To be or not to be: Is this an emergency?
COPE: 31412-SD

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Emergency Questions by Patients

- Can you take these bumps off my eye?
- Was it good that I washed my hands before calling you?
- Can I lose my vision from eating dessert? (diabetic patient)

Case 1

Can you take these bumps off my eye?

Patient presentation

37 yo BM presents for initial evaluation for FBS and redness OU for over a year. He reports 2 bumps in his lower eyelid OD for 6 mos that he wants removed.

He has used topical antibiotic drops his wife gave him without any improvement of his symptoms. He also has used Visine without relief.

Patient presentation: Medical history

Allergic rhinitis
GERD
Restless leg syndrome
Sleep apnea
Hypertension
Right shoulder pain
Arthralgia involving hips/knees/ankles
Chronic sinusitis
Possible mumps 1 year ago.

Zyrtec
OTC omeprazole
OTC decongestant

Patient presentation: Ocular exam

Externals normal
Pupils crisp responses/(-) APD
BVA 20/20 OD
20/20 OS

SLE lids, cornea, iris normal
 conjunctiva .............
AC deep and quiet
TA 17 OD
16 OS
Ocular assessment:

- Dry eye from bilateral dacryoadenitis. Started topical lubricant gtts and UNG.
- Initial working diagnosis of sarcoidosis, cat scratch, and mumps.
- Schedule biopsy of conjunctival lesion/lacrimal gland.
- Chest x-ray, ACE, PPD, Bartonella titer, CBC.
- RTC in 2 weeks for evaluation for conjunctival biopsy.

Dacryoadenitis

Bilateral, chronic involvement is more commonly associated with systemic conditions such as sarcoidosis, lymphoma, Sjögren syndrome, malnutrition, metabolic derangement such as diabetes mellitus, and cystic fibrosis, or drugs such as thiouracil.

Acute dacryoadenitis with unilateral or bilateral involvement commonly results from viral (i.e., mumps and Epstein Barr) and bacterial infections.

**Patient 2 week follow-up**

Patient returned for pre-op for lesional excision of conjunctiva or lacrimal gland. Surgery was cancelled due to "eyes feeling better".

Patient did not go for any lab or radiology testing since his previous visit. He did continue on lubricant tx. He was sent to obtain ACE, PPD and Bartonella and CBC.

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**4 month visit**

MB did not return for follow-up for 4 mos

Pt started on CPAP for sleep apnea

Worsening articular pain not controlled by oral NSAIDs

Parotid gland enlargement right side over 2 month period

No change in visual or ocular health exam from initial exam.

Testing results: Bartonella IgG and IgM: negative

ACE 65

CBC: normal

PPD: no reaction

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**Recommendations after 4 month evaluation**

- Progressive involvement of parotid gland associated with no resolution of lacrimal involvement warrants definitive diagnosis.
- Discussion with PC whose concern was potential carcinoma of parotid
- Referral to pulmonologist (repeated ACE 72)
- Referral to rheumatologist for progressive arthropathy

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**CHEST X-RAY RESULTS**

- Clear chest x-ray
- Hilar lymphadenopathy

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**Increasing suspicion of sarcoidosis**

A rare case of sarcoidosis without pulmonary involvement with:

- clear chest x-ray
- elevating ACE levels
- bilateral dacryoadenitis
- conjunctival granuloma
- parotiditis
- arthropathy

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**BIOPSY WHICH TISSUE?**
Lacrimal biopsy and sarcoid Dx

Weinreb (1984 N=27) patients with suspected sarcoidosis confirmed dx in:

- 5 non caseating granuloma
- 3 of 5 with enlarged glands
- 5 of 7 with gallium scan uptake

Conjunctival biopsy and sarcoid Dx

Blind biopsy without defined lesion:

- Weinreb (1987) <10% positive yield
- Bonifoli (2005) 7-55% positive yield
- Spaide (1990) 61% positive yield

Biopsy of defined lesion:

- Bonifoli (2005) 85% positive yield

Tissue to be biopsied

Primary care concern of potential parotid tumor

Parotid gland biopsy results

Multiple non-caseating granulomas. AFB and fungal stains negative.

Rheumatology evaluation after biopsy

Impression:
1) Concurrence with optometry impression of non-pulmonary sarcoidosis (left parotid tenderness which began 2 mos prior).

2) Systemic treatment necessary – patient started on plaquenil and 60mg prednisone secondary to:
- polyarthritis
- dry eye with lacrimal gland enlargement
- granulomatous parotid infiltration

Evolution of sarcoidosis

1898 Johnathon Hutchinson describes a dermatologic condition due to the presence of erythema nodosum

1899 Caesar Boeck felt the dermatologic condition resembled a sarcoma naming the condition “sarkoid”

1909 Schumaker described uveitis in a patient with sarcoidosis
Sarcoidosis: more than a lung disease

Multisystem granulomatous disease with few signs or symptoms in early stages which are dependent on specific organ system involvement.

Affecting 10-30/100,000 in US (.8% white and 2.4% Black LTR)

1/2 of patients go into remission in 3 years
2/3 within 10 years

1/3 of patients have a chronic/protracted course resulting in life altering physical impairment

3-5% mortality associated with severe pulmonary, cardiac or neurologic involvement

Sarcoidosis etiology

Specific etiology unknown with probable multiple factors with varying patterns of the disease.

- Pathogenic infection
- Environmental agents exposure (ie: titanium and crop dust)
- Genetic predisposition?

Organ system involvement

90% pulmonary involvement
>50% muscle involvement
35% bone/joint
25% dermatologic
20% liver
17% bone marrow
10% neurologic
5% cardiac
5% parotid gland
5% mucous membrane
30% initially present with extra-pulmonary involvement

Ocular involvement and sarcoidosis

Can be presenting symptom in 5% of cases with overall incidence of 20-25% of sarcoid patients:

- 60-80% uveitis
- 25% posterior segment (choroid and retina)
- 5% optic nerve
- 12-27% eyelid lesions
- 20-50% conjunctival granulomas
- 4-66% lacrimal gland/keratoconjunctivitis sicca

Sarcoidosis diagnostic challenges

Diagnosis made on clinical presentation > 60% of cases as varying organ involvement and severity makes a “hallmark clinical picture” difficult

No definitive laboratory test exists

Pulmonary involvement may be minimal or absent

Tissue biopsy warranted for definitive diagnosis in many cases

Diagnosis of Sarcoidosis

3 clinical elements are needed for diagnosis:

A. Compatible clinical and radiographic findings
B. Exclusion of other diseases that present similarly
C. Tissue biopsy results revealing histopathologic confirmation of noncaseating granuloma
Lacrimal gland and sarcoid diagnosis

<table>
<thead>
<tr>
<th>Studies with lacrimal gland involvement</th>
<th>Initially normal chest X-ray</th>
<th>Elevated ACE</th>
<th>Elevated lysozyme</th>
<th>Systemic involvement</th>
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</thead>
<tbody>
<tr>
<td>Prabhakaran et al. N=11 of 26</td>
<td>46.15%</td>
<td>81.80%</td>
<td>25%</td>
<td>100%</td>
</tr>
<tr>
<td>Yanardag and Pamuk N=9</td>
<td>55.60%</td>
<td>NA</td>
<td>NA</td>
<td>100%</td>
</tr>
<tr>
<td>Mavrikakis and Rootman N=11 of 20</td>
<td>50%</td>
<td>20%</td>
<td>NA</td>
<td>50%</td>
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Indications for systemic treatment

Not all patients require treatment.

Treatment is indicated when target organ damage warrants intervention.

Systemic treatment with oral steroids and non-steroidal agents comprise the mainstay of treatment for both pulmonary and non-pulmonary involvement

Pulmonary Staging of Sarcoid disease

Stage 0: normal chest x-ray

Stage 1: bilateral hilar adenopathy without infiltration (65% at initial diagnosis)

Stage 2: bilateral hilar adenopathy with pulmonary infiltration (22% at initial diagnosis)

Stage 3: pulmonary fibrosis present

Indications for systemic treatment

No treatment

Asymptomatic stage 0-3

Oral NSAIDs

Stage 1 pulmonary c mild symptoms

Arthralgia/rheumatic symptoms

Oral Steroids

(40-60mg daily 3-6 mos)

Symptomatic pulmonary involvement in stages 1-3

Symptomatic extra-pulmonary involvement

Nonsteroidal treatment of sarcoidosis

Methotrexate effective alternative to prednisone

Chloroquine/plaquenil acute and chronic pulmonary, dermatologic neurologic and boney involvement

Azathioprine (Imuran) effective steroid sparing agent

Chlorambucil (Leukeran) progressive disease when steroids are contraindicated or ineffective

Cyclophosphamide (Cytoxin) modest effectiveness compared to steroid in refractory cases

Cyclosporine (Sandimmune) limited effectiveness in refractory cases

Infliximab (Remicade) used in refractory cases that primarily involve extra pulmonary tissues

Overview of clinical outcome

<table>
<thead>
<tr>
<th>Arth</th>
<th>ACE</th>
<th>Oral Tx</th>
<th>Dacryo</th>
</tr>
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<tbody>
<tr>
<td>08/06</td>
<td>65</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>01/07</td>
<td>72</td>
<td>started</td>
<td>+</td>
</tr>
<tr>
<td>04/07</td>
<td>35</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>05/07</td>
<td>27</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>12/08</td>
<td>66</td>
<td>+/-</td>
<td>-</td>
</tr>
<tr>
<td>01/09</td>
<td>10</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>07/09</td>
<td>60</td>
<td>+/-</td>
<td>-</td>
</tr>
<tr>
<td>12/09</td>
<td>15</td>
<td>+</td>
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</tr>
<tr>
<td>09/12</td>
<td>32</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>05/13</td>
<td>30</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>
**Dacryoadenitis and treatment**

Baseline | 6 mos | 1 year

**Conjunctival granuloma and treatment**

Baseline | 1 year later

**CASE CLOSURE**

Chronic dry eye: Patient managed on topical lubricant gts and UNG with adequate control of symptoms.

Rheumatology: Chronic arthritis managed on MTX-oral steroid used for 8 mos after initial diagnosis. On chronic MTX treatment.

Pulmonary: No ongoing management

**Salient points of the case**

Histopathologic findings played a primary role in the definitive diagnosis.

Ocular manifestations were instrumental in the guiding diagnostic decision making.

The medical treatment of patients with sarcoidosis may best be managed by non-pulmonary medical providers depending on the target organ involvement.

**Frey's syndrome after parotid dissection**

- Gustatory sweating on the cheek following parotid gland removal superficial to the facial nerve.
- This results from aberrant innervation of cutaneous sweat glands by postganglionic parasympathetic salivary nerves.
- Reported in 2-80% of patients.

**Case 1**

Should patients wash their hands before seeing us?
Case 1:

BM is a 57 yo WM in for emergency visit. He states he noticed a hemorrhage in his OS when washing his hands after moving his bowels in the bathroom.

PMH: Type 2 DM x 1 year e 6.2 A1c
HT x 10 yrs c good control (127/76 that morning)
HL x 8 yrs on statin med
CAD s/p bypass 2 years ago on 81mg ASA daily in addition to fish oil
Obesity
Sleep Apnea
Nonsmoker

Last eye exam 5 mos ago with no vision change since that time. He has been using lubricant drops PRN for dry eye with relief.

Entering VA 20/20 OD/OS
Externals no APD
SLE dry eye with lower lid laxity hemorrhage OS
Case 1: Hyphema

Causes of Iris Neovascularization

Ocular Ischemia

- Proliferative diabetic retinopathy
- Retinal vein occlusion
- Ocular ischemic syndrome

What applies to this patient?

Diabetic: but no retinopathy
No active or compensated RVO evident

Ocular Ischemic Syndrome (OIS)

- >90% carotid occlusion
- M>F over age 50 (greatest over 60)
- usually presents unilaterally
- 25% of patients with OIS have previous CVA

Symptoms:

- 10% have no symptoms
- Vision loss in 90% of patients
- ocular angina in 40% of patients
- amaurosis seen in 10% of patients
- delayed light and dark adaptation

Clinical Findings of OIS

* Anterior Segment:
  - Sluggish pupillary responses
  - Neovascularization: NVI/NVA 67%, NVG 33%
  - AC Flare 18% (Pseudo-iritis)
  - Relative hypotony

* Posterior Segment:
  - Asymmetric retinopathy
  - Blot hemes at the equatorial region and beyond
  - NVD/NVE rarely

Pertinence to Case 1

No carotid bruit
No NVA on gonioscopy
IOP's were 15 OD and 16 OS
Same day carotid ultrasound and MRA (1 week later)
93% R stenosis
97% L stenosis
Case 1: Outcome of Patient WM

Patient referred for:
• evaluation carotid surgery (performed left side in 1 week)
• bilateral PRP (performed 1 week after initial visit)

Clinical findings on f/u:
• Hyphema resolved in 2 days
• Regression in the NVI by 1 mo
• IOP elevation of 23 mm

So....

Should patients wash their hands before seeing us?

YES... it may do more than stop the spread of germs!

Case 3

Does eating dessert cause vision loss?

Case 3: Medical history

PMH:
DM x 5 yrs A1c 6.7 and av BS at home 122
Colon cancer dx in 2009 and ongoing chemotherapy
Anemia from chemo
HTN on meds 124/82
HL on meds with good control

Case 3: Ocular history

OAG with AR dx and tx OD since 2010 determined to be stable OD since 2010 determined to be stable at last visit 5 mos age

Severe NPDR OU a DME 1 year prior age and also at last exam 5 mos earlier

Case 3

CK is a 55 yo WM presenting with a complaint of sudden change in vision OS since the previous day.

He states he has been treated for DM x 5 years and has been eating desserts frequently for the past few months and wants to know if it caused him to lose vision
**Case 2: Clinical findings**

- BVA 20/20 OD/OS
- P3/4RRL (-) APD
- SLE: pinguecula
- no NVI
- TA 11 OD
- 14 OS
- 3 clock hours of AR OD

- .65/.7 vessel barring
- 12 and 6
- .45/.5 respects ISNT

- ASII
- No DME
- VH OS>OD

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**Do I expect severe NPDR OU to progress bilaterally to PDR with VH in 4 mos?**

- A1c of 6.7%

**Anything in the medical history to explain the rapid progression of retinopathy?**

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**Do you expect diabetics to progress from Severe NPDR to bilateral PDR in 5 mos??**

**Charts:**

- DCCT
- ETDRS
- UKPDS
Ocular ischemia

Conceptual problems:
1) Impaired perfusion due to vessel wall disease (ie: RVO/RAO/carotid disease)
2) Impaired perfusion due to blood constituents
   - decreased flow rate (ie: hyperviscosity)
   - decreased oxygen carrying capability (ie: anemia)

Case 2: Lab findings in past year

DM:
- HbA1c 7.3 9 mos ago to 6.7
- average BS at home 132 with FS of 122 this morning

Anemia:
- RBC 3.25-3.51 (3.7-4.3)
- HGB 10.6-12.0 (12.2-16.3)
- HCT 31.3-33.5 (35.5-52)

HTN: 124/82 no recent med changes

Hematocrit and Hemoglobin

Hematocrit: the ratio of the volume of red blood cells to the total volume of blood as determined by separation of red blood cells from the plasma usually by centrifugation. (M: 42-54% F: 38-46%)

*** patients HCT is 31-33 over past year

Hemoglobin: oxygen carrying component in red blood cells

*** patients' HGB 10.6-12.0 (12.2-16.3)

Anemic retinopathy

Mixed level hemorrhaging with or w/o retinal

Can mimic DM or HT retinopathy

Erythropoetin and RBC formation

Up to 25% of DM patients have anemia

Diabetes and anemia

Mikajiri and Nishikawa* reported 2 cases of diabetic retinopathy in patients with combined diabetes and anemia. Both cases had reversible "diabetic retinopathy" following treatment of their anemia.

Diabetes and anemia

In 1985, Shorb reported 3 cases of rapid progression to PDR with the onset of severe anemia. Berman and Friedman reported 3 cases of resolution of diabetic retinal exudation with treatment of anemia.

ETDRS and anemia as risk factor

- Identified 4 additional risk factors for retinopathy: history of diabetic neuropathy, decreased hematocrit, increased triglyceride, and decreased albumin.
- Progressive increase in risk (2x) for high-risk PDR adds substantially to the evidence supporting the importance of anemia as a risk factor for diabetic retinopathy.

Aspects of anemia

Causes:
- 1/3 due to malnutrition/malabsorption
- 1/3 due to chronic disease/kidney disease (arthritis/diabetes, etc.)
- 1/3 due to various other conditions

- Can be seen in as high as 51% M and 41% of apparent healthy adults in the US

World Health Organization’s (WHO) Hemoglobin thresholds used to define anemia

<table>
<thead>
<tr>
<th>Age or gender group</th>
<th>HGB threshold (g/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children (0.5–5.0 yrs)</td>
<td>11.0</td>
</tr>
<tr>
<td>Children (5–12 yrs)</td>
<td>11.5</td>
</tr>
<tr>
<td>Teens (12–15 yrs)</td>
<td>12.0</td>
</tr>
<tr>
<td>Women, non-pregnant (&gt;15yrs)</td>
<td>12.0 (&lt;11 severe)</td>
</tr>
<tr>
<td>Women, pregnant</td>
<td>11.0</td>
</tr>
<tr>
<td>Men (&gt;15yrs)</td>
<td>13.0 (&lt;10 severe)</td>
</tr>
</tbody>
</table>

Patient HGB 10.6–12.0 (12.3–16.3)

Anemia and other disease

Not certain if anemia is a direct or indirect cause for morbidity and functional loss.

Increased risk for “all causes” of death with HGB level < 12.

Relative risk of death is 1.6 for men and 2.3 for women.

ETDRS and anemia as risk factor

- Identified 4 additional risk factors for retinopathy: history of diabetic neuropathy, decreased hematocrit, increased triglyceride, and decreased albumin.
- Progressive increase in risk (2x) for high-risk PDR adds substantially to the evidence supporting the importance of anemia as a risk factor for diabetic retinopathy.
Patient CK: DR and anemia

Patient referred for urgent PRP OS and OD.

Carotid evaluation

Chemotherapy not stopped but transfusion/EPO considered

Question 2: Does eating dessert cause vision loss in diabetics?

Thank You!