Autoimmune Disease and the Eye
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Disclosure
I have no financial disclosures

Goals
Manifestations
Diagnosis/Treatment
Referral

Autoimmune Disease
Ankylosing Spondylitis    Myasthenia Gravis
Chon’s Disease            Psoriasis
Giant Cell Arteritis      Rheumatoid Arthritis
Graves’ Disease           Sarcoidosis
Lupus Erythematosus       Sjögren’s Syndrome
Multiple Sclerosis        Ulcerative Colitis

External
Ptosis
Exophthalmos
Diplopia

Anatomy of the Eye

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Ptosis

Myasthenia Gravis

Any patient with Diplopia or Ptosis

Myasthenia Gravis

Greek and Latin meaning
“grave muscle weakness”

Myasthenia Gravis

Chronic autoimmune neuromuscular disease
Muscle weakness and fatigue
Eyelid muscles first affected in most cases

Myasthenia Gravis

15% have Ocular only
80% have some ocular manifestation

Myasthenia Gravis

Can involve breathing and swallowing
Myasthenic Crisis

Myasthenia Gravis

Antibodies destroy or alter receptors for acetylcholine
Myasthenia Gravis

In office testing
- Ice-pack test
- Upgaze test
- Cogan lid twitch
- Orbicularis resistance

Other testing
- Tensilon
- Acetylcholine receptor antibodies
- Anti-MuSK antibody (muscle specific kinase)

Treatment
- Cholinesterase inhibition (pyridostigmine)
- Corticosteroid
- Immunosuppressants
- Plasmapheresis
- Intravenous IVlg

Surgery
- 15% of MG patients have tumor of Thymus
- Often require Thymectomy
Myasthenia Gravis

RH - 55 yo WM
Healthy eyes
New CN IV Palsy
+DM, +HTN
NO neuro symptoms

Myasthenia Gravis

Resolved 6 weeks later

Myasthenia Gravis

4 months later
Ptosis
Ice pack
Pre 2mm
Post 9 mm

Myasthenia Gravis

Upgaze fatigue
+ Cogan lid twitch
AchR Antibodies very elevated

Myasthenia Gravis

RH has difficulty with meds
Variable diplopia!!
Remains ocular only

Exophthalmos

Graves’ Disease
Graves’ Disease

Autoimmune Disease
Skin
Thyroid
Orbit
Mental Health

Patient DS

20/25 OD and OS
IOP 18/18
No APD
Diplopia in lateral and downgaze
Pain in lateral gaze

Exam

Exophthalmos OS
Hertel 19/23
Lagophthalmos
Conjunctival edema and injection
Eyelid edema

Labs

TSH = 0.003 (normal = 0.47-5.00)
T4 = 20.3 (normal = 4.5-12)
Referral

Endocrine
Oculoplastics
Inform PCP of findings

5 months later

IOP 18/24
? APD OS
Start IOP Timolol 0.5%
Start Oral Pred (40 mg)

6 months later

IOP as high as 38/28
Oral Pred now 80 mg
+ APD OS
IOP 19/19 on Travatan, Cosopt, Alphagan
Refer for Orbital Decompression

After Orbital Decompression

Develops Diplopia
But...IOP 12/14 on meds

Now S/P:
Orbital Decompression
Strabismus Surgery
Eyelid Retraction
Now has 20/80 cataract
Last Month

20/20
Single vision
Normal IOP

Graves’ Disease

80% are Hyperthyroid
Sweat, tremor, weight loss
10% are Hypothyroid
Cold, weight gain, hair loss
10% are Euthyroid

Graves’ Disease

30-50% of Graves’ patients have orbitopathy

2-5% serious complications

Graves’ Disease

Increased antithyroid antigens
TSH receptor antibodies
Increased T3, T4
Decreased TSH

Graves’ Disease

Dry eye
Injection
Eyelid retraction
Diplopia
Compressive Optic Neuropathy
Graves' Disease

Increase in
- Fibroblasts
- Hyaluronic Acid
- Collagen
- Adipose

Graves' Disease

Exophthalmos

Hertel
- Asian upper limit = 18
- White upper limit = 21
- Black upper limit = 24

Graves' Disease

Free T3 and T4
- TSH
- Anti-thyroglobulin (TSI)
- Thyrotopin-Binding Inhibitory Immunoglobulin (TBII)
- Thyroid Peroxidase (TPO)
- Refer to Endocrine

Graves' Disease

CT allows measurement of
- Orbital fat
- Lacrimal gland
- Extraocular muscles

MRI for serial imaging

Graves' Disease

Treatment
- Quiet inflammation - Steroid
- Stabilize Thyroid
- Medication
- Surgery
- Radioiodine

Graves' Disease

Treatment
- Ocular Comfort
- Prism
- Surgery
Graves’ Disease

Surgery
Orbital Decompression
Strabismus
Eyelid
Cataract

Graves’ Disease

Affects up to 1/3 of Graves’ patients
Attention
Mood
Anxiety

Graves’ Disease

Smoking makes disease worse
Smoking makes treatment less effective

Diplopia

Graves’ Disease (common)
Myasthenia Gravis (common)
Multiple Sclerosis (common)
Giant Cell Arteritis (uncommon)

Multiple Sclerosis

Is MS an autoimmune disease?

Multiple Sclerosis

Demyelinating disease
Can cause diplopia
Transient
Multiple Sclerosis

Consider testing if:
- Young patient
- Other neurologic symptoms
  - Lhermitte symptom
  - Uhthoff phenomenon
- Optic Neuropathy

Episcleritis

Not as likely to be autoimmune
Consider testing if:
- Recurrent
- Nodular

Scleritis

Rheumatoid Arthritis*
Lupus
Ulcerative Colitis
Ankylosing Spondylitis
Reactive Arthritis
Psoriatic Arthritis

Episcleritis vs Scleritis

<table>
<thead>
<tr>
<th></th>
<th>Episcleritis</th>
<th>Scleritis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vision</td>
<td>Normal</td>
<td>May reduce</td>
</tr>
<tr>
<td>Hyperemia</td>
<td>Focal</td>
<td>Focal</td>
</tr>
<tr>
<td>Focal/Diffuse</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>Mild/Mod</td>
<td>Mod/Severe</td>
</tr>
</tbody>
</table>

Scleritis

http://www.aao.org/theeyeshaveit/red-eye/scleritis.cfm

Rheumatoid Arthritis

Inflammatory damage to small joints
- Mostly hands and feet
- Pain, swelling, and possible deformity
- Can cause pain in larger joints
  - Hip, shoulder, knees, ankles, and elbows
Rheumatoid Arthritis

Diagnosed with a combination
Blood work
X-ray
Clinical signs/symptoms

Rheumatoid Arthritis

Treated with NSAIDs for mild cases
Steroids
DMARDs (i.e. Methotrexate)
Immune modulating drugs (i.e. Enbrel)

Rheumatoid Arthritis

Most likely systemic cause of scleritis is RA
Only 50% of patients with scleritis have associated condition
Patients with RA and scleritis have
Widespread and aggressive systemic disease
May need more aggressive therapy

Lupus

Autoimmune disease that affects
Joints, skin, kidneys, blood cells, brain, heart and lungs
Symptoms include
Fatigue, shortness of breath, chest pain

Lupus

Classic "butterfly" rash on cheeks and nose
Lupus

Most commonly seen in women of childbearing age

Difficult to diagnose

Lupus

NSAID
Corticosteroid
Plaquenil
Immune suppression

Cornea/Dry Eye

Graves’ Disease
Sjögren’s Syndrome
Lupus
Rheumatoid Arthritis

Sjögren’s Syndrome

Autoimmune disease that mainly causes: dry eye and dry mouth

Can also have joint pain, fatigue, persistent cough

Typically in women over 40

Sjögren’s Syndrome

Can have association with RA or Lupus

Diagnosis is made by signs/symptoms, blood test

Lip biopsy?

Sjögren’s Syndrome

Treat specific symptoms

Dryness
Dry eye

Treat salivation (pilocarpine), may also use Plaquenil
Uveitis

Possible association with autoimmune disease
Less than 50% have known cause

Tailored approach
Examine/Classify
Working List
Case History

Uveitis

Ankylosing Spondylitis
Inflammatory Bowel
Reactive Arthritis
Psoriasis
Sarcoidosis
JIA

Uveitis

Examine/Classify
Anterior/Posterior/Pan
Granulomatous/Non
Acute/Chronic
Unilateral/Bilateral

Uveitis

Scatter approach
Tailored approach

Case History
Ask specific questions
Decide if special testing needed
Uveitis

Acute Anterior Unilateral Nongranulomatous
Ankylosing Spondylitis
Inflammatory Bowel
Psoriasis
Reactive Arthritis

Ankylosing Spondylitis
Lower Back Pain
Worse with Rest
Wake up with pain
Better with NSAIDS

Inflammatory Bowel
GI symptoms
Cramps, diarrhea, bloody stools
Diet modification, Immune modulation, Surgery
Refer to GI

Psoriasis
Skin plaques - joints, scalp
Arthritis ~ 5%
Steroid creams, Immune modulation
Refer to Dermatology

Psoriasis

Reactive Arthritis
Acute Arthritis
Typically knee, ankle, foot
Skin lesions, urethritis, diarrhea
Pain modification
Refer to Rheumatology
Uveitis

Chronic Anterior Bilateral Granulomatous Sarcoidosis

90% have lung involvement
Skin involvement common
Order chest x-ray
ACE is non-specific

Uveitis

Asymptomatic Anterior Unilateral Nongranulomatous Juvenile Idiopathic Arthritis

Joint pain/stiffness/swelling
Unilateral cataract
Pediatrician/Rheumatology referral

Retina

Plaquenil

Ganglion, Photoreceptor, RPE
Atrophy
Scotoma
Irreversible Damage
Plaquenil

HCQ
1000 g
400 mg/day
>7 years

Plaquenil

Quantify risk
1-7 years
1/1000
>7 years
1/100

Plaquenil

Find HCQ toxicity before visible on fundus evaluation
Prevent irreversible vision loss

Plaquenil

Testing
mfERG
FAF
VF
OCT

Plaquenil

VF
24-2, 30-2 not sufficient
10-2 white on white (or red)
False Positives

What is Sensitivity/Specificity?
Consider risk of developing toxicity

Plaquenil

Risk before 7 years = 1/1000
Risk after 7 years = 1/100
If Specificity = 90%

10-100 times more FALSE positives than TRUE

Plaquenil

Pro:
- Available
- Inexpensive
- Interpretation

Con:
- Subjective
- Patients dislike
- False Positives

Plaquenil

Flying Saucer
OCT

Pro:
Available
Objective
Interpretation

Con:
Early detection
Cost

Plaquenil

2002 Recommendations

High risk if > 6.5 mg/kg/day
Color vision
10-2 or Amsler

Plaquenil

2011 Recommendations

High risk if 1000g cumulative dose
NO Color vision or Amsler Grid
10-2 combined with
OCT, FAF, mfERG

Plaquenil

(+) HVF, (+) SD-OCT
(+) HVF, (-) SD-OCT
(-) HVF, (+) SD-OCT
(-) HVF, (-) SD-OCT
**Plaquenil**

**Frustrations**
- False positives
- No gold standard
- We are the authority
- Benefits of Plaquenil

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**Case**

**86 Year Old White Male**
Blur at distance
Ocular History: Early AMD

**Medical History**
Psoriatic Arthritis
HTN

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**Case**

**Medications**
- Plaquenil
- Fluocinonide
- Coreg
- ASA 325 mg

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**Case**

Patient at VA since 1999
Every exam: RPE changes OS>OD
Called AMD
20/20- OD and OS

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**Case**

September 2010
Ring shaped atrophy OS
Fundus Photos/OCT

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**Fundus OS**
Case 2

71 Year Old White Male
Evaluation for Plaquenil Maculopathy
No vision complaints
Case 2

On Plaquenil for 7 years
200 mg BID
RA/Lupus
Normal kidney, liver
Normal BMI

BCVA 20/20 OD/OS
Anterior Segment Unremarkable
Posterior Segment - Mild ERM OD
Case 2

Normal macula
Normal OCT

?HVF

Case 2

Plan
Continue medication
RTC 6 months - retest

Vascular

Arterial Disease
Vasculitis
Arterial Disease

CRAO
Giant Cell Arteritis
5-15%

Vasculitis

Wegener’s
Polyarteritis Nodosa
Giant Cell Arteritis

Optic Nerve

Optic Nerve Edema
Optic Atrophy

Giant Cell Arteritis

Profound Vision Loss
Bilateral in 14 days in 1/3 if Untreated
Systemic Complications
Treatable

Optic Nerve

Giant Cell Arteritis
Graves’ Disease
Lupus
Multiple Sclerosis
Sarcoidosis
Systemic Symptoms

Jaw Claudication (Odds Ratio 9.0)
Neck Pain (Odds Ratio 3.4)
Anorexia (Odds Ratio 2)


Less Predictable

Headache
Fever
Scalp Tenderness
Malaise


Headache

A-AION - 46% had Headache
NA-AION – 54% had Headache
Could Mislead


Testing

Labs – ESR, CRP, CBC, Platelets
Fluorescein Angiography
Ultrasound, PET, MRI – Limited Benefit
Temporal Artery Biopsy

Labs

ESR
> 33 mm/h
Sensitivity 90%
Specificity 90%
CRP
> 2.45 mg/dl
Sensitivity 100%
Specificity 82%
CBC
ESR + CRP

Sensitivity 100%
Specificity 97%


Platelets

Odds Ratio:
ESR > 47 mm/hr = 1.5
CRP > 2.45 mg/dL = 5.3
Platelets > 400,000/μL = 4.2
All 3 elevated = 8


Additional Testing

Temporal Artery Biopsy
Gold Standard
Case by Case
Side Effects
Necrosis, Infection, Nerve Damage
Bilateral?

MR. A

63 y/o White Male
New onset headache, temporal pain, neck pain
NO vision complaints
EOM full
NO APD
MR. A

Labs
ESR = 56
CRP = 1.37
Pending Temporal Artery Biopsy

MR. A

 Started on 40 mg Pred
When he tapers, headaches return
What about vision?
20/70 and VF reduction

MR. A

When Pred resumed, vision returned to 20/25
Visual Field improved
Goals

Manifestations
Diagnosis/Treatment
Referral

Thank you

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