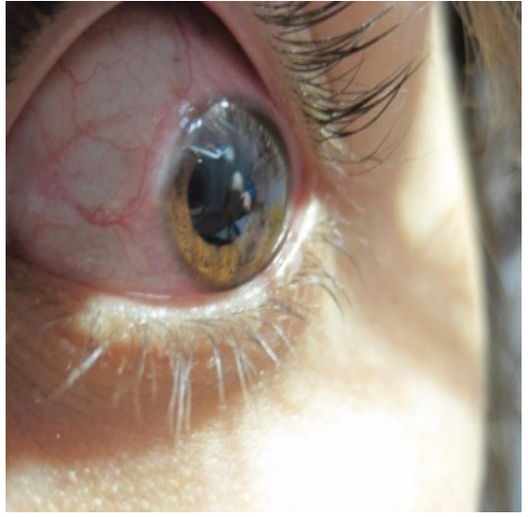
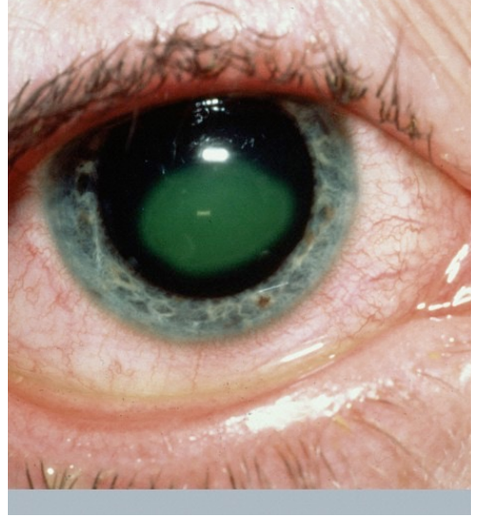




Eye Casualty & the Oncology Patient

Miss Stella Hornby
Consultant Ophthalmologist Oxford Eye Hospital

Overview

- Ocular toxicity from anti-cancer therapy
- Not uncommon but underestimated and under-reported
- Vision related quality of life v imp to patients
- Treatable often without stopping the biologic

Differential Diagnosis

- Metastasis/ infiltration
- Paraneoplastic syndrome
- Side effect of the treatment
- Opportunistic infection
- Unrelated to either cancer or treatment

Audit 2016

Age	Sex	Eye problem	Type of cancer	Drug?
56	F	Old toxo scars	Breast ca	Pre-chemo Amblyopia ? Risk of reactivation with chemo
50	F	Papillodema	Lung ca Brain mets	No
74	F	Uveitis & CMO	Lung cancer	Side effect of erlotinib Responded to steroids
71	M	Retinal haemorrhages & Roth spots	ALL	new diagnosis
44	F	Blepharitis & dry eye	Myeloma	Ixazomib
28	M	Dry eyes	Sarcoma	Worse after chemo
55	F	Multiple chalazia	Myeloma	Bortezomib (velcaid)
49	M	Retinal haemorrhage	NHL	on chemo ? Candida
40	F	Uveitis bilateral	Skin melanoma	Pembrolizumab
62	M	HZO on chemo & VMT in other eye	Bowel ca	Chemo
69	F	Blurred vision Dry eye and cataracts	Pancreatic cancer	Trial drug
64	M	Blurred vision swollen disc	Prostate cancer with skull base disease	rucaparib
51	F	Bilateral uveitis R>L with fibrin	Breast ca with spine mets	? Diabetic or paraneoplastic VA maintained with topical steroids

Side effects of Biologics

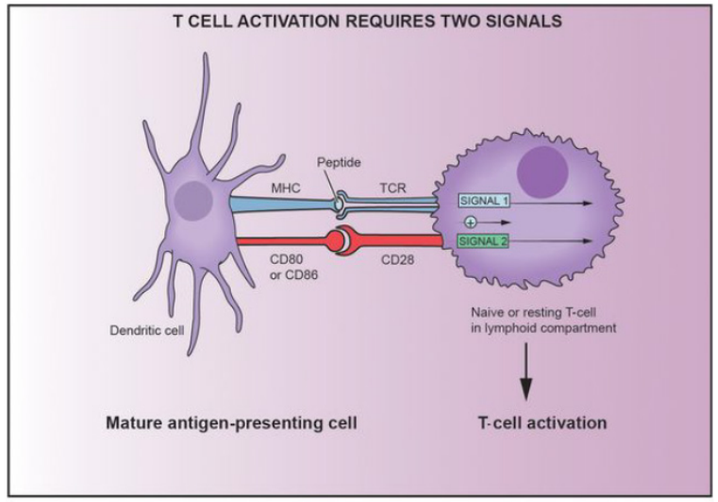
- Ocular Surface Problems
- Uveitis
- Retinal Problems
- Orbital inflammation
- Reactivation of infections from immunosuppression

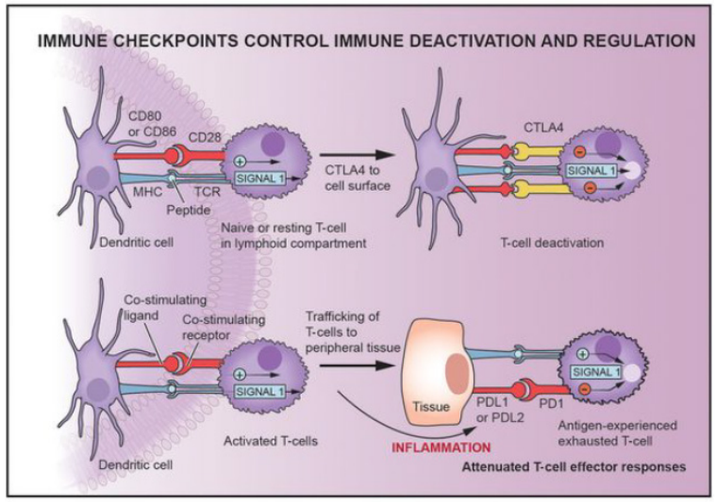
Mechanism of action

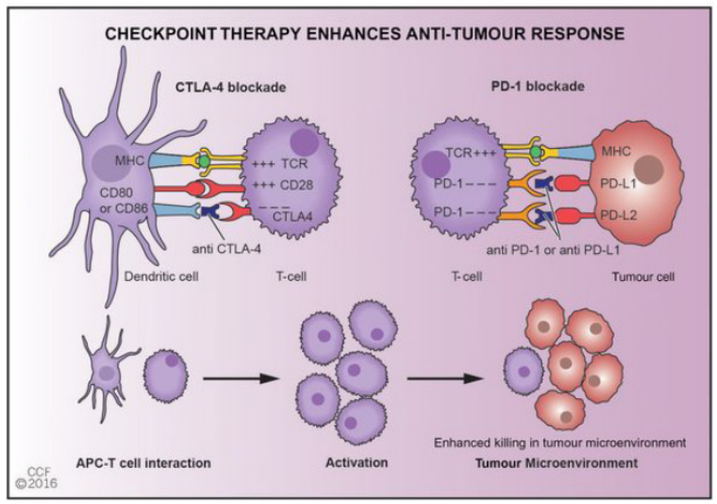
- Long dreamed of harnessing the power of the immune system to fight cancer
- These therapies have provided significant and sometimes prolonged survival advantages in patients with metastatic melanoma, non-small cell lung cancer, renal cell carcinoma and others

TABLE 1. IMMUNOTHERAPEUTIC AGENTS

AGENT	MOLECULAR TARGET	MALIGNANCY APPROVED FOR	YEAR APPROVED
Pembrolizumab	PD-1	Non-small cell lung cancer	2015
		Melanoma	2014
Nivolumab	PD-1	Hodgkin lymphoma	2016
		Renal cell carcinoma	2015
		Non-small cell lung cancer	2014
		Melanoma	2013
Atezolumab	PDL-1	Urothelial carcinoma	2016
Ipilimumab	CTLA-4	Melanoma, in combination with nivolumab	2014
		Melanoma	2011







Ocular Surface Problems

- Dry eye
- Chalazia
- Blepharitis
- Sore, itchy, burning, fb sensation, red, blurring when reading
- Conjunctivitis
- Conjunctival oedema (chemosis)

Cases

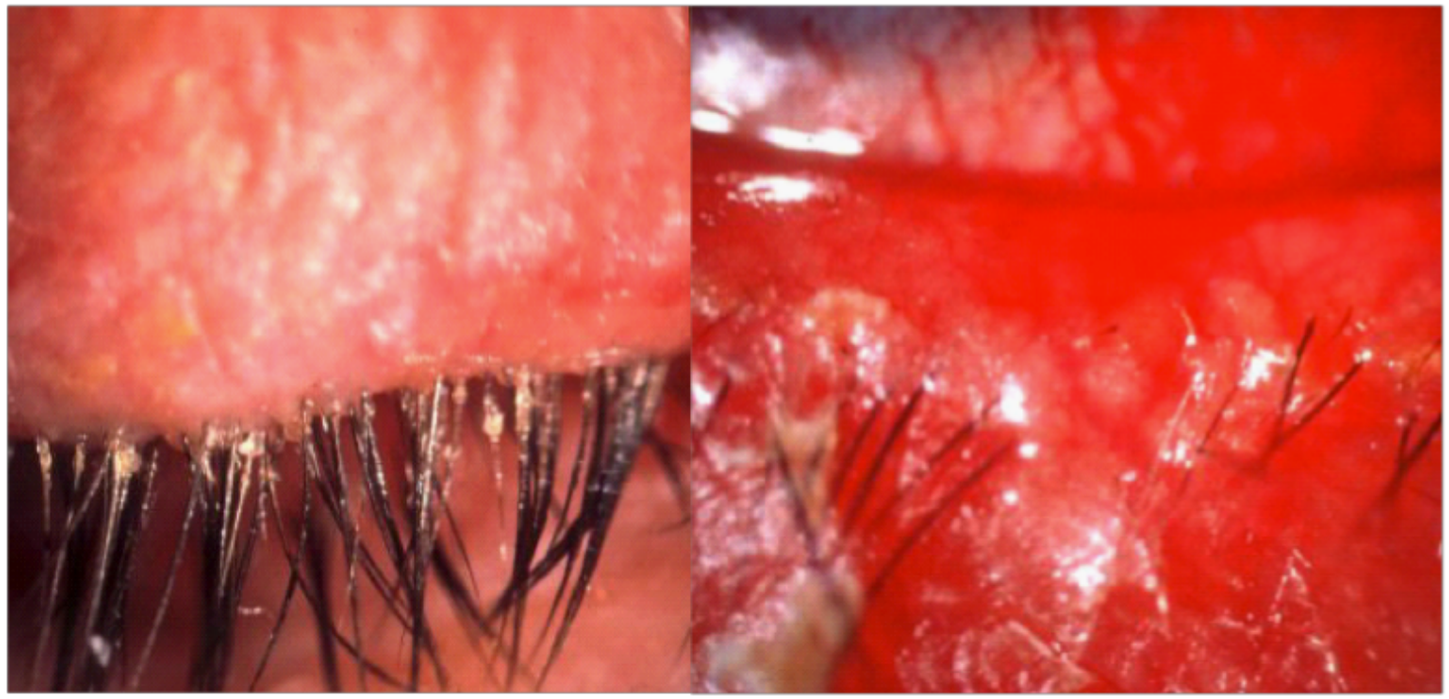
- 55 year old female with myeloma on bortezomib (velcade) Multiple chalazia - 9 or 10!

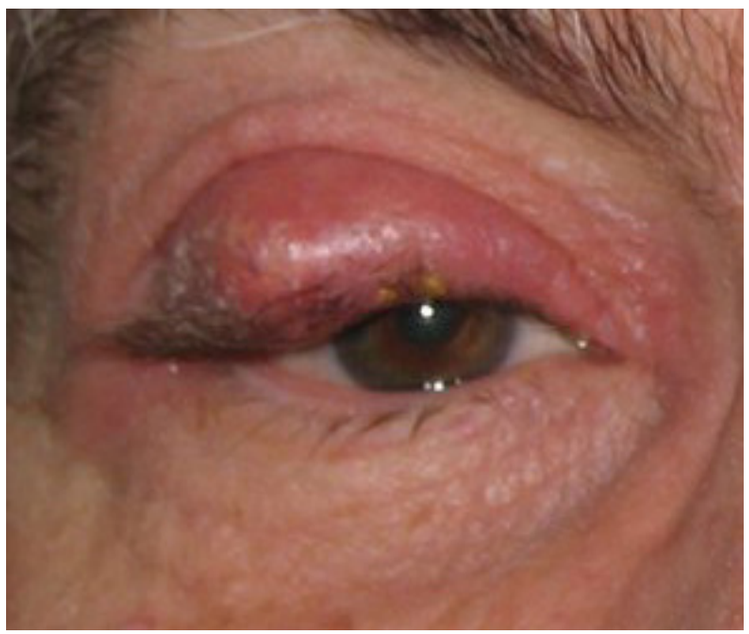
- 44 year old female with myeloma on ixazomib with dry eye and blepharitis

- Proteasome inhibitor may enhance the release of pro-inflammatory cytokines which incite systemic inflammation (rashes and blepharitis)

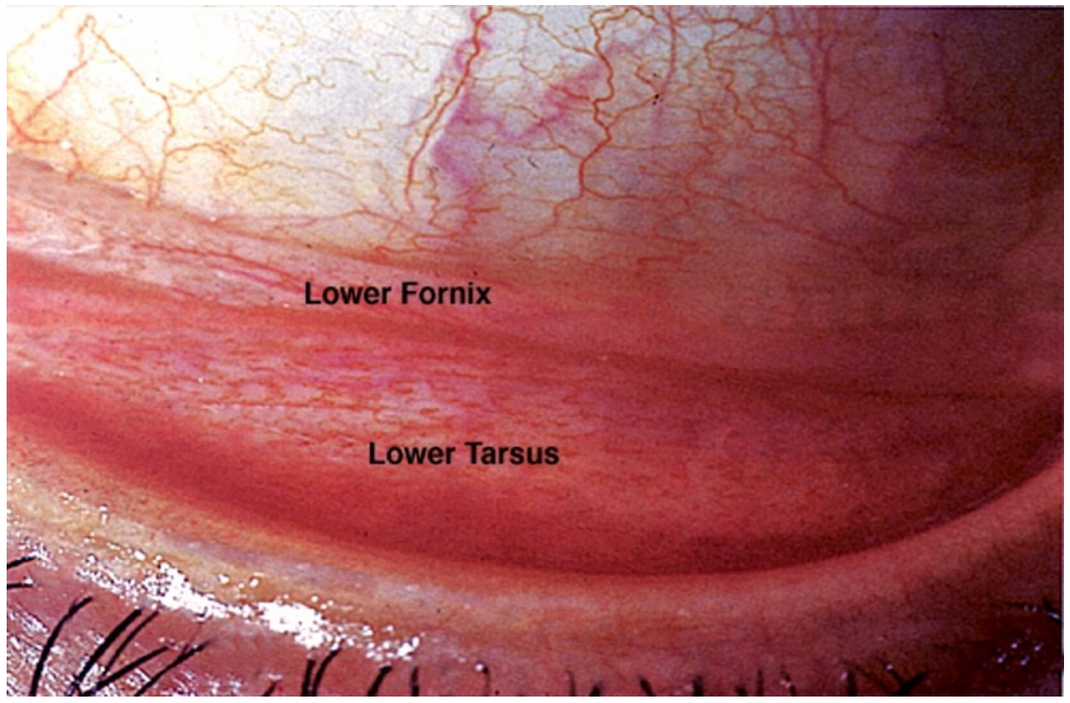
Blepharitis

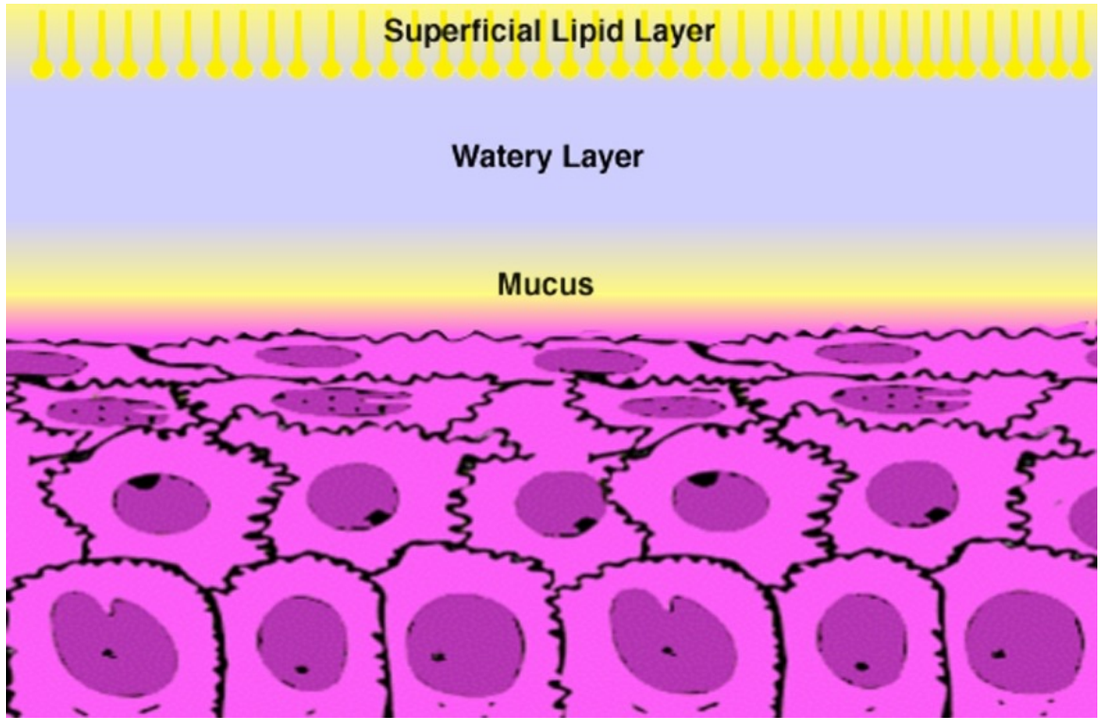
- Stingy/Burning
- Scratchy
- Red
- Sore
- Crusty
- Cysts
- Dry, blurry





Dry eye


Lower Fornix
Lower Tarsus


Superficial Lipid Layer
Watery Layer
Mucus

Blepharitis Mangement

- Heat (warm compresses or eyebag) & Lid massage

- Lid scrubs (ocusoft available from Boots or bicarbonate of soda solution)

- Oral tetracycline e.g. doxycycline 100mg po od for months or lymecycline 408mg po od

- Weak steroid e.g. FML drops or maxitrol ointment bd

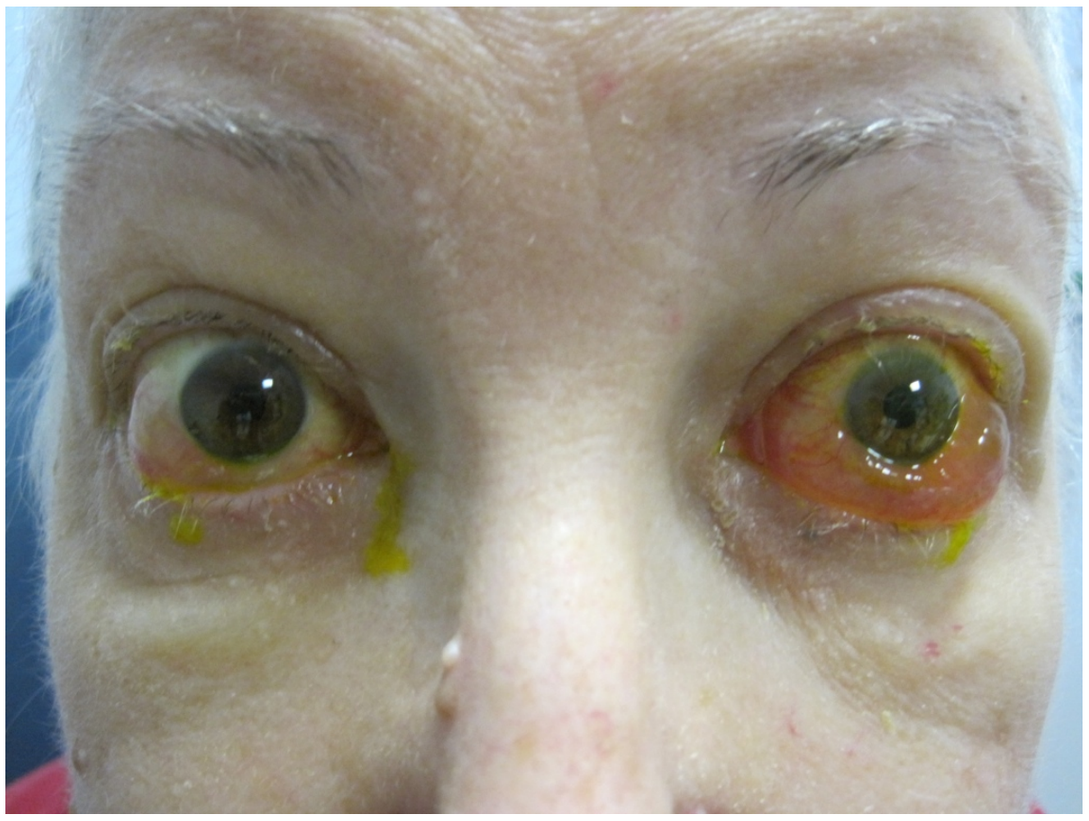
- Dry eye drops - Any but some marketed for lipid deficient dry eye Optive Plus NHS price £7.49 for 10ml bottle (can keep open for 6/12) or Systane Balance

Dry Eye Mangement

- Eye Drops
- Gels
- Ointments (nocte)
- Environmental modifications
- Tear conservation (punctal plugs)
- Botox ptosis if lagophthalmos or neurotrophic ulcer

Chemosis

- Metastatic renal cell carcinoma
- On Sunitinib (sutent)
- Asymmetrical due to posture
- Multitarget tyrosine kinase inhibitor
- Facial & eyelid oedema

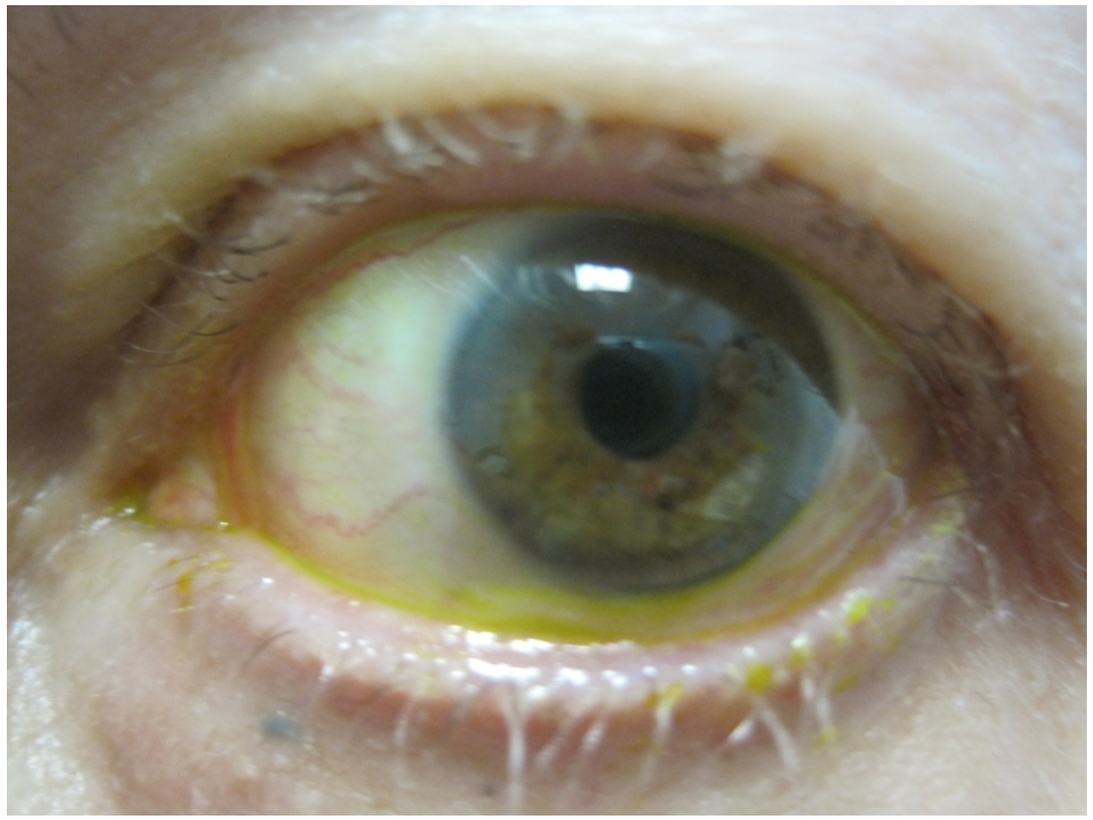


Management

- Preservative free dexamethasone 0.1% every 2 hours

- Lacri-lube ointment twice a day

- Xailin night / VitA pos ointment (Available over the counter)



Ocular surface

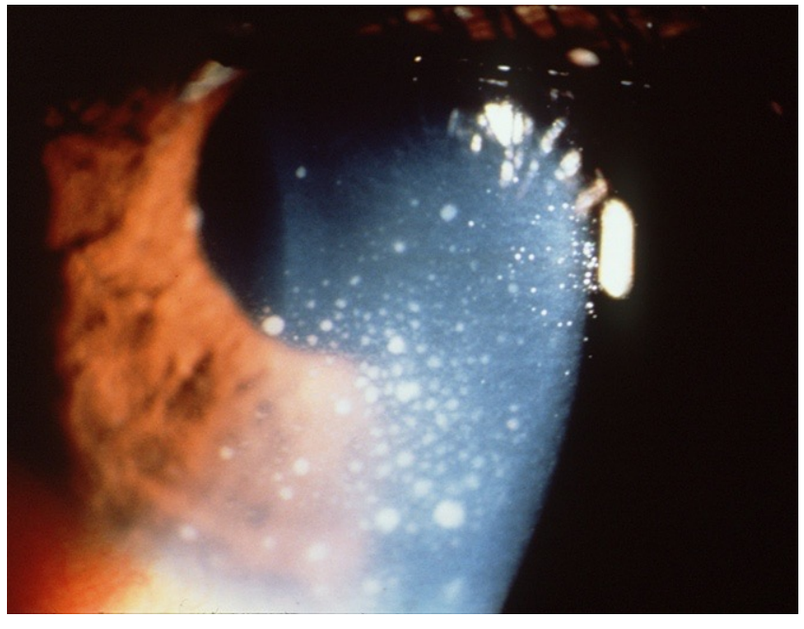
- Dry eye
- Chalazia
- Blepharitis
- Sore, itchy, burning, fb sensation, red, blurring when reading
- Conjunctivitis
- Conjunctival oedema (chemosis)

Symptoms of uveitis

- Onset usually sudden, unilateral
- Pain (dull/ache)
- Photophobia
- Redness
- Decreased vision
- Lacrimation
- Floaters - suspect vitreous involvement

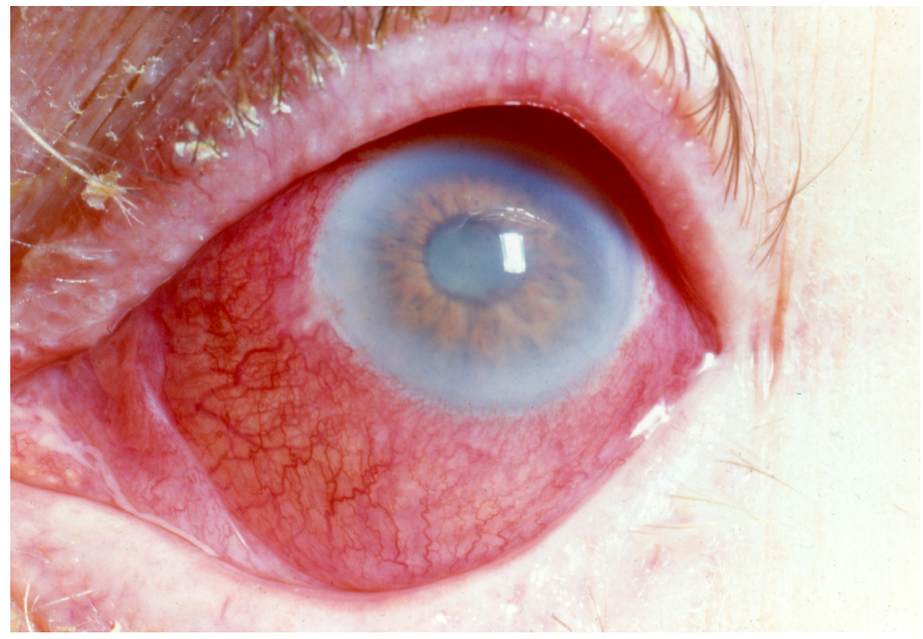
Signs of uveitis

- Red eye Circumlimbal injection
- Decreased vision
- Cells/ flare/ fibrin/ hypopyon
- Posterior synechiae
- Keratin precipitates
- Iris transillumination



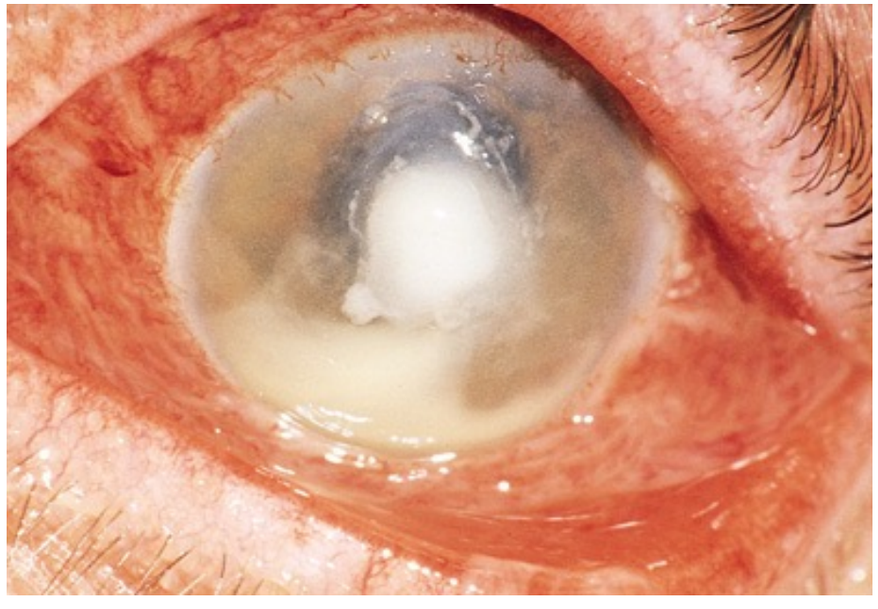
Differential Diagnosis

- Acute Angle Closure Glaucoma



- Intraocular foreign body

- Other forms of posterior uveitis including infections e.g herpes zoster, toxoplasmosis



- Infectious keratitis

Cases

- 74 year old female with lung cancer on erlotinib (tarceva) Blurred vision

- Bilateral anterior uveitis and cystoid macular oedema

- 40 year old male with skin melanoma on pembrolizumab (Keytruda)

- Bilateral anterior uveitis

-

Uveitis Mangement

- Sunglasses & Do not drive
- If infection excluded - topical steroids (dexamethasone 0.1%/ prednisolone acetate 1%)
- Mydriatics (Cyclopentolate 1%)
- Periocular steroid injection or Oral steroids
- Manage glaucoma (drops)
- Remove cataract

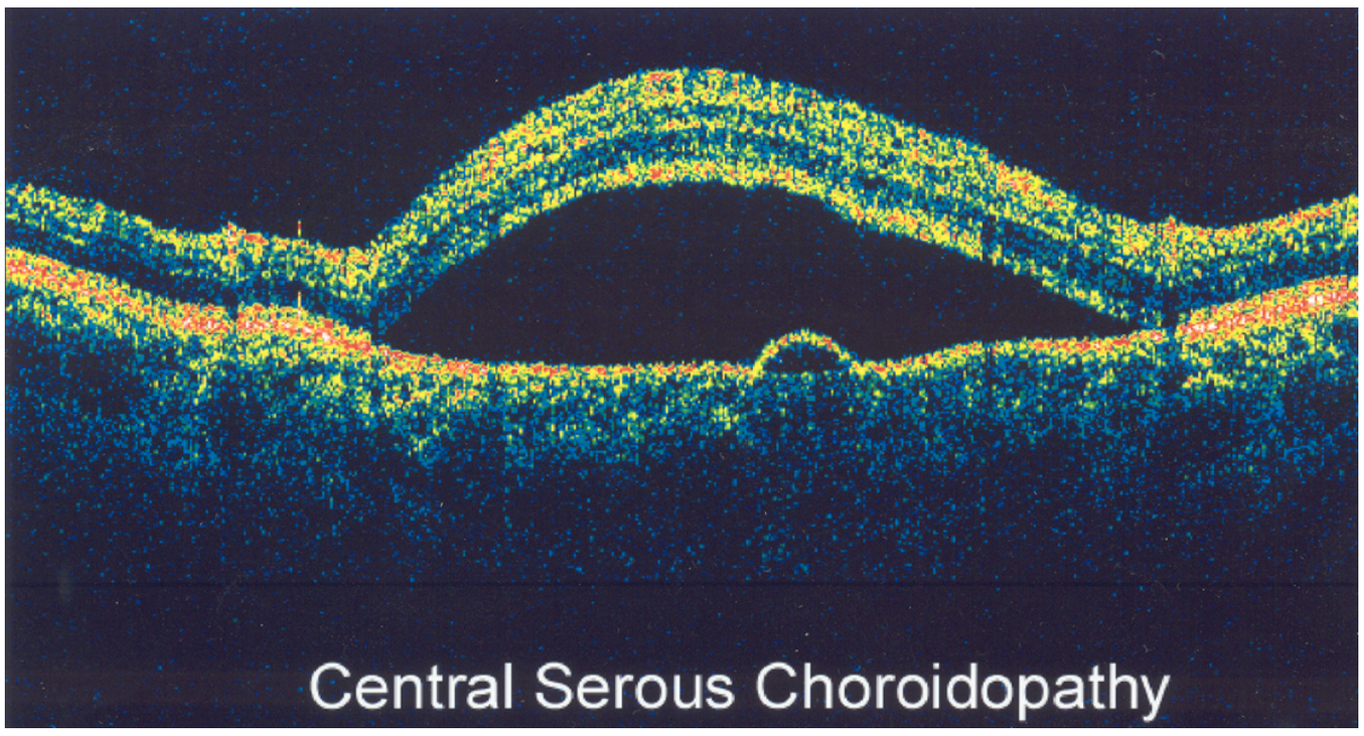
Symptoms of retinal disease

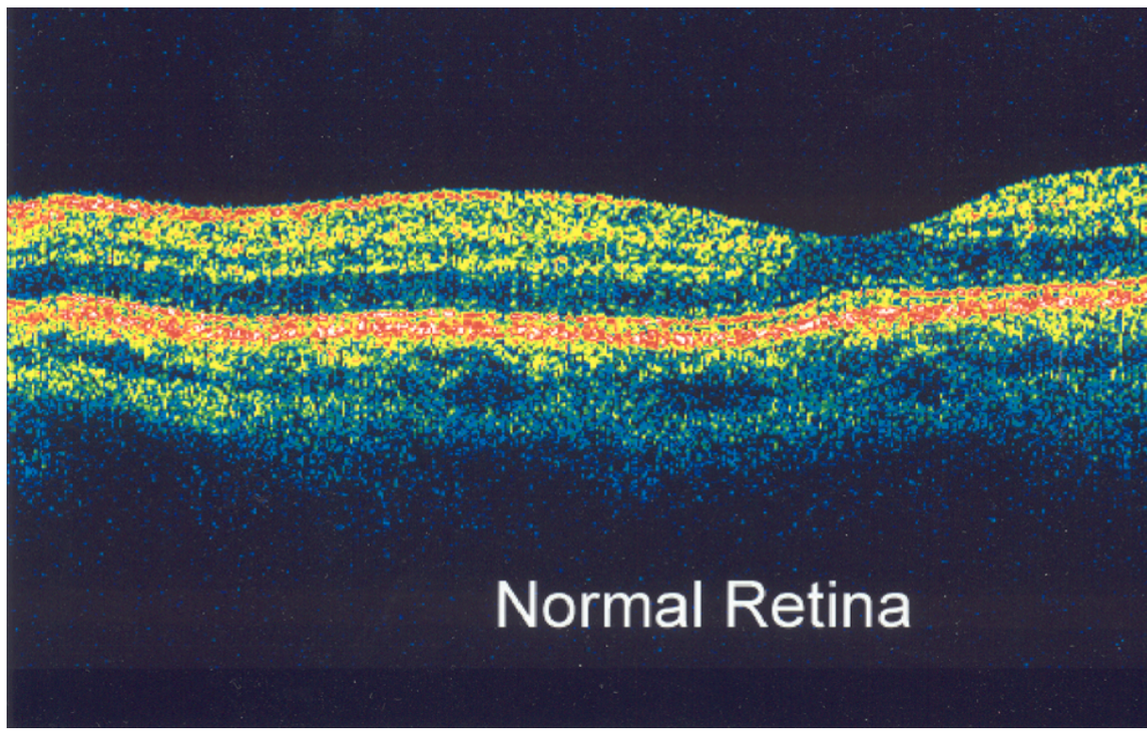
- Flashes
- Floaters
- Blurring, distortion or change in image size
- Abrupt loss of vision
- Progressive loss of vision
- Night blindness

Retinal vein occlusions

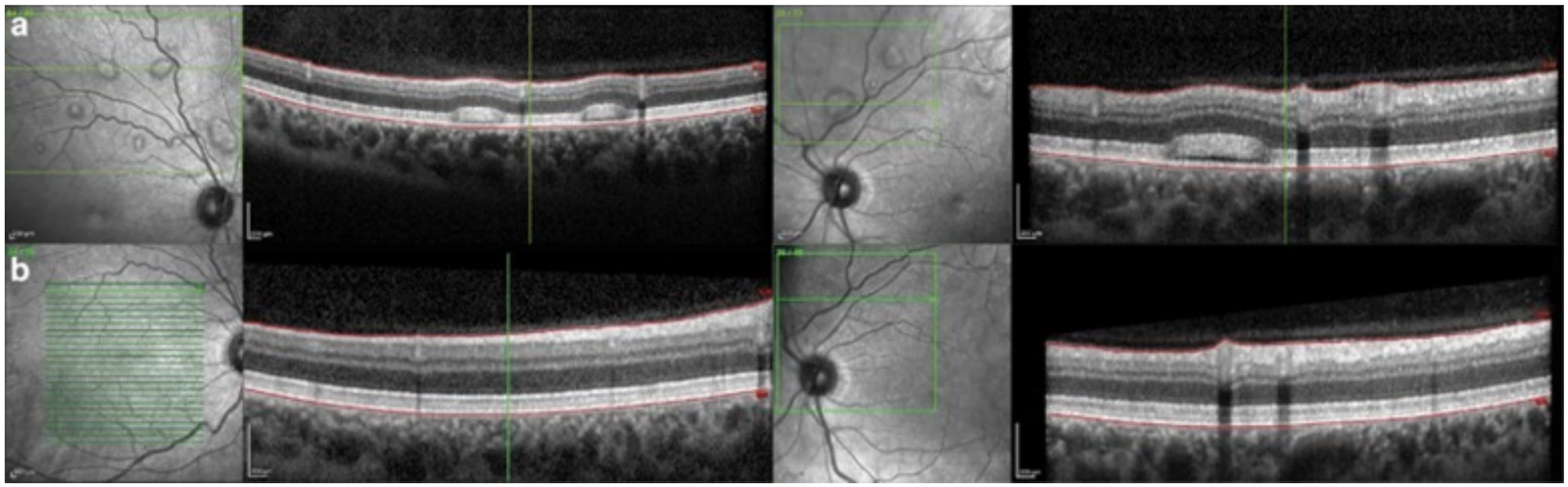
Wellcome Images

Central Serous Retinopathy





Multifocal Serous Retinal Detachments



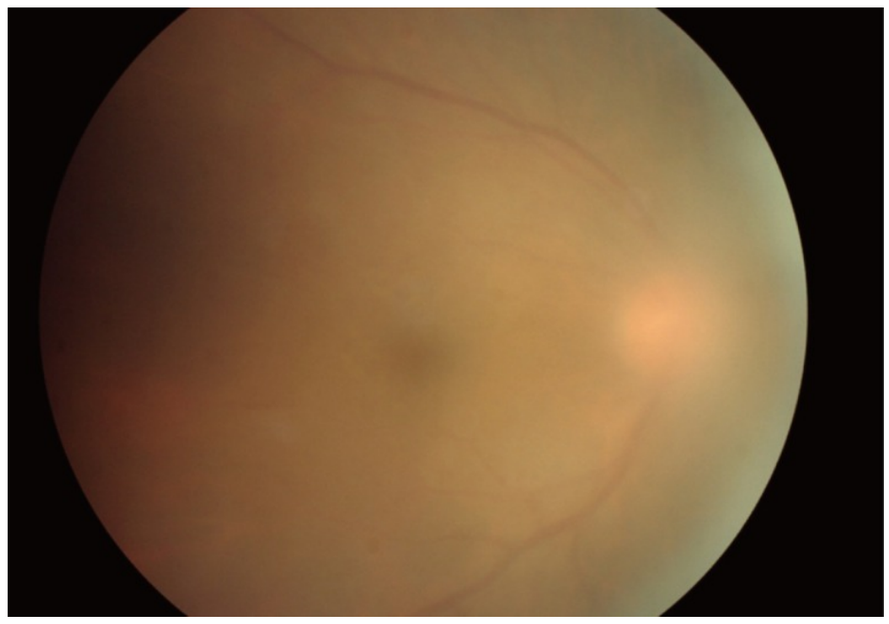
Oxford Study on MEK inhibitors

- JAMA Oncology Feb 2017
- 7 of 40 (18%) patients on 3 different MEK inhibitors developed ocular side effects
- MEK1A 3/11 (11%) bilateral CSR
- MEK1B 2/19 (11%) 1 CRVO, 1 multifocal CSR
- MEK 1C 2/10 (20%) 1 multifocal CSR, 1 IOP rise

Other reported side effects

- Severe bilateral uveitis, retinal detachments

- Papillitis



MEK inhibitors

- Very little known about mechanism of action
- If CRVO occurs in one eye may have to stop the drug to prevent second eye involvement.
- Options for management - intravitreal injections of
- steroids and/or anti-VEGF

Pt on Pembrolizumab

Enquiry Details
Who is calling (Onc Triage) : Patient
Contact No. (Onc Triage) :
Consultant (Onc Triage) :
Previously contacted Triage (Onc Triage) : Yes
Drop in (Onc Triage) : No

Assessment
Action taken (Onc Triage) : Specialist team informed for advise.
d/w Spr patient needs to be seen in eye casualty.
I have informed patient to attend eye casualty tomorrow at JR.
If there's any concerns to liaise with Triage Unit

Reason for call (Onc Triage) : PMH: melanoma

PC: complaining of dry eyes since last cycle, "feels like I'm in a steamy bathroom and everything looks grey"
Feels very fatigued the last couple days.
Her son has noticed that her eyes looks yelow.

Denies any pain, headaches, blurred or double vision.

Was seen by opticians prior to starting treatment.
Eating and drinking

Oxford Eye Hospital, Oxford UK
OPTOS, 200Tx
Laterality: R
Red: 50%
Green: 50%
Zoom: 1.56
Presentation: Multiple
1/2
1

Oxford Eye Hospital, Oxford UK
OPTOS, DAYTONAPLUS
Laterality: L
Red: 50%
Green: 50%
Zoom: 2.09
Presentation: Multiple
1/1

Birdshot-like

- One case report with pembrolizumab
- Garden variety is a rare form of autoimmune posterior uveitis
- Presents with floaters and blurred vision
- HLA -29 association

68 F ipilimumab- acute eye pain and unable to move eyes

1 External photos. External photos taken of the subject taken at presentation, with bilateral periorbital swelling, upper eyelid

Graves-like orbitopathy

- CT showed proptosis and enlarged eye muscles consistent with TED (patient remained euthyroid)

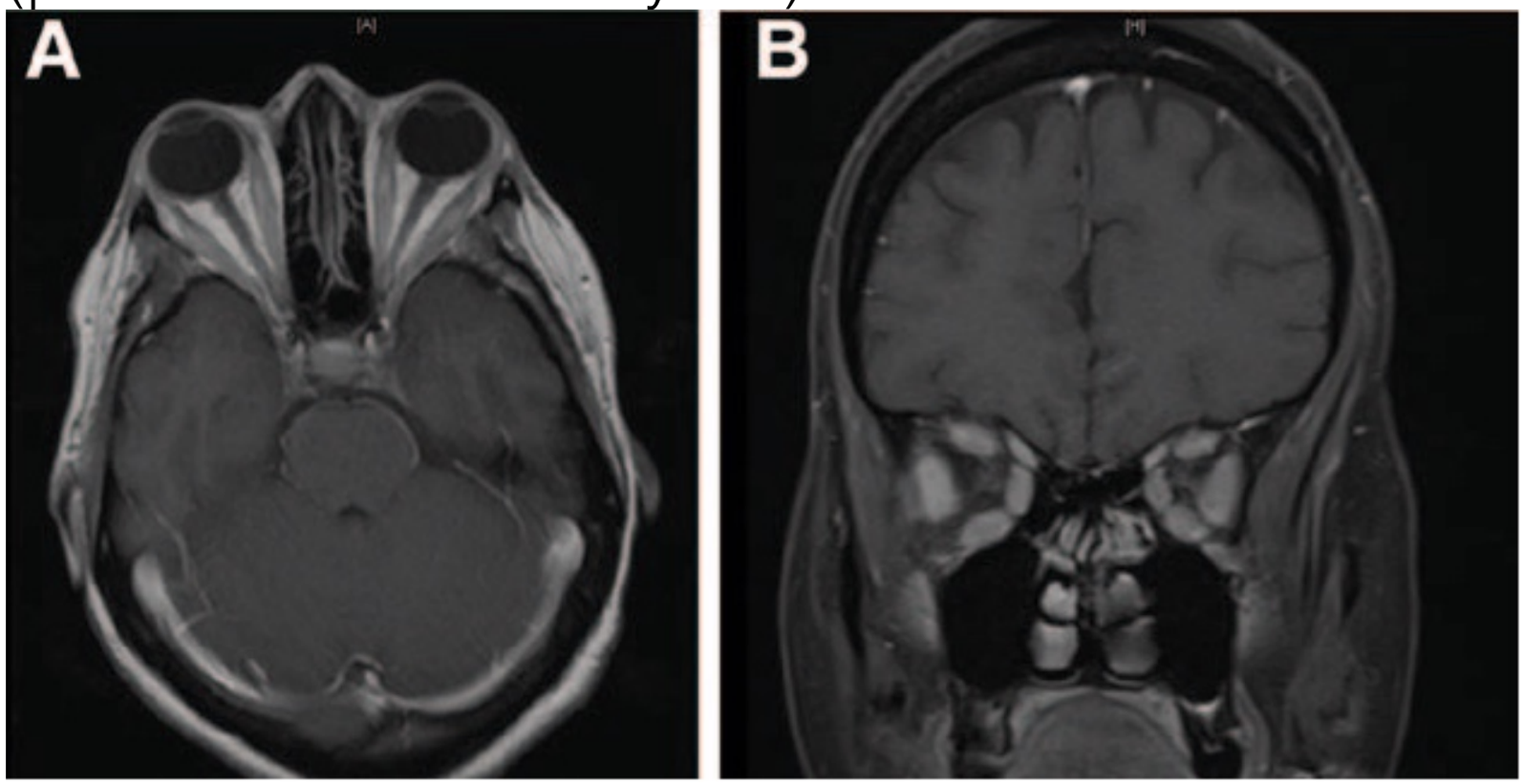


FIG. 2. **A**, Axial T1-weighted postcontrast image; (**B**) coronal

54 yr female

- “ Had surgery for right occipital meningioma 10 days ago. When went home after 7 days everything seemed dark & dull and muted colours, difficulty reading because of left visual field defect

- Not seen a blue sky since (November in UK!)

Details

Next visit	none planned at present
Last episode	20-Nov-2019 Miscellaneous / referral to eye cas (pdf)
Last visit	08-Nov-2019 Miss Stella Hornby OEH
GP	Dr Davi Copping ...

Active diagnoses

visual disturbance

Both eyes - homonymous hemianopia (08-Nov-2019)

Management plan 08-Nov-2019 Miss Stella Hornby

Plan:

Had surgery for right occipital meningioma 10 days ago. When she went home after 7 days she noticed everything seemed dark and dull and muted colours and difficulty reading because left visual field defect.

Her ocular examination was normal with normal optic discs. The visual

History

Allergies	None known
MRSA	Not recorded
SH	

Examination 08-Nov-2019

UA 6/4	**VA**	UA 6/4
(Peak: 19 on 08-Nov-2019) **19**	**IOP (Rebound)**	**20** at 12:49 (Peak: 20 on 08-Nov-2019)
no RAPD	**Pupil / Iris**	no RAPD
normal optic disc Ishihara score 11/17	**Optic disc**	normal optic disc Ishihara score 12/17
homonymous hemianopia	**Motility / Fields**	homonymous hemianopia

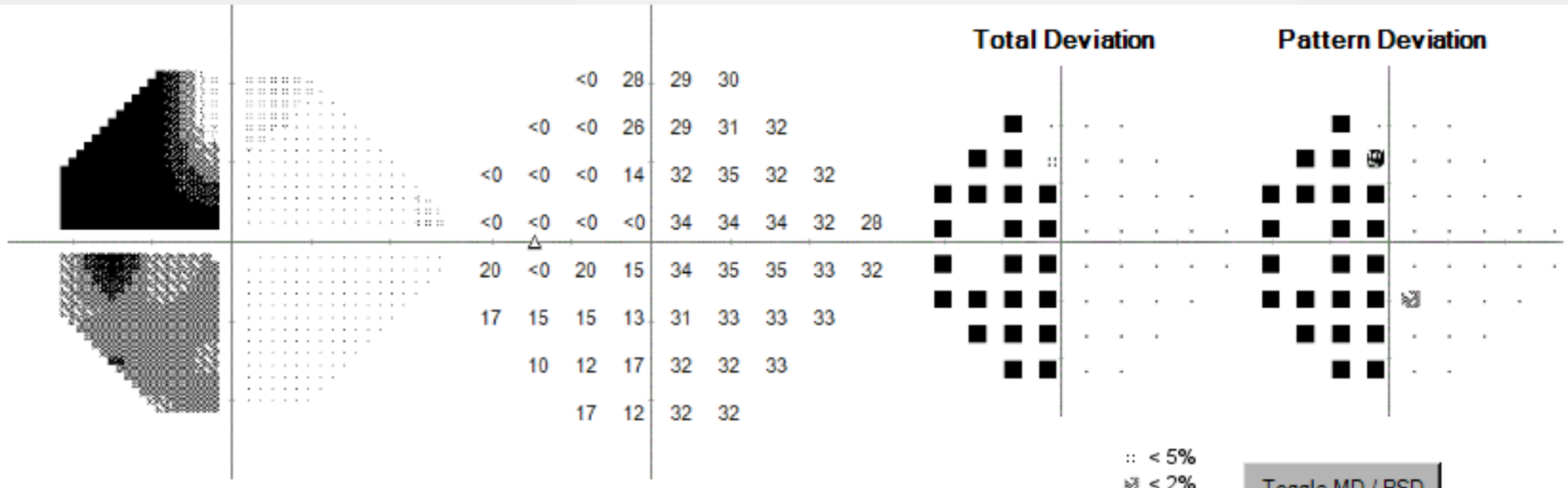
OphthView

Humphrey visual fields

○ Right ◉ Left Central 24-2 threshold DIANE LE

Latest

Date: 08-11-2019 13:10:17
Age: 54
Fixation target: Central
Fixation losses: 0/11
False POS errors: 2 %
False NEG errors: 10 %
Test duration: 03:32
Fovea: OFF
Stimulus: III, White on 31.5 ASB
Strategy: SITA fast
RX: +2.00
GHT: Outside Normal Limits
VFI: 68%
MD: -7.58 Db P < 0.5%
PSD: 13.45 Db P < 0.5%
AGIS*: 4 / 20 CIGTS*: 9 / 20
Central defect (1 of 4 points)
Paracentral defect Temporal vertical step Partial peripheral rim defect Enlarged blind spot



:: < 5%
▨ < 2%
◉ < 1%
■ < 0.5%

Toggle MD / PSD intensity / shading

☑ Include in progression calculations

Show printer dialog screen ☐ Print test

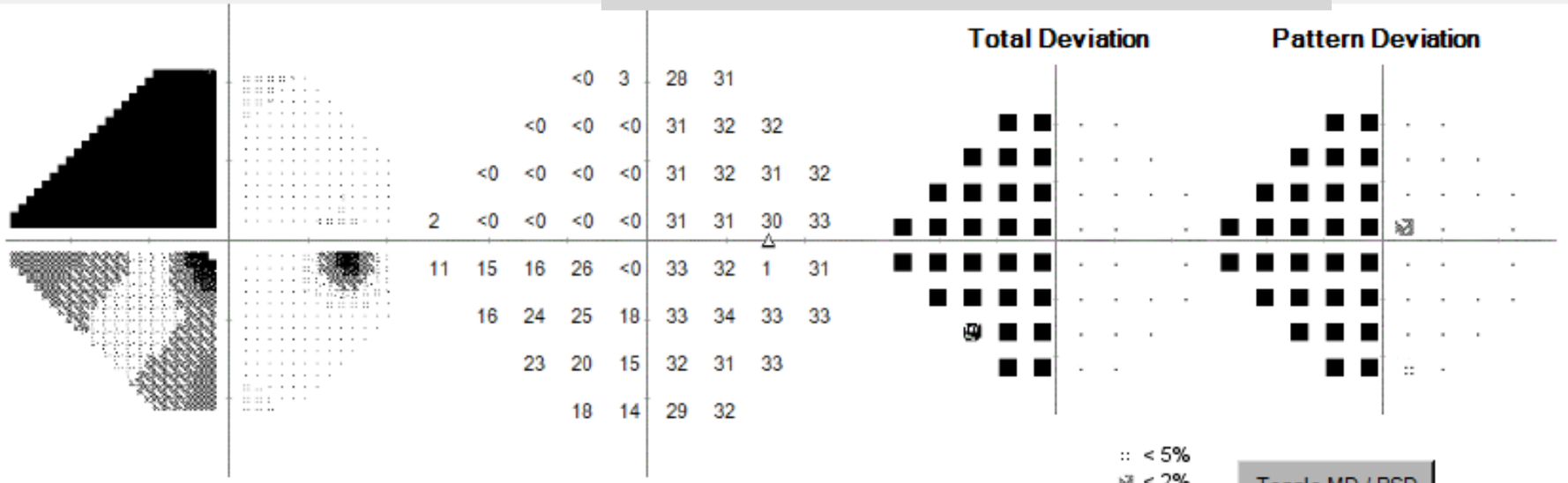
OphthView

Humphrey visual fields

◉ Right ○ Left Central 24-2 threshold DIANE LESL

Latest

Date: 08-11-2019 13:03:44
Age: 54
Fixation target: Central
Fixation losses: 0/13
False POS errors: 5 %
False NEG errors: 10 %
Test duration: 04:20
Fovea: OFF
Stimulus: III, White on 31.5 ASB
Strategy: SITA fast
RX: +2.00
GHT: Outside Normal Limits
VFI: 59%
MD: -13.13 Db P < 0.5%
PSD: 15.01 Db P < 0.5%
AGIS*: 10 / 20 CIGTS*: 11 / 20
Superior arcuate scotoma
Central defect (2 of 4 points)
Paracentral defect Nasal



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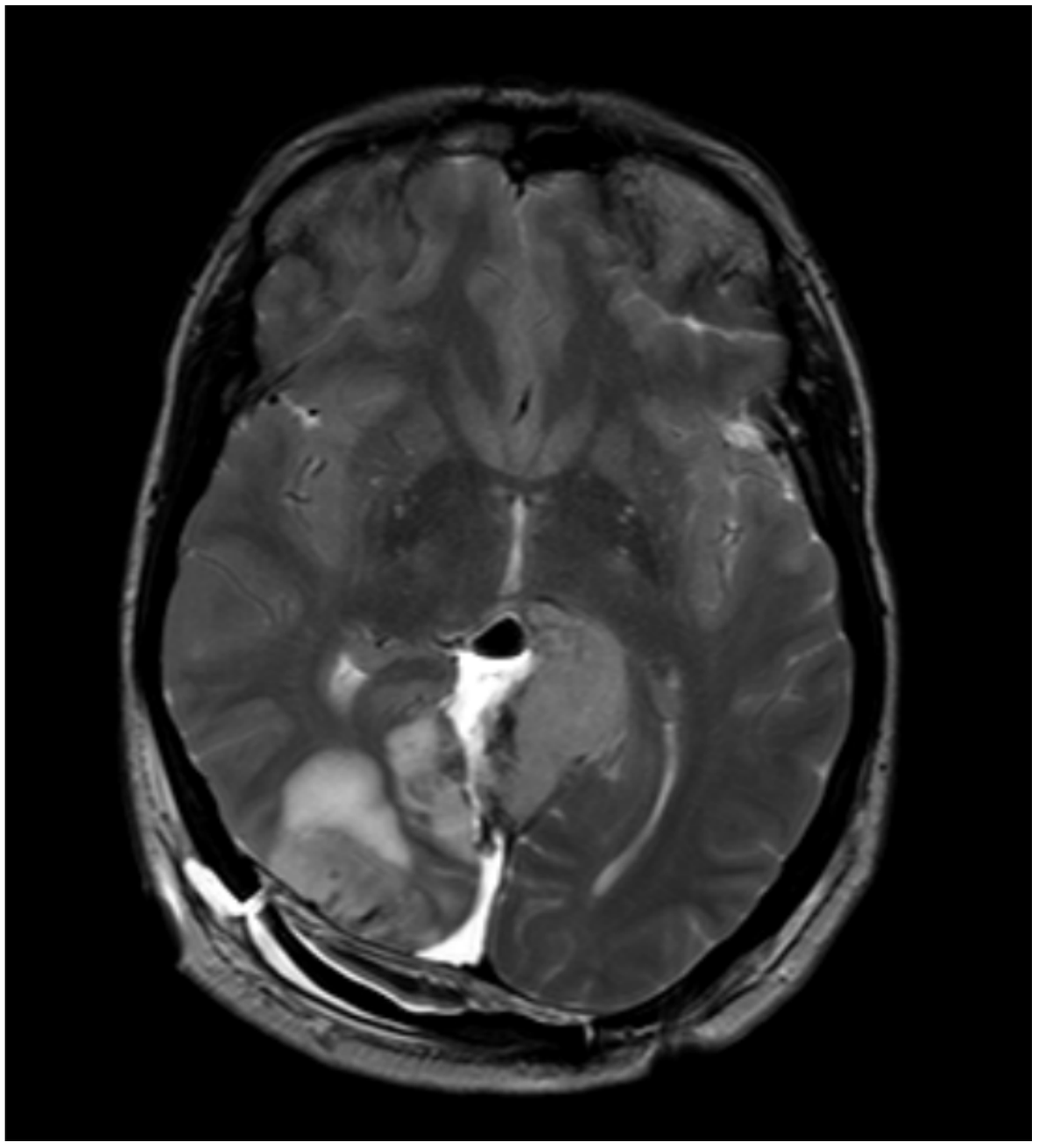
■ < 0.5%

Toggle MD / PSD intensity / shading

☑ Include in progression calculations

Post op MRI



What is going on?

- Reading problem left homonymous hemianopia

- Colour vision problem - cerebral achromatopsia

- ventral occipital cortex colour processing

- The case of the colour blind painter Oliver Sacks

Follow up

- Phone call to patient

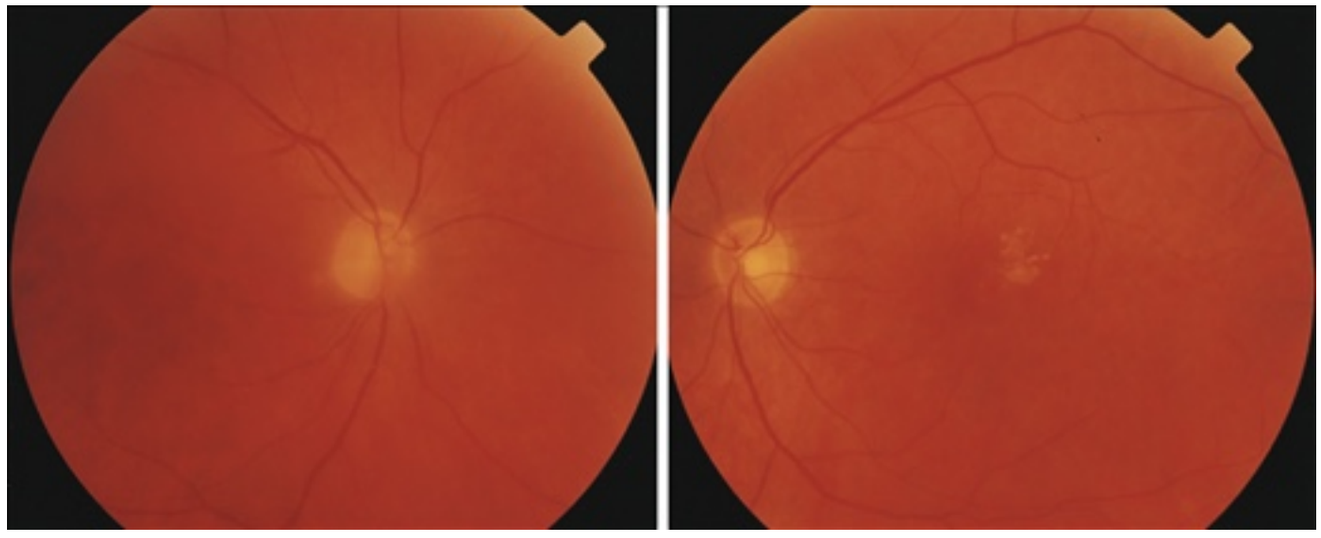
- Peripheral vision improving but everything still looks dull and drab through a veil

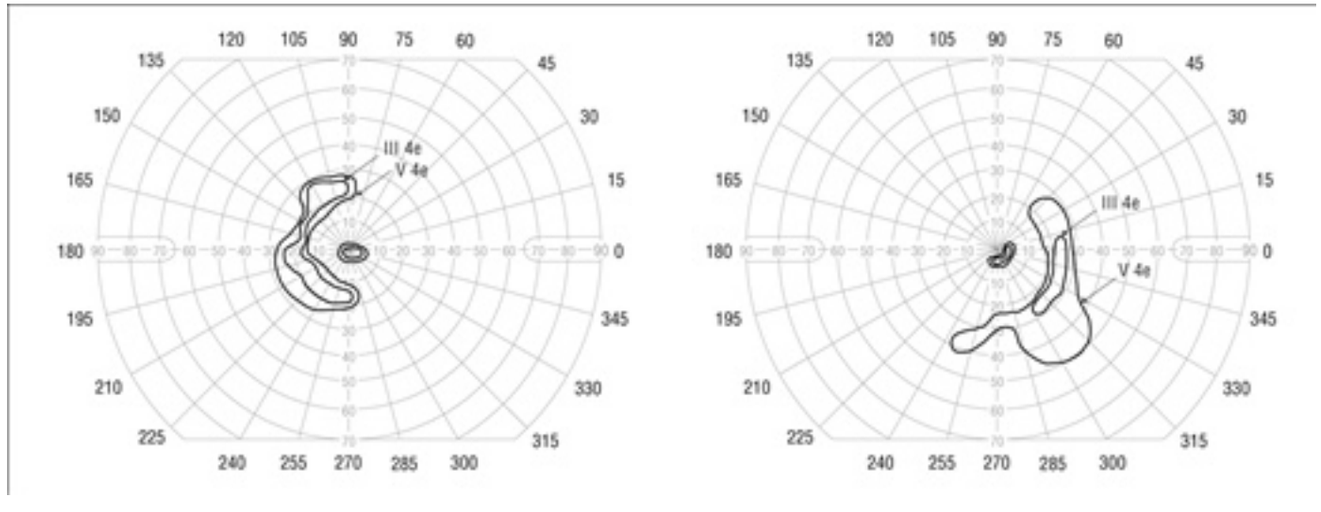
- Can tell if something is red, orange or purple

Paraneoplastic syndromes

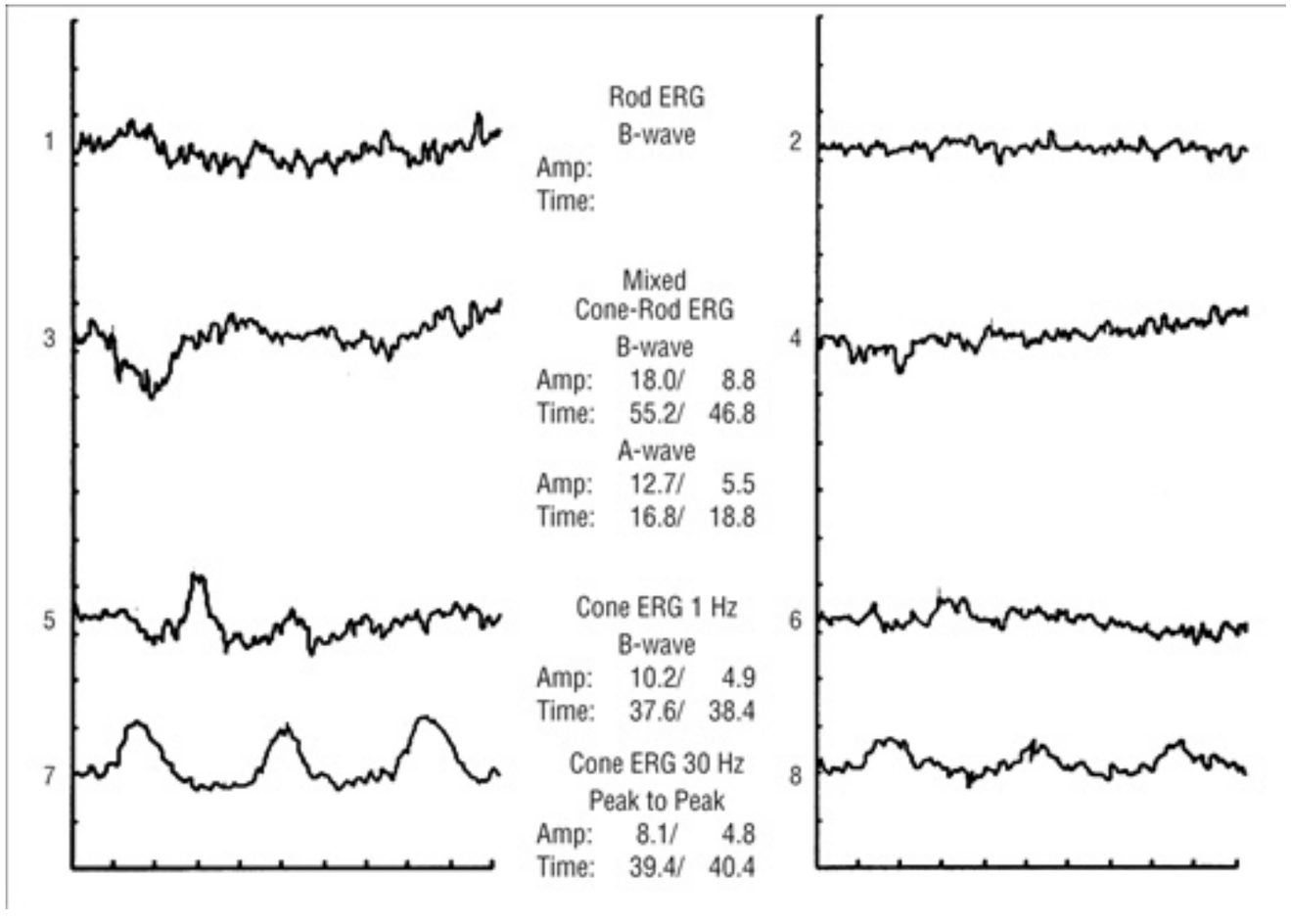
- Cancer associated retinopathy (CAR)
- Melanoma associated retinopathy (MAR)
- Paraneoplastic optic neuropathy (CRMP-5)

Cancer-associated retinopathy





Cancer associated retinopathy



Case History

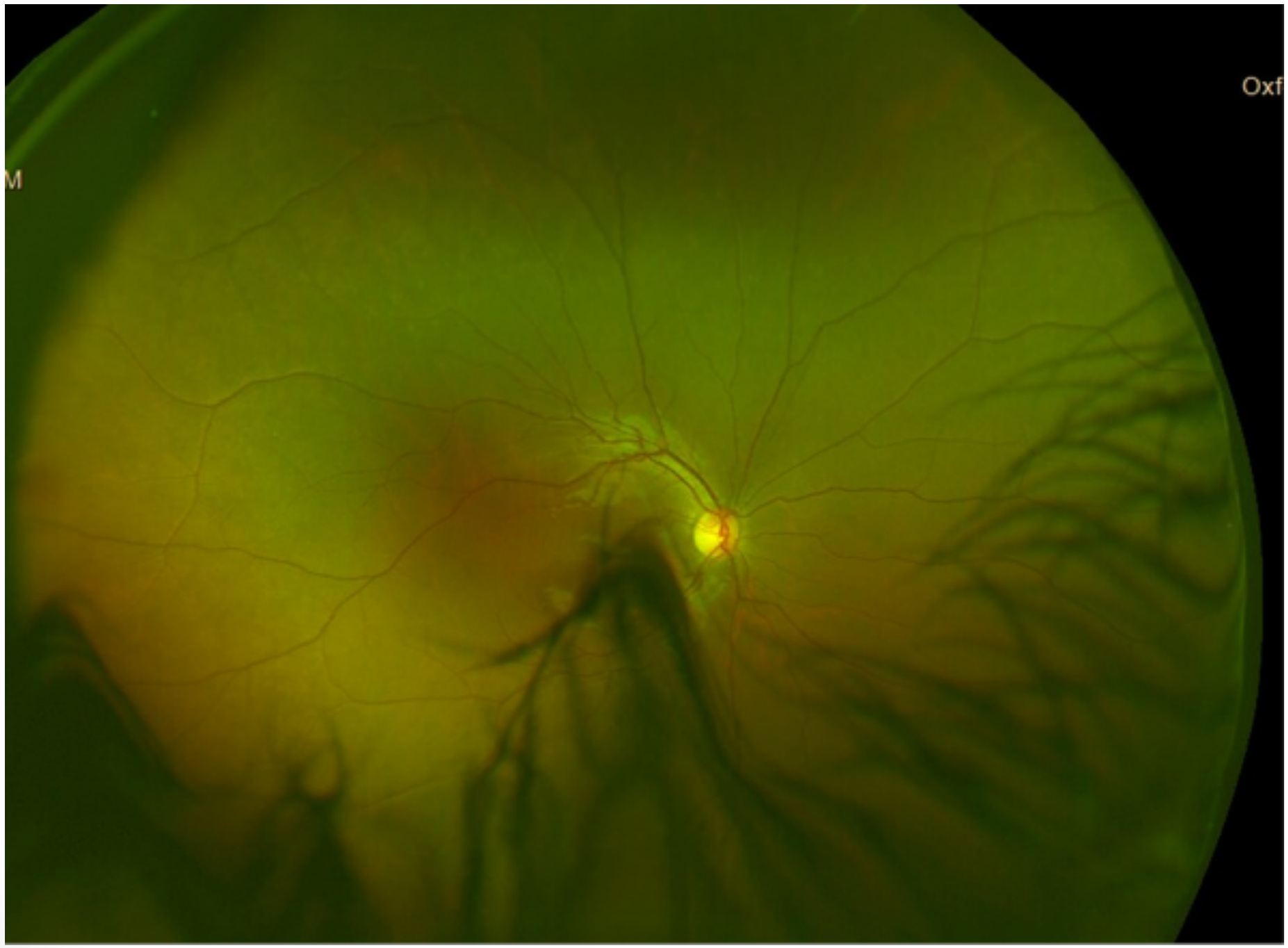
Patient
16 year old boy

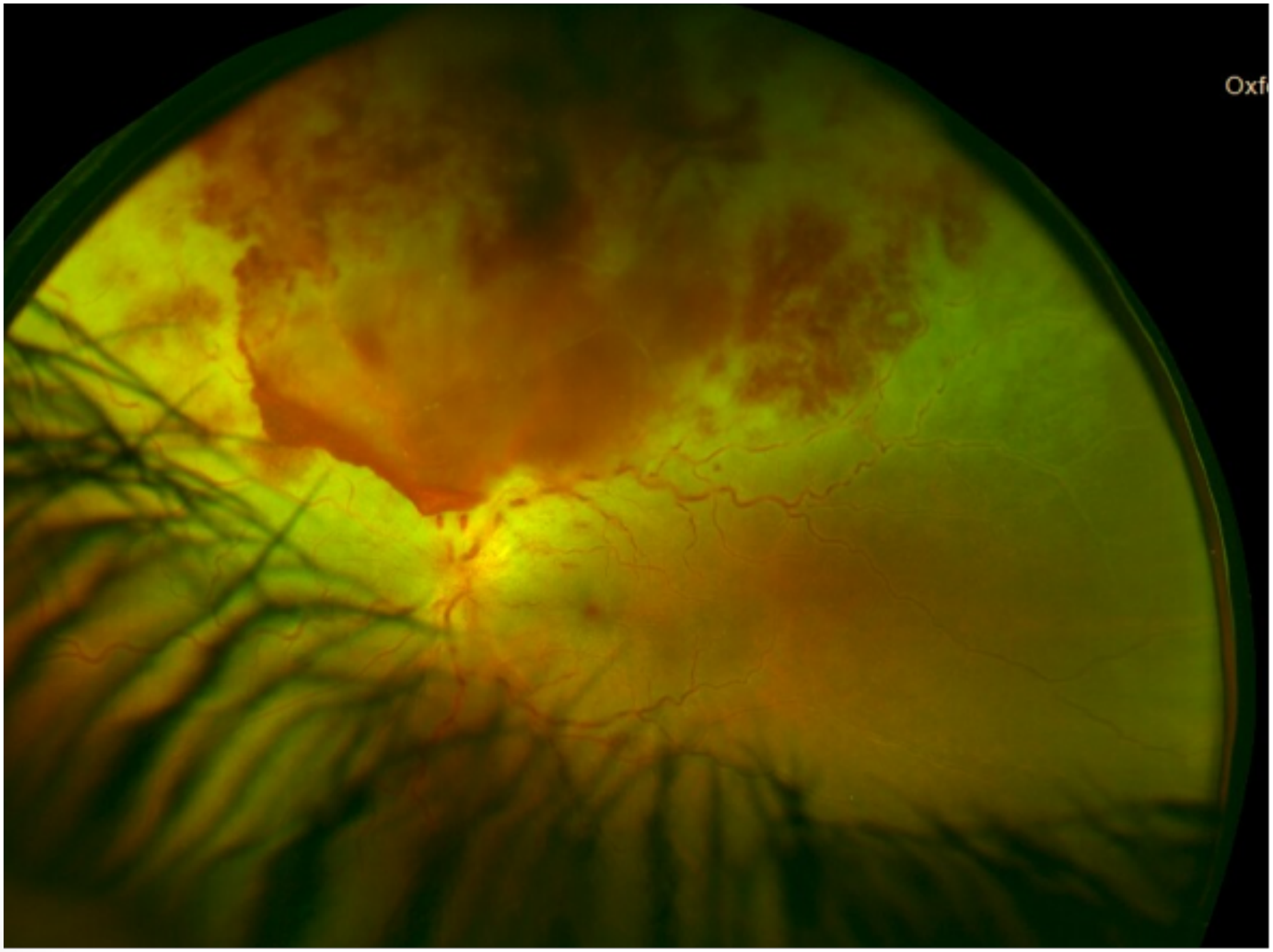
- Attending his final Haematology clinic appointment prior to a planned Bone Marrow Transplant in Bristol
- mentioned that he had “suddenly lost vision the day before in the left eye”
- Asked by haematologist to be seen in ophthalmology outpatients

Medical History
- Acute Lymphoblastic Leukaemia (ALL)
- Lymphocytes 0.58 (Sept 30th).
- On prophylactic anti viral and anti toxoplasmosis treatment

Ocular History
- Diagnostic Vitrectomy (June 2019)
- Previous Left Eye OD disc swelling thought to be secondary to lymphocytic infiltration of the CNS or demyelination secondary to Methotrexate treated successfully with oral steroids, with nil residual visual deficit.
- Nil other ocular history

Optos





Summary

- Many side effects of biologics are treatable without stopping the drug
- Need to exclude infections in uveitis
- Supporting visual impaired patient - cataract surgery, magnifiers, advice
- Paraneoplastic syndromes rare but devastating