

1

Autoimmune Disease and the Eye

Anthony DeWilde, OD FFAO

2

Disclosure

Financial disclosures: No financial disclosures

3

Goals

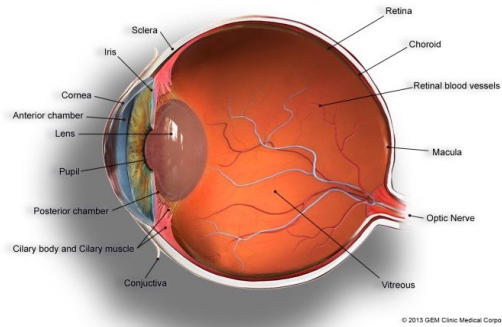
Manifestations
Diagnosis/ Treatment
Referral

Autoimmune Disease

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

4

Anatomy of the Eye



5

External

Ptosis
Exophthalmos
Diplopia

6

Ptosis

Myasthenia Gravis

Any patient with Diplopia or Ptosis

Especially women under 40, men over 60

7

Myasthenia Gravis

Greek and Latin meaning

“grave muscle weakness”

8

Myasthenia Gravis

Chronic autoimmune neuromuscular disease

Muscle weakness and fatigue

Eyelid muscles first affected in most cases

9

Myasthenia Gravis

15% have Ocular only

80% have some ocular manifestation

10

Myasthenia Gravis

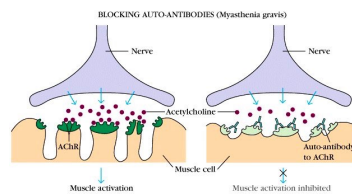
Can involve breathing and swallowing

Myasthenic Crisis

11

Myasthenia Gravis

Antibodies destroy or alter receptors for acetylcholine



12

Myasthenia Gravis

In office testing

Ice-pack test

Utgaze test

Cogan lid twitch

Orbicularis resistance

13

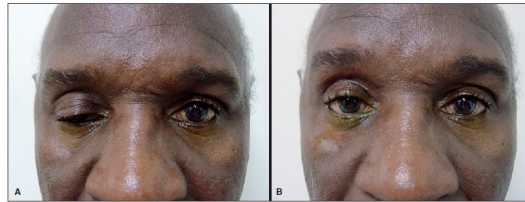


Figura 1 - Aspecto clínico da ptose palpebral miastênica. A) Pré-teste do gelo; B) Pós-teste.

Arq. Bras. Oftalmol. vol.73 no.2 São Paulo Mar. / Apr. 2010

14

Myasthenia Gravis

Other testing

Tensilon

Acetylcholine receptor antibodies

Anti-MuSK antibody (muscle specific kinase)

EMG

15

Myasthenia Gravis

Treatment

Cholinesterase inhibition (pyridostigmine)

Corticosteroid

Immunosuppressants

Plasmapheresis

Intravenous IVIg

16

Myasthenia Gravis

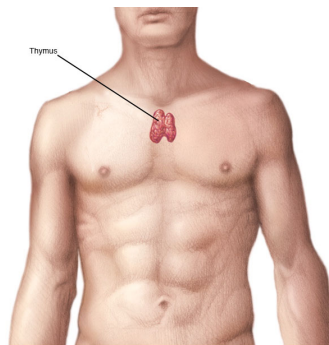
Surgery

15% of MG patients have tumor of Thymus

Every patient needs Chest X-Ray or CT

Often require Thymectomy

17



<https://goo.gl/images/SZbv3L>

18

Myasthenia Gravis

19

Refer to Neurology

Test Thymus

Test for generalized Myasthenia Gravis

Myasthenia Gravis

20

RH - 55 yo WM

Healthy eyes

New CN IV Palsy

+DM, +HTN

NO neuro symptoms

Myasthenia Gravis

21

Resolved 6 weeks later

Myasthenia Gravis

4 months later

Ptosis

Ice pack

Pre 2 mm

Post 9 mm

22

Myasthenia Gravis

Upraze fatigue

+ Cogan lid twitch

AchR Antibodies very elevated

23

Myasthenia Gravis

RH has difficulty with meds

Variable diplopia!!

What's best Tx for this?

Remains ocular only

24

Myasthenia Gravis

TH is 65 y/o black male

Complains of diplopia 10/2015

Dx: Medial Rectus Palsy with ptosis

25

Myasthenia Gravis

TH has DM, HTN

No other neuro complaints

Pupils normal

What tests do you order?

26

Myasthenia Gravis

Resident said RTC 6 weeks

27

Myasthenia Gravis

TH complains of diplopia 12/2015

No improvement

What tests?

28

Myasthenia Gravis

Ice pack 3mm -> 5mm

Cover test showed greater exo and hypo

Ptosis!

Ordered labs

29

Myasthenia Gravis

ACHr mod AB – 83 (normal 0-32)

ACH Binding AB – 7.1 (normal 0-0.3)

ACH receptor blocking AB – 46 (normal 0-15)

Chest x-ray and Chest CT normal

EMG performed looking for Generalized MG

30

Myasthenia Gravis

31

Under care of Neuro

Pyridostigmine

Eye patch

Exophthalmos

32

Graves' Disease

Graves' Disease

33

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

34



35

Exam

Exophthalmos OS

Hertel 19/23

Lagophthalmos

Conjunctival edema and injection

Eyelid edema

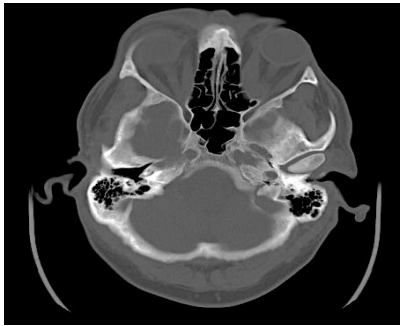
36

Labs

TSH = 0.003 (normal = 0.47-5.00)

T4 = 20.3 (normal = 4.5-12)

37



38



39

Referral

Endocrine

Oculoplastics

Inform PCP of findings

40

5 months later

IOP 18/24

? APD OS

Start IOP Timolol 0.5%

Start Oral Pred (40 mg)

41

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

42

After Orbital Decompression

43

Develops Diplopia

But...IOP 12/14 on meds

Now S/P:

Orbital Decompression

Strabismus Surgery

Eyelid Retraction

Now has 20/80 cataract

44

Last Month

45

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

46

Graves' Disease

30-50% of Graves' patients have orbitopathy

2-5% serious complications

47

Graves' Disease

Dry eye

Injection

Eyelid retraction

Diplopia

Compressive Optic Neuropathy

48

Graves' Disease

Increased antithyroid antigens

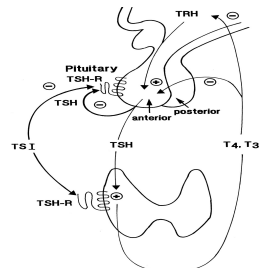
TSH receptor antibodies

Increased T3, T4

Decreased TSH

49

Graves' Disease



50

Graves' Disease

Increase in

Fibroblasts

Hyaluronic Acid

Collagen

Adipose

51

Graves' Disease

Exophthalmos

Hertel

Asian upper limit = 18

White upper limit = 21

Black upper limit = 24

52

Graves' Disease

Free T3 and T4

TSH

Anti-thyroglobulin (TGI)

Thyrotropin-Binding Inhibitory Immunoglobulin (TBII)

Thyroid Peroxidase (TPO)

Refer to Endocrine

53

Graves' Disease

CT allows measurement of

Orbital fat

Lacrimal gland

Extraocular muscles

MRI for serial imaging

54

Graves' Disease

Treatment

Quiet inflammation - Steroid

Stabilize Thyroid

Medication

Surgery

Radioiodine

55

Graves' Disease

Treatment

Ocular Comfort

Prism

Surgery

56

Graves' Disease

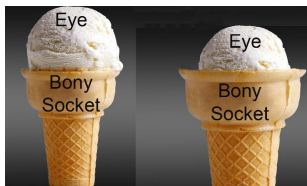
Surgery

Orbital Decompression (plus radiation)

Strabismus

Eyelid

Cataract



<http://thyroideyes.org/resources/Thyroid>

57

Graves' Disease

Affects up to 1/3 of Graves' patients

Attention

Mood

Anxiety

58

Graves' Disease

Smoking makes disease worse

Smoking makes treatment less effective



59

Diplopia

Graves' Disease (common)

Myasthenia Gravis (common)

Multiple Sclerosis (common)

Giant Cell Arteritis (uncommon)

60

Multiple Sclerosis

61

Is MS an autoimmune disease?

Multiple Sclerosis

62

Demyelinating disease

Can cause diplopia

Transient

Multiple Sclerosis

63

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

64

Scleritis

Rheumatoid Arthritis*

Lupus

Ulcerative Colitis

Ankylosing Spondylitis

Reactive Arthritis

Psoriatic Arthritis

65

Scleritis



<http://www.aaopt.org/theeyehaveit/red-eye/scleritis.cfm>

66

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

67

Rheumatoid Arthritis



68

Rheumatoid Arthritis

Diagnosed with a combination

Blood work

X-ray

Clinical signs/symptoms

69

Rheumatoid Arthritis

Treated with NSAIDs for mild cases

Steroids

DMARDs (i.e. Methotrexate)

Immune modulating drugs (i.e. Enbrel)

70

Rheumatoid Arthritis

Most likely systemic cause of scleritis is RA

Only 50% of patients with scleritis have associated condition

71

Rheumatoid Arthritis

Patients with RA and scleritis have

Widespread and aggressive systemic disease

May need more aggressive therapy

72

Lupus

Autoimmune disease that affects

Joints, skin, kidneys, blood cells, brain, heart and lungs

Symptoms include

Fatigue, shortness of breath, chest pain

73

Lupus

Classic "butterfly" rash on cheeks and nose



74

Lupus

Most commonly seen in women of childbearing age

Difficult to diagnose

75

Lupus

NSAID

Corticosteroid

Plaquenil

Immune suppression

76

Cornea/Dry Eye

Graves' Disease

Sjögren's Syndrome

Lupus

Rheumatoid Arthritis



Image: Will's Eye

77

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

78

Sjögren's Syndrome

Can have association with RA or Lupus

Diagnosis is made by signs/symptoms, blood test

Lip biopsy?

79

Sjögren's Syndrome

Treat specific symptoms

Dryness

Dry eye

Treat salivation (pilocarpine), may also use Plaquenil

80

Uveitis

Possible association with autoimmune disease

Less than 50% have known cause

81

Uveitis

Scatter approach



82

Uveitis

Tailored approach



83

Uveitis

Tailored approach

Examine/Classify

Working List

Case History

84

Uveitis

Examine/Classify

Anterior/Posterior/Pan

Granulomatous/Non

Acute/Chronic

Unilateral/Bilateral

85

Uveitis

Ankylosing Spondylitis

Inflammatory Bowel

Reactive Arthritis

Psoriasis

Sarcoidosis

JIA

86

Uveitis

Case History

Ask specific questions

Decide if special testing needed

87

Uveitis

Acute Anterior Unilateral Nongranulomatous

Ankylosing Spondylitis

Inflammatory Bowel

Psoriasis

Reactive Arthritis

88

Uveitis

Ankylosing Spondylitis

Lower Back Pain

Worse with Rest

Wake up with pain

Better with NSAIDS



89

Uveitis

Ankylosing Spondylitis

Lower back X-Ray

Refer to Rheumatology

90

Uveitis

Inflammatory Bowel

GI symptoms

Cramps, diarrhea, bloody stools

Diet modification, Immune modulation, Surgery

Refer to GI

91

Uveitis

Psoriasis

Skin plaques - joints, scalp

Arthritis ~ 5%

Steroid creams, Immune modulation

Refer to Dermatology

92

Psoriasis



93

Uveitis

Reactive Arthritis

Acute Arthritis

Typically knee, ankle, foot

Skin lesions, urethritis, diarrhea

Pain modification

94

Uveitis

Reactive Arthritis

No test for this

Refer to Rheumatology

95

Uveitis

Chronic Anterior Bilateral Granulomatous

Sarcoidosis

96

Uveitis

Sarcoidosis

Multisystemic, Granulomatous Disease

90% have lung involvement

Skin involvement common

Order chest x-ray

ACE is non-specific

97

Uveitis

Sarcoidosis

Order chest x-ray

ACE is non-specific

IL2R lab test - very specific

May need Pulmonary consult

98

Uveitis

Asymptomatic Anterior Unilateral Nongranulomatous

Juvenile Idiopathic Arthritis

99

Uveitis

Juvenile Idiopathic Arthritis

Joint pain/stiffness/swelling

Unilateral cataract

Pediatrician/Rheumatology referral

100

Retina

Plaquenil

101

Plaquenil

Ganglion, Photoreceptor, RPE

Atrophy

Scotoma

Irreversible Damage

102

Plaquenil

HCQ

1000 g

400 mg/day

>7 years

103

Plaquenil

Quantify risk

1-7 years

1/1000

>7 years

1/100

104

Plaquenil

Quantify risk

Under 5 years = 1%

10 years = 2%

20 years = 4%

105

Plaquenil

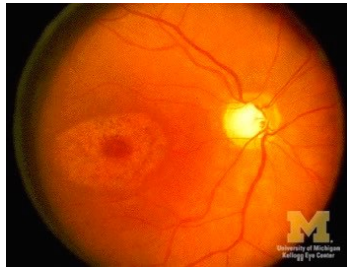
Find HCQ toxicity before visible on fundus evaluation

Prevent irreversible vision loss

Modify risk if possible*

106

Plaquenil



107

Plaquenil

2002 Recommendations

High risk if > 6.5 mg/kg/day

Color vision

10-2 or Amsler

108

Plaquenil

2011 Recommendations

High risk if 1000g cumulative dose

NO Color vision or Amsler Grid

10-2 combined with

OCT, FAF, mfERG

109

Plaquenil

2016 Recommendations

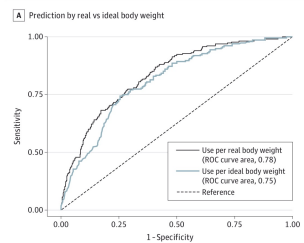
High risk if >5 mg/kg/day REAL weight

or 6.5 mg/kg/day IDEAL weight

110

Plaquenil

Figure 2. Hydroxychloroquine Retinal Toxicity and Daily Use by Real Body Weight vs Ideal Body Weight



111

Plaquenil

2016 Recommendations

Continues testing recommendations from 2011

112

Plaquenil

Low risk drug if correct dosage

If proper dosage, should never see "bull's eye maculopathy"

113

Plaquenil

Consider modifying risk by modifying dosage

Only come in 200 mg tablets

Patient may want to take fewer than 14 tablets/week

114

Plaquenil

Study of 500 patients started on Plaquenil
50% were on too high dose for ocular safety

Ophthalmology 2017;124:604- 608

115

Plaquenil

Height to take med safely based on IDEAL weight
Men - 5'5"
Women - 5'7"

116

Plaquenil

For every 2" below ideal, subtract 1 tablet per week

117

Plaquenil

Safe weight for 400 mg/day - based on REAL weight

180 lbs

For every 13 lbs less than this subtract 1 tablet/week

118

Plaquenil

Testing

mfERG

FAF

VF

OCT

119

Plaquenil

VF

24-2, 30-2 not sufficient (but consider if Asian)

10-2 white on white (or red)

120

Plaquenil

Risk before 7 years = 1/1000

Risk after 7 years = 1/100

If Specificity = 90%

10-100 times more FALSE positives than TRUE

124

HVF

Pro:

Available

Inexpensive

Interpretation

125

HVF

Con:

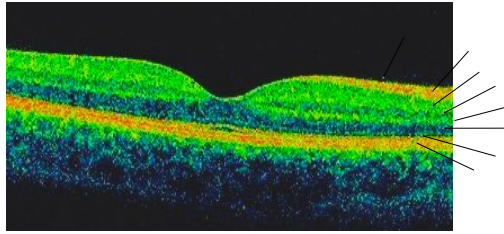
Subjective

Patients dislike

False Positives

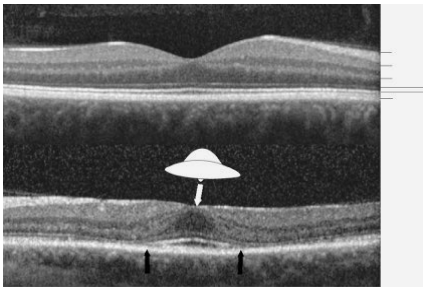
126

Plaquenil

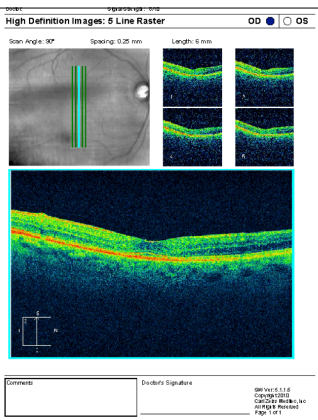


127

Flying Saucer



128



129

OCT

Pro:

Available

Objective

Interpretation

130

OCT

Con:

Early detection

Cost

131

Plaquenil

(+) HVE, (+) SD-OCT

(+) HVE, (-) SD-OCT

(-) HVE, (+) SD-OCT

(-) HVE, (-) SD-OCT

132

Plaquenil

Frustrations

False positives

No gold standard

We are the authority

Benefits of Plaquenil

133

Case 1

60 Year Old White Female

Blur at distance

Photophobia

Dry eye

134

Case 1

Plaquenil x 20 years

400 mg/day

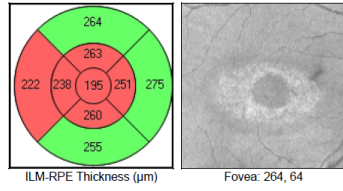
Lupus

5'4"

105 lbs - safe dosage is 200 mg

135

Case 1 - OD OCT

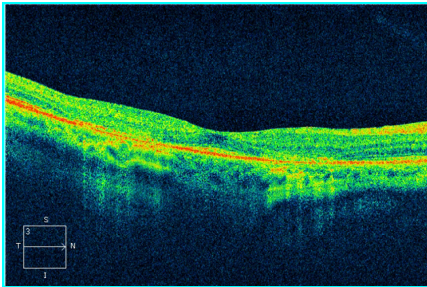


ILM-RPE Thickness (μm)

Fovea: 264, 64

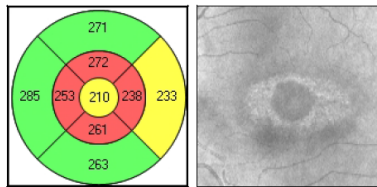
136

Case 1 - OD OCT



137

Case 1 - OS OCT

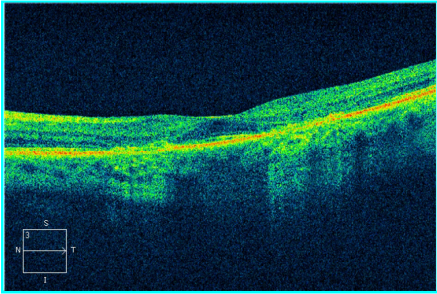


ILM-RPE Thickness (μm)

Fovea: 260, 66

138

Case 1 - OS OCT



139

Case 1

- Plaquenil toxicity
- Should have been on lower dose
- Need to discontinue medicine

140

Case 2

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

141

Case 2

Medical History

Psoriatic Arthritis

HTN

CAD

Hyperlipidemia

142

Case 2

Medications

Plaquenil

Fluocinonide

Coreg

ASA 325 mg

143

Case 2

5'7" tall

130 lbs - would need 10 tablets/week

144

Case 2

Patient at VA since 1999

Every exam: RPE changes OS>OD

Called AMD

20/20- OD and OS

145

Case 2

September 2010

Ring shaped atrophy OS

Fundus Photos/OCT

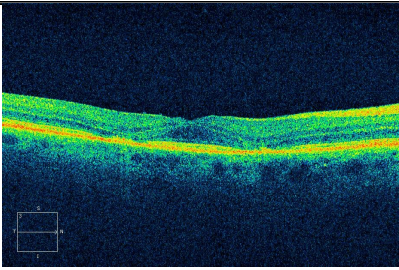
146

Fundus OS



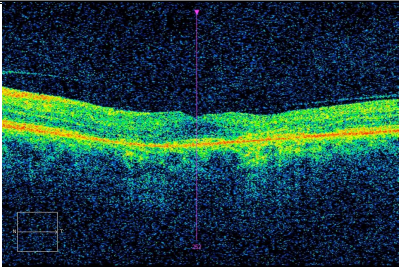
147

SD-OCT - OS



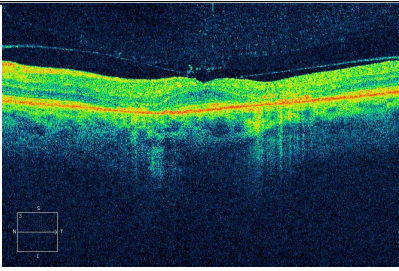
148

SD-OCT - OS



149

SD-OCT - OD



150

Management

Discontinue Plaquenil

See Rheumatologist -- Patient refused initially

151

Management

Patient eventually discontinued meds

Asymptomatic

Good outcome?

152

Case 3

71 Year Old White Male

Evaluation for Plaquenil Maculopathy

No vision complaints

153

Case 3

On Plaquenil for 7 years

200 mg BID

RA/Lupus

Normal kidney, liver

Normal BMI

154

Case 3

5'11" tall

155 lbs - should be on 12 tablets/week

155

Case 3

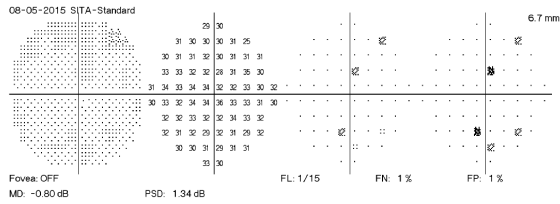
BCVA 20/20 OD/OS

Anterior Segment Unremarkable

Posterior Segment - Mild ERM OD

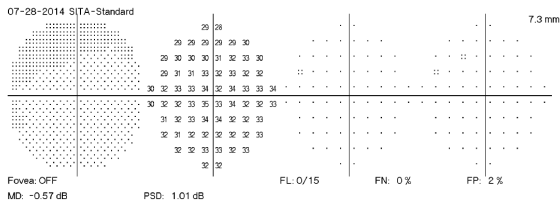
156

HVF- OD



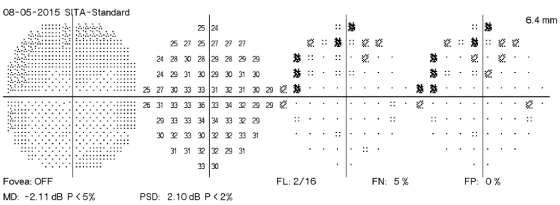
160

HVF- OS



161

HVF- OS



162

Case 3

Normal macula

Normal OCT

?HVF

163

Case 3

Do we continue medication?

Do we discontinue medication?

164

Case 3

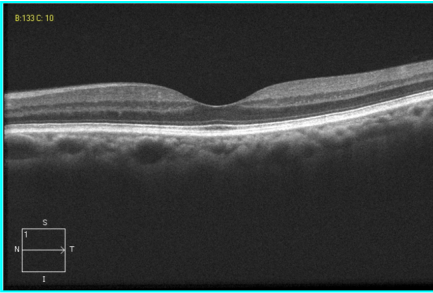
Plan

Continue medication

RTC 6 months - retest

165

Case 4 - OCT OS



172

Case 4

Informed Rheumatologist
They discontinued Plaquenil
Was this the right call?
Could we have done better?

173

Vascular

Arterial Disease
Vasculitis

174

Arterial Disease

CRAO

Giant Cell Arteritis

5-15%

175

Vasculitis

Wegener's

Polyarteritis Nodosa

Giant Cell Arteritis

176

Optic Nerve

Optic Nerve Edema

Optic Atrophy

177

Optic Nerve

Giant Cell Arteritis

Graves' Disease

Lupus

Multiple Sclerosis

Sarcoidosis

178

Giant Cell Arteritis

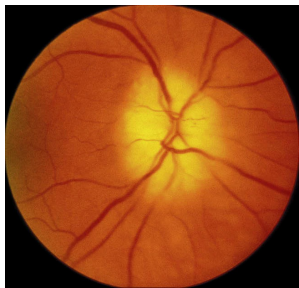
Profound Vision Loss

Bilateral in 14 days in 1/3 if Untreated

Systemic Complications

Treatable

179



180

Systemic Symptoms

Jaw Claudication (Odds Ratio 9.0)

Neck Pain (Odds Ratio 3.4)

Anorexia (Odds Ratio 2)

Hayreh SS, et al. Giant Cell Arteritis: Validity and Reliability of Various Diagnostic Criteria. Am J Ophthalmol 1997;123:285-96

181

Less Predictable

Headache

Fever

Scalp Tenderness

Malaise

Hayreh SS, et al. Giant Cell Arteritis: Validity and Reliability of Various Diagnostic Criteria. Am J Ophthalmol 1997;123:285-96

182

Headache

A-AION - 46% had Headache

NA-AION - 54% had Headache

Could Mislead

Hayreh SS, et al. Giant Cell Arteritis: Validity and Reliability of Various Diagnostic Criteria. Am J Ophthalmol 1997;123:285-96

183

Average Number of Symptoms = 3

184

Testing

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

185

Labs

ESR
> 33 mm/h
Sensitivity 92%
Specificity 92%

186

Labs

CRP

> 2.45 mg/dl

Sensitivity 100%

Specificity 82%

187

ESR + CRP

Sensitivity 100%

Specificity 97%

Hayreh SS, et al. Giant Cell Arteritis: Validity and Reliability of Various Diagnostic Criteria. Am J Ophthalmol 1997;123:285-96

188

Don't Forget CBC

Check for inflammation

Check for Anemia, Polycythemia

Platelets

189

Platelets

Odds Ratio:

ESR > 47 mm/hr = 1.5

CRP > 2.45 mg/dL = 5.3

Platelets > 400,000/ μ L = 4.2

All 3 elevated = 8

Walvick MD, Walvick MP. Giant Cell Arteritis: Laboratory Predictors of a Positive Temporal Artery Biopsy. Ophthalmology 2011;118:1201-1204

190

Additional Testing

Temporal Artery Biopsy

Gold Standard

Case by Case

Side Effects

Necrosis, Infection, Nerve Damage

Bilateral?

191

Treatment

IV/Oral corticosteroids

Methotrexate

Actemra injections



192

MR. A

193

63 y/o White Male

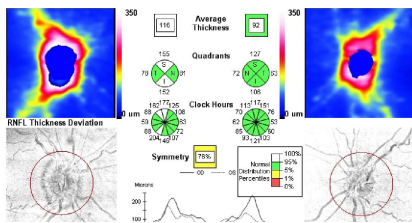
New onset headache, temporal pain, neck pain

NO vision complaints

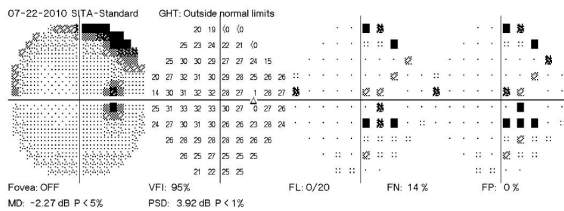
EOM full

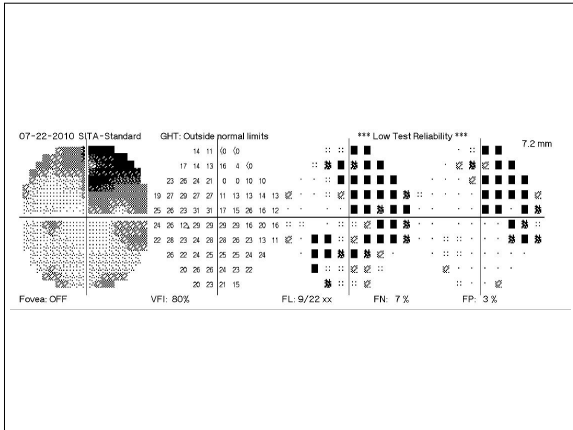
NO APD

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196

MR. A

Labs

ESR = 56

CRP = 1.37

Pending Temporal Artery Biopsy

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MR. A

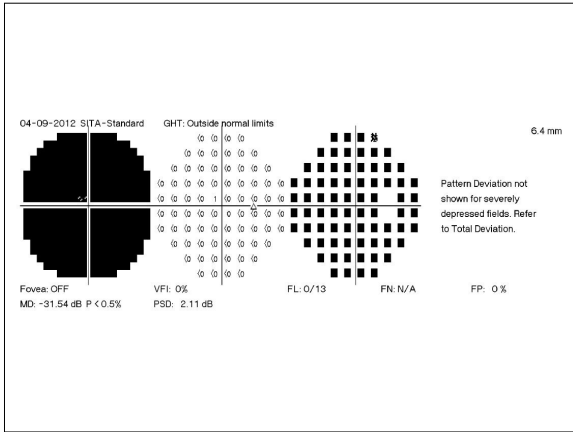
Started on 40 mg Pred

When he tapers, headaches return

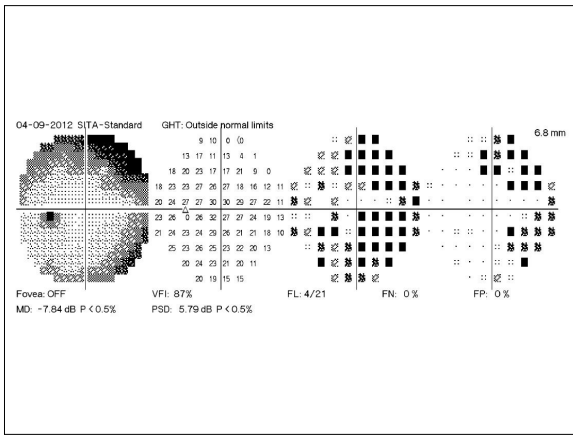
What about vision?

20/70 and VF reduction

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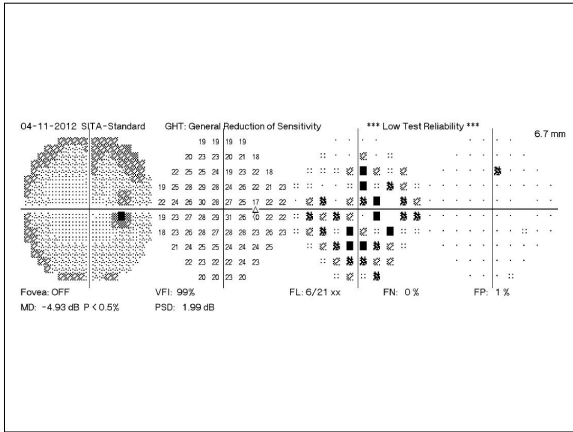
200

MR. A

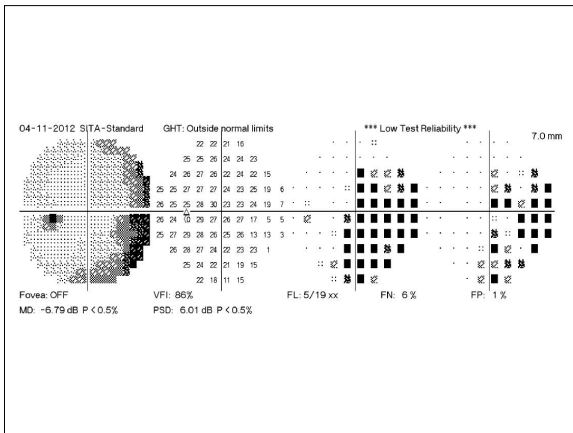
When Pred resumed, vision returned to 20/25

Visual Field improved

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Goals

Manifestations

Diagnosis/ Treatment

Referral

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Thank you
anthony.dewilde@va.gov
