possible herpetic conjunctivitis without keratitis; Birmonidine bid OU in addition to Cosopt for IOP control

3. August 24th:
   a. had not taken Viroptic because pharmacy never released it to him, over-brow headaches had subsided, patient reported symptoms of fever the night before but did measure his temperature, subjective decrease in conjunctival injection
   b. physical exam: full range of motion of neck without stiffness or pain to further evaluate for meningitis, parotid gland tenderness has resolved and the swelling has decreased bilaterally with right side more than left
   c. Goldmann IOP: 24/18 @ 0757
   d. 1+ bulbar injection, resolving papillary reaction
   e. anterior chamber reaction resolving
   f. assessed as “subacute bilateral conjunctivitis with trabeculitis and mild anterior uveitis”
   g. ordered additional serologic testing (see above), continue topical steroid

4. August 26th:
   a. headaches almost resolved, redness almost resolved, no noticeable size difference in parotid gland swelling and still without tenderness
   b. physical exam: decreased swelling left parotid, stable amount of swelling right parotid, both are non-tender
   c. Goldmann IOP: 18/15 @ 0757
   d. bulbar conjunctiva: white and quiet
   e. anterior chamber: rare cell and trace flare OD, rare cell without appreciable flare OS
   f. discontinue brimonidine, discontinue Viroptic in the patient's electronic health record
   g. next follow-up scheduled for August 30th

ii. Telephone consult with the chief of infectious disease concerning immunoglobulin levels in adults diagnosed with mumps
III. Differential Diagnosis
   a. Primary/leading: Heerfordt’s syndrome → precursor to sarcoid
   b. Others: mumps (significantly elevated IgG), Sjögren’s Syndrome (dry mouth complaints)

IV. Diagnosis and Discussion
   a. The presumptive diagnosis after considering all of the diagnostic information available at the time of writing this outline is Heerfordt’s syndrome, although further follow-up, possibly over several years, will need to be conducted to derive a definitive diagnosis. Heerfordt’s syndrome is a precursor to sarcoidosis involving any combination of parotitis, uveitis, fever, and facial nerve palsy. This patient had a positive history for the first two clinical features, and a questionable history for fever. No facial nerve palsy was observed in clinic or reported by history, but facial nerve palsy may possibly develop over the course of follow-up (Snell and Karish).
   b. Sarcoid is a systemic inflammatory condition resulting in the formation of noncaseating granulomas throughout multiple systems and mediated by T-cell lymphocytes (Kanski). The lungs are affected in 90% of all cases. This condition affects mostly young adults; elderly patients with newly diagnosed sarcoid are rare but do occur frequently with sub-clinical findings. This patient presents without materialization of hilar lymphadenopathy and a normal ACE level, but considering that sub-clinical findings are common in this patient’s age range, diagnosis is a matter of exclusion in this case.
      i. Heerfordt’s Syndrome: very rare. Tamme and Evanchan report that only 6-8% of formally-diagnosed sarcoid patients present with parotid gland swelling; Evanchan states that about 0.3% of sarcoid patients have Heerfordt’s syndrome, but any combination of the four components may be present at any time. These characteristics make this diagnosis extremely difficult. Additionally, Snell and Karnish published a case report for the British Journal of Medicine in 1976 that cited authors who found 8 out of 388 cases of sarcoidosis with incomplete Heerfordt’s syndrome; only 1 of the 388 cases reviewed had a occurrence of facial nerve palsy. Evanchan also cites an author who states that facial palsy is present in about only 5% of all cases (Joseph and Scolding 2007).
      ii. According to C.F. Heerfordt, who described Heerfordt’s syndrome in 1909 as "uveoparotid fever", the clinical presentation of parotid gland swelling, uveitis, and facial nerve palsy was originally associated with mumps (Evanchan, Heerfordt). Sarcoid and Heerfordt’s were directly linked in 1937. Like sarcoid, there is no known cause for Heerfordt’s syndrome. Literature review available in 2007 suggested infectious agents like M. tuberculosis or DNA viruses could be responsible, but no definitive findings could support the theories (Tamme).
      iii. Arthritis: the patient was seen in the rheumatology clinic at the VA hospital because of small joint complaints. A search on UpToDate.com found that almost 25% of sarcoid patients have arthritic complaints,
especially in the lower limbs, linked to sarcoid (Sequeira and Aggarwal). While a link between the patient’s arthritis and uveitis/parotitis is weak, the argument for a diagnosis of sarcoid is much stronger when considering the whole clinical picture.

iv. Dyspnea: in the early stages of sarcoid revealed that 50% of all patients are asymptomatic at onset and 25% have cough/dyspnea (Dempsey 2009).

v. Generally speaking, ocular manifestations of sarcoid include: acute and chronic anterior uveitis, intermediate uveitis, periphlebitis, choroidal infiltrates, multifocal choroiditis, retinal granulomas, peripheral retinal neovascularization, optic nerve head edema or granulomas (Kanski).

c. Mumps is included on the current differential diagnosis list because of the parotid gland swelling. Although this diagnosis is usually reserved for children, Mumps may affect the elderly and a resurgence of infection is being seen in this age group. Serological testing is necessary for proper diagnosis and is confirmed by detection of a 4-fold rise in acute and convalescent phase IgG titer or detection of IgM in a convalescent phase serum sample (CDC). Mumps may also be confirmed by culturing mumps virus from saliva or cerebrospinal fluid (Mumps 1167). This patient did report that he thought he was vaccinated against mumps in his youth, but the vaccine was introduced in 1967 when the patient was in his 30s. In concordance with the patient’s history, his mumps IgM level was not significantly elevated; however, his IgG antibodies resulted in a significantly elevated titer. We plan to obtain convalescent phase titers on September 7th to compare for a four-fold increase. Sjögren’s syndrome is on the differentials list as a minor possibility because of the patient’s complaint of a new-onset dry mouth. Sjögren’s can have similar initial presentations as sarcoid, or vice versa, and a labial biopsy may possibly be the only way to differentiate the two (Melsom 1988).

d. Expound on unique features:

i. The patient is much older than the typical age at which sarcoid is diagnosed. The patient also had no significant pulmonary findings on chest x-ray and his ACE level was well within the normal range.

ii. Increased intraocular pressure is a very unique finding. Trabeculitis was essentially confirmed after starting the Pred Forte. Initially, there was no significant decrease in intraocular pressure when the patient was on the Cosopt. Within 24 hours, the intraocular pressure was reduced by 43% OD and 57% OS when Pred Forte and Brimonidine 0.2% were started. Such a dramatic decrease in IOP would not be expected from the effect of adding brimonidine alone.

iii. Observing the amount of injection without an anterior chamber reaction for the first two visits is a difficult judgment on the nature of the redness. It was not until the third visit that uveitis was assessed and properly treated.

V. Treatment and Management
a. Continuation of the Pred Forte on a very slow taper and discontinue ocular hypotensive agents
b. No systemic steroids to treat sarcoid at this time due to lack of symptoms and systematic findings. Rheumatology consult ordered.
c. Parotid gland swelling: no treatment at this time, monitor for the return of tenderness, development of mucous secretion into mouth, and refer to ENT if these symptoms present or if parotitis persists.
d. Consider in future follow-ups:
   i. labial salivary gland biopsy indicated in order to confirm presence/absence of granulomas
   ii. conjunctival biopsy not indicated because lack of concretions/granulomas visible along tarsal plate
   iii. high resolution CT of lungs due to negative chest x-ray; also, high resolution CT of head to rule out metastases

VI. Conclusion
a. Persistence of the clinical features of conjunctivitis may introduce a systemic inflammatory or infectious condition. When any combination of uveal inflammation, parotitis, fever, and or facial nerve palsy presents, Heerfordt’s syndrome should be considered as a precursor to sarcoidosis.

b. A careful physical examination of the head and neck is required in cases of red eyes, otherwise attributes such as subtle glandular changes may go undetected and a misleading diagnosis may be conferred.

VII. Bibliography


