Uveitis and treatments; What's new?

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Communication to GP’s & Optometrist

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Date Patient Seen: 

Patient Details: 

Following is the outcome of your patient’s visit to the Eye Clinic as a new patient:

Diagnosis:
- Presbyopic Both eyes Jul 2017
- Dry Eyes Both eyes Jul 2017
- Ultraphats both eyes Jul 2017

Vision:
RE: UA: 5/9
LE: UA: 5/9

IOP:
RE: 16 mmHg
LE: 16 mmHg

Plan:
- Treat

Treatment:
- O Hyloforte - 2% QDS 5 Weeks Both Eyes
- O FML - TDS 3 Weeks Both Eyes

Rx Advice:
- New treatment added
- Lid Hygiene, Leaflets
- Follow up - 2 months

Outcome:
- Advised regarding lid hygiene, massaging the eyelids with warm compresses and using lubricant eye drops whenever required.
- Patient needs an Optic disc scan for the optic nerves baseline as his grandmother had glaucoma. This will be done at St Helen hospital.
- He will also need a orthoptic workup which I will arrange at St Helen hospital or over here.

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Ocular Inflammatory Disease

- How does ocular inflammation or uveitis happen?
- Infection
- Trauma
- Cancer
- Autoimmunity
JIA related uveitis treated with steroids; traditional Cushingoid features
UVEITIS

• What is it?
• What is its importance?
• What is the history of its therapy?
• What does the future hold?
UVEITIS

• What is it?
Etymology

- Uvea, from uva (Latin = grape)
- itis, (Greek = inflammation)

Therefore, inflammation of the uvea

Ophthalmia and flegmoni, general terms
Anatomy

The uvea or uveal tract is the middle, highly vascular layer of the eyeball

- Iris
- Ciliary body
- Choroid
UVEITIS

• What is it?
• What is its importance?
The Problem

Uveitis is the third leading cause of preventable blindness in developed countries.
How Does Uveitis Blind?

- Glaucoma
Pthisis and Hypotony
How Does Uveitis Blind?

- Glaucoma
- Hypotony
- Maculopathy
  - CMO
How Does Uveitis Blind?

- Glaucoma
- Hypotony
- Maculopathy
  - Edema
  - Cysts/holes
How Does Uveitis Blind?

- Glaucoma
- Hypotony
- Maculopathy
  - Edema
  - Cysts/holes
  - Membrane
How Does Uveitis Blind?

• Glaucoma
• Hypotony
• Maculopathy
  – Edema
  – Cysts/holes
  – Membrane
• Optic neuropathy
How Does Uveitis Blind?

- Glaucoma
- Hypotony
- Maculopathy
  - Edema
  - Cysts/holes
  - Membrane
- Optic neuropathy
- Retinopathy
How Does Uveitis Blind?

- Glaucoma
- Hypotony
- Maculopathy
  - Edema
  - Cysts/holes
  - Membrane
- Optic neuropathy
- Retinopathy
- Neovascularization
Active uveitis; Toxo scar at macula
Better imaging; posterior uveitis with vascular shutdown
It was during this era that a very young French boy was blinded in one eye by an accidental puncture of that eye with an awl in his father’s saddle shop. Sympathetic ophthalmia uveitis blinded the other eye by the time the child was 9 years old.
History of immune suppression for Uveitis

Prevalence of Visual Disability and Blindness Despite Corticosteroid Therapy

Evidence-based analysis of peer-reviewed literature indicates that the prevalence of visual disability and blindness secondary to uveitis has not measurably changed in the past 40 years. Why is that? How can that possibly be?
Steroid Monotherapy
Stuck in second gear

• Few departments of Ophthalmology have an Ocular Immunologist on their faculty
• Most ophthalmologists completing their training have never been exposed to uveitis patient management with anything other than with steroids
Lessons from Rheumatology

- Rheumatologists learned the lesson the hard way too: steroid and NSAID therapy first, reserving immunomodulatory therapy for patients with advanced disease, resulted in progressive joint damage and great disability.
Lessons from Rheumatology

The battle-cry throughout the world of rheumatology “The Mission is Remission”
Lessons from Rheumatology

• Early employment of steroid-sparing immunomodulatory, disease-modifying agents results in vastly superior outcomes

• The toxicity of medication side effects is less with this approach too
Lessons from Rheumatology

• Ophthalmologists should embrace this model of early steroid-sparing, remission-inducing therapy with even more vigor than does rheumatology, since the eye is so much less forgiving of chronic inflammation than is the joint, with profound life-altering consequences
So, Where Are We Today?

IMMUNOMODULATORY THERAPY

• Clear evidence for safety and effectiveness in saving vision in selected populations with uveitis patients doomed to a life of blindness without such therapy
So, Where Are We Today?

IMMUNOMODULATORY THERAPY

• Clear evidence for insufficient employment of such therapy by ophthalmologists worldwide
A View to the Future

• International Uveitis Study Group
• International Ocular Inflammation Society
• Uveitis Subspecialty Day – American Academy of Ophthalmology
Uveitis entities (not an exhaustive list)

- HLA B27 + related (most common)
- JIA related (childhood arthritis)
- Sympathetic uveitis (Trauma)
- Toxoplasma Uveitis (infection)
- Behcets disease (Autoimmune)
- Intermediate uveitis (autoimmune)
- Sarcoidosis, MS, vasculitis, CT diseases etc
- TB related uveitis, HIV related uveitis
Drugs available

• Topical steroids & cycloplegics (most common)
• Oral steroids
• Periorbital steroids
• Intraocular steroids (Ozurdex, Triasensce, IVTA)
• Methotrexate
• Infliximab, Adalilumab
• Etanercept
• Azathioprine
A View to the Future

New initiatives by “Big Pharma” on clinical trials of medications capable of affecting the immune system and ocular inflammatory disease.
Cataract surgery and Uveitis
Liverpool Adult Uveitis database

- Based at RLUH / St Pauls
- MU Saeed
- IA Pearce
- NAV Beare

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Liverpool Adult Uveitis database

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Etanercept in uveitis; Summary

• 4/5 patients with uveitis have achieved control of uveitis with etanercept
• 1 patient was a true non responder & continues to have variable control with infliximab and methotrexate
• 4/4 patients without uveitis (arthritis only) have not shown any signs of “new uveitis”
Etanercept in Paediatric Uveitis Experience at Alder Hey

Usman Saeed, Sue Goyal, Arvind Chandna, William D. Newman, Gavin Cleary
Treatment aims:
Immune modulators; why not commonly used; so a trained physician only

• **Monitoring**
  • Patients must report mouth ulcers, sore throat, fever, epistaxis, unexpected bruising or bleeding, shortness of breath, and any unexplained illness/infection and should be seen urgently for full blood count and liver function tests and CXR if pulmonary symptoms.

  — *Prior to starting therapy* ,
  • Chest x-ray
  • Assessment of renal and liver function, fbc

  — *Ongoing Monitoring*:
  • It is recommended that all blood counts are monitored and recorded carefully.
  • FBC, renal function and LFTs fortnightly for 3 months and monthly thereafter. If there is evidence of renal impairment check that renal function has not deteriorated after 4 weeks.
  • FBC should be measured one week after any increase in dose.
  • In order to monitor disease activity a 3 monthly CRP would be helpful.

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Side effects

- **Side effects**

  - Very common/Common:
    - Mouth ulcers
    - Nausea and diarrhoea
    - Hair loss
  
    - Uncommon:
      - Headaches
      - Bone marrow suppression
      - Lung and liver inflammation
      - Renal impairment
  
    - Very rare:
      - Drowsiness
      - Anaphylactic reaction
Why should cataract surgery in uveitits happen with a uveitis specialist

- White cataracts
- Small pupils
- Posterior synaechae (stuck pupils)
- Increased post operative uveitis
- Increased post Operative macular odema
- Increased incidence of post op IOP rise
Cataract surgery in small pupil caused by uveitis
What are special measures needed in cataract surgery
Make the pupil bigger
Take the cataract out
New lens in

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NICE Guidance for uveitis

- Ozurdex approved for treatment of DMO in July 2017, only if:
  1. the implant is to be used in an eye with uveitis
  2. the macular oedema does not respond to topical corticosteroid treatment, or such treatment is unsuitable.
UK recommendations

Adalimumab and dexamethasone for treating non-infectious uveitis

1 Recommendations

1.1 Adalimumab is recommended as an option for treating non-infectious uveitis in the posterior segment of the eye in adults with inadequate response to corticosteroids, only if there is:
- active disease (that is, current inflammation in the eye) and
- inadequate response or intolerance to immunosuppressants and
- systemic disease or both eyes are affected (or 1 eye is affected if the second eye has poor visual acuity) and
- worsening vision with a high risk of blindness (for example, risk of blindness that is similar to that seen in people with macular oedema).

1.2 Stop adalimumab for non-infectious uveitis in the posterior segment of the eye in adults with inadequate response to corticosteroids if there is 1 of the following:
- new active inflammatory choroidal or inflammatory retinal vascular lesions, or both or
- a 2-step increase in vitreous haze or anterior chamber cell grade or
- worsening of best corrected visual acuity by 3 or more lines or 15 letters
Adalilumab

1 Recommendations

1.1 Adalilumab is recommended as an option for treating non-infectious uveitis in the posterior segment of the eye in adults with inadequate response to corticosteroids, only if there is:

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- systemic disease or both eyes are affected (or 1 eye is affected if the second eye has poor visual acuity) and
- worsening vision with a high risk of blindness (for example, risk of blindness that is similar to that seen in people with macular oedema).

1.2 Stop adalilumab for non-infectious uveitis in the posterior segment of the eye in adults with inadequate response to corticosteroids if there is 1 of the following:

- new active inflammatory chorioretinal or inflammatory retinal vascular lesions, or both or
- a 2-step increase in vitreous haze or anterior chamber cell grade or
- worsening of best corrected visual acuity by 3 or more lines or 15 letters.
• Each Ozurdex implant delivers 700mcg dexamethasone for 6 months or more
• Implant lasts in vitreous for 270 days before fully dissolving
• The summary of product characteristics states that after initial treatment, re-treatment can be performed after approximately 6 months
Dexamethasone

1.3 Dexamethasone intravitreal implant is recommended as an option for treating non-infectious uveitis in the posterior segment of the eye in adults, only if there is:

- active disease (that is, current inflammation in the eye) and
- worsening vision with a risk of blindness.

1.4 These recommendations are not intended to affect treatment with adalimumab and dexamethasone that was started in the NHS before this guidance was published. Adults having treatment outside these recommendations may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.
Ocular adverse events observed in MEAD were as expected for an ophthalmic intravitreal corticosteroid therapy
Summary

• Uveitis is a potentially blinding eye problem
• It is a problem of younger patients hence economic importance
• Excellent therapy exists today for uveitis
• Yet far too few ophthalmologists avail themselves and their patients of such therapy
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Patient Details: 

Following is the outcome of your patient's visit to the Eye Clinic as a new patient:

Diagnosis: 
- Presbyopic Both eyes Jul 2017
- Dry Eyes Both eyes Jul 2017
- Ultephants Both eyes Jul 2017

VSPC: 
- RE: UA: 59
- LE: UA: 59

IOP: 
- RE: 16 mm/Hg
- LE: 16 mm/Hg

Plan: 
- Treat

Treatment: 
- Gy Hyloforte 2% QDS 5 Weeks Both Eyes
- Gy FML 3 Weeks Both Eyes

Rx Advice: 
- New treatment added
- Lid hygiene, Leaves

Outcome: 
- Follow up 2 months
- Advised regarding lid hygiene, massaging the eyelids with warm compresses and using lubricant eye drops whenever required.
- Patient needs an Optic disc scan for the optic nerves baseline as his grandmother had glaucoma. This will be done at St Helen hospital.
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Conclusions

• Research dedicated to uveitis
• Should be seen by a specialist who has experience in uveitis
• Steroids is not the only answer
• Immune modulators and cytotoxics can and should be used
Thank you for listening

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