

# LEUKEMIC RETINOPATHY

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OST1

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- Case Study
  - Chronic Myeloid Leukemia
  - Leukemic Retinopathy
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## THE CASE – MRS. D.A.

- 42 year old Caucasian female referred to WEH EyeCas [ Dec 2013] by Haematology with a 5/7 hx:
  - Reduction in visual acuity RE
  - Field loss in right upper nasal quadrant

# THE CASE – MRS. D.A.

- **BACKGROUND:**
  - **CML with CNS involvement** → diagnosed **May 2013** at Hammersmith Hospital.
    - Incidental finding: visited **opticians** previously c/o 1/52 hx of flashing lights
      - O/E: “tortuous, dilated b.v. with dot, flame and blot haemorrhages with macular involvement” → GP to please arrange **FULL BLOOD WORK UP** and refer to r/o active ocular pathology within <1/52.
  - Treated with FLAG-IDA (4x chemotherapy) → cytopenia
  - Neutropenic sepsis → prolonged Abx
  - Fungal lung disease → HRCT

# THE CASE – MRS. D.A.

- PMH: nil
- POH: nil
- Dx:
  - Omeprazole
  - Aciclovir
  - Tranexemic
  - Ciprfloxacin
  - Voriconazole

# THE CASE – MRS. D.A.

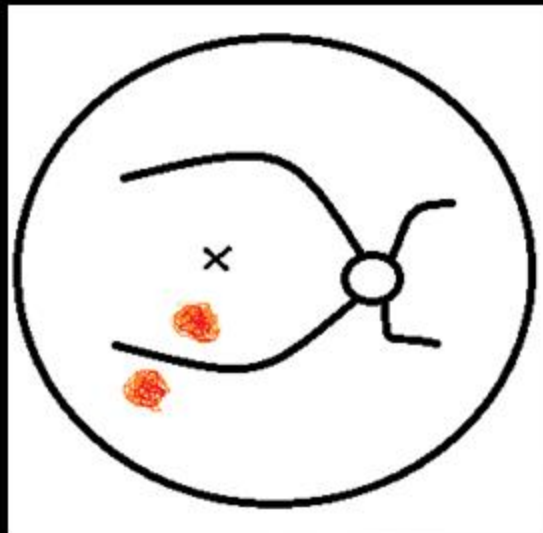
- Examination:

6/60	VA	6/4
13/17	Ishihara	17/17
Upper nasal quadrant defect	Confrontational VF	full
no	RAPD	no
N	Lids	N
white	Conj	white
Clear, no staining	Cornea	Clear, no staining
d+q	A/C	d+q
N	Iris/Lens	N
16	IOP	13

# THE CASE – MRS. D.A.

- Examination:

pigment	Vitreous	syneresis
	Retina	NAD

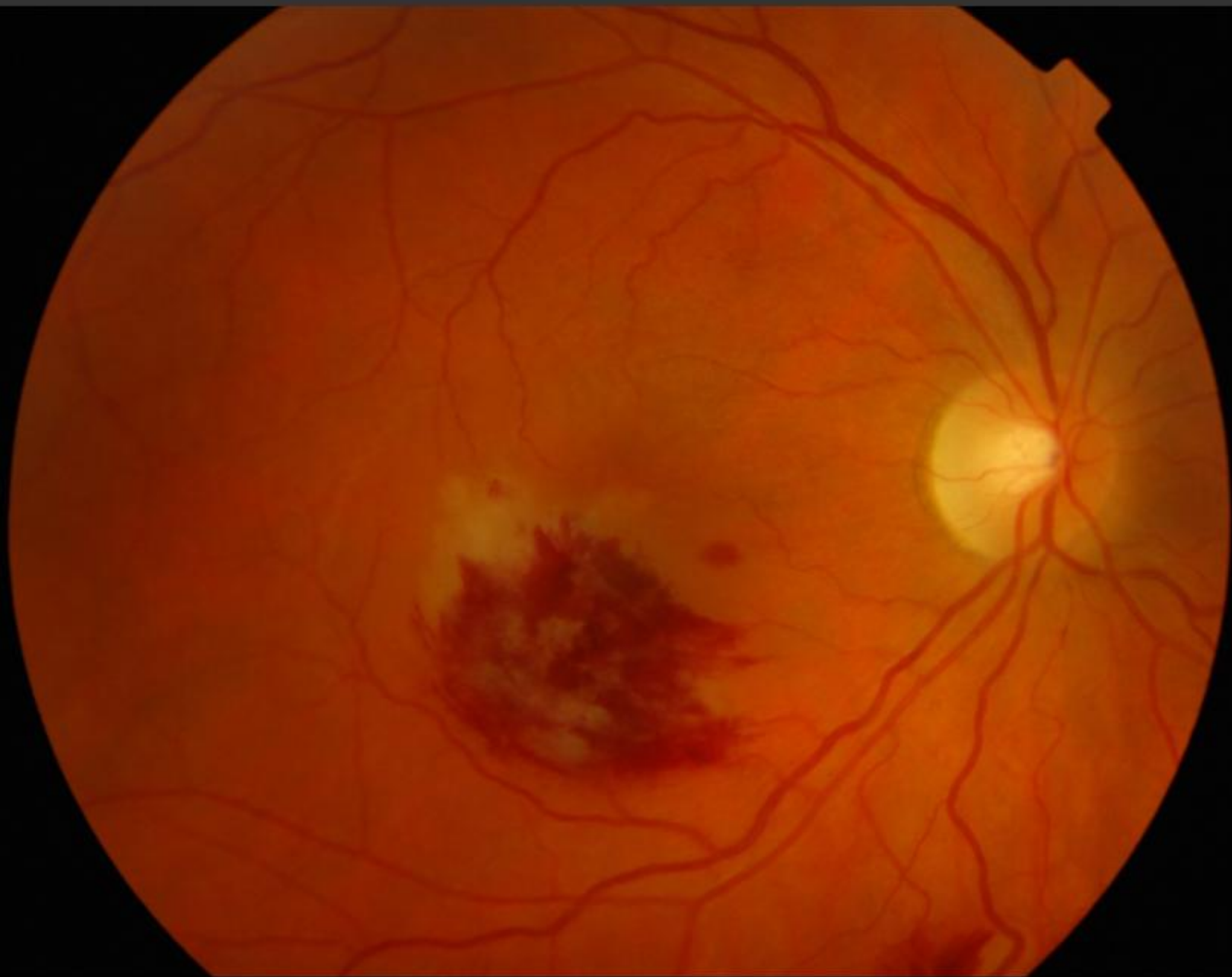


→ Swollen elevated pale lesion with overlying haemorrhage

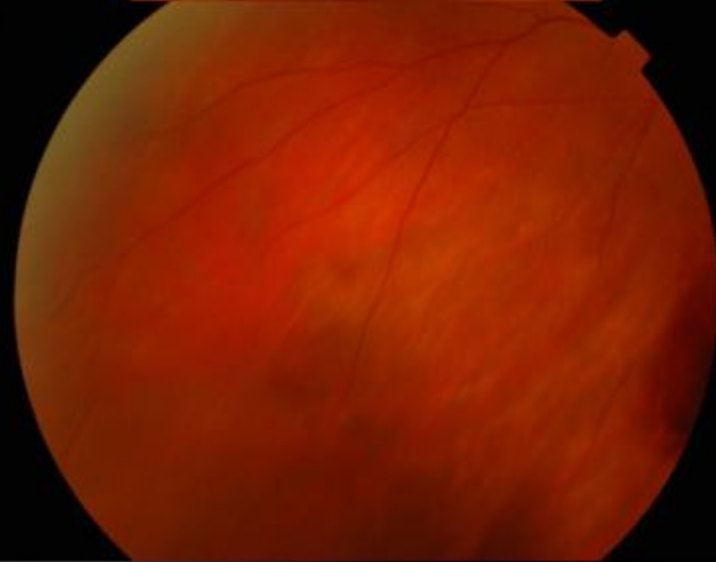
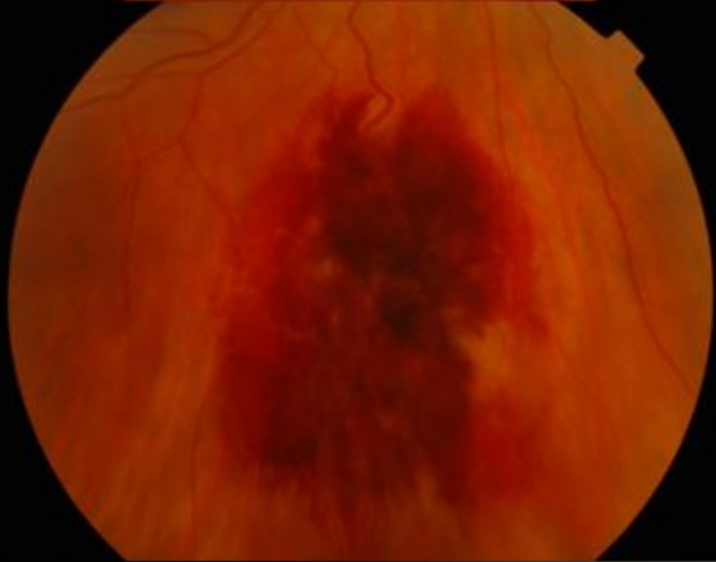
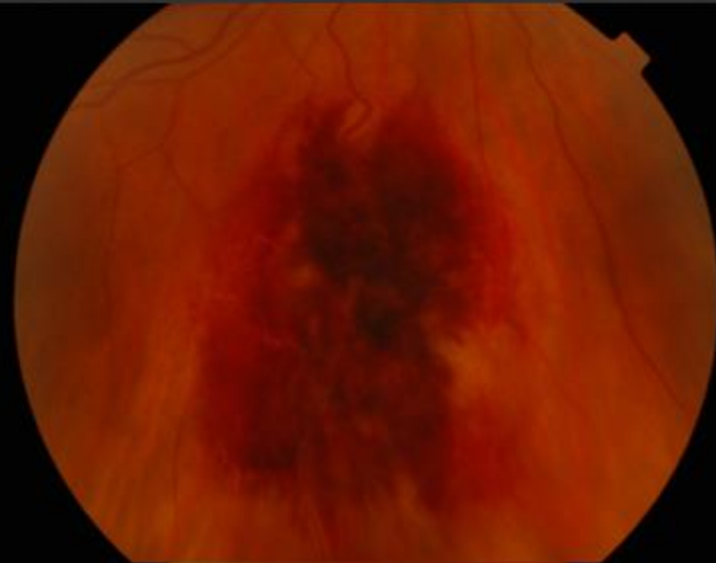
→ No signs of vitritis, retinitis

## Blood Count (18/2/2013)

WCC: **1.4** (4-11 x 10<sup>9</sup> /L)  
Hb: **90 g/l** (140-180 g/L)  
Plt: **13** (150-400 x 10<sup>9</sup> /L)  
Neu: **0.9** (2.5-7.5 x 10<sup>9</sup> /L)

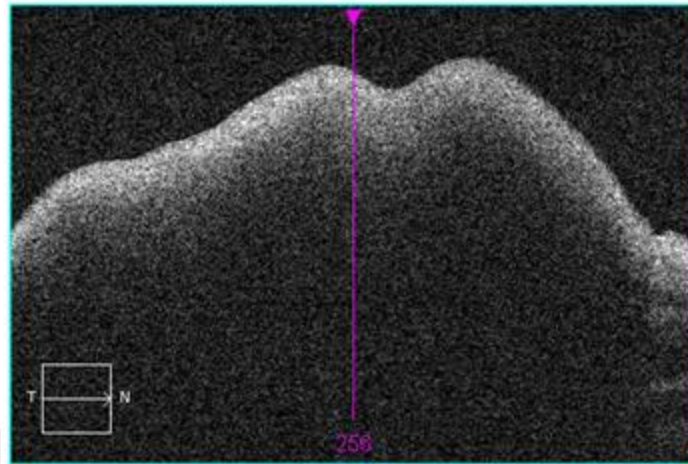
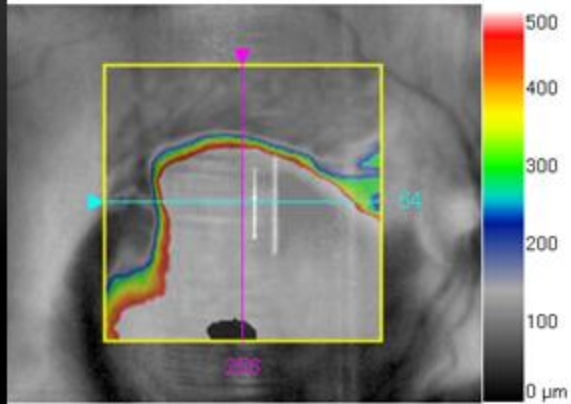




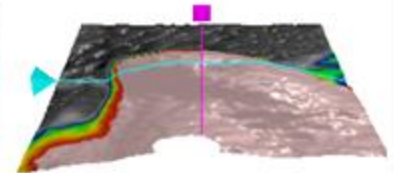




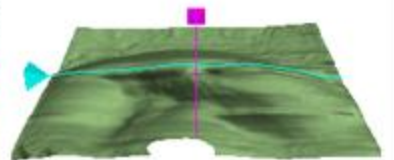
Signal Strength 6/10



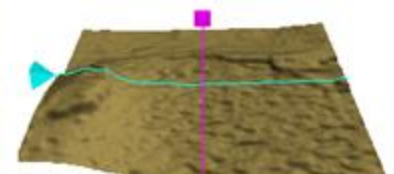
ILM - RPE



ILM



RPE

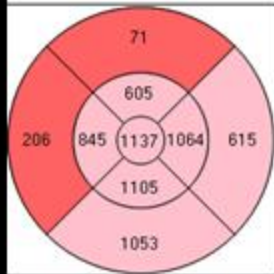


Overlay   
Transparency

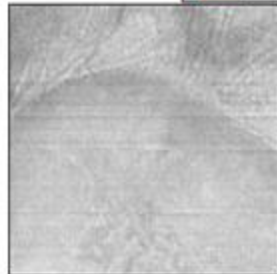
	Thickness Central Subfield ( $\mu\text{m}$ )	Volume Cube ( $\text{mm}^3$ )	Thickness Avg Cube ( $\mu\text{m}$ )
ILM - RPE	1137	19.8	554

Diversified: Distribution of Normals

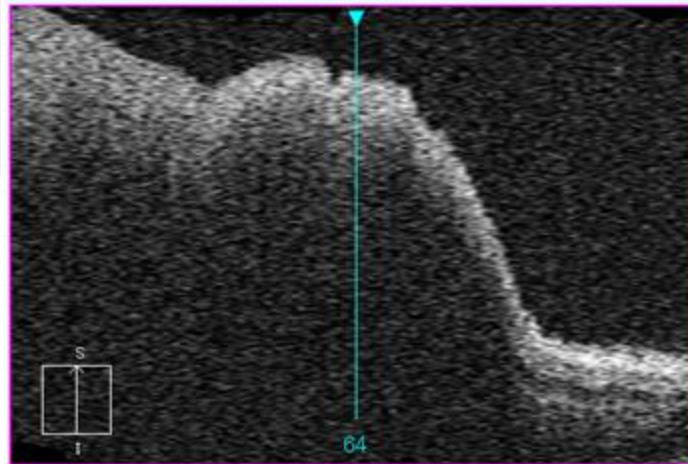
- 99%
- 95%
- 5%
- 1%



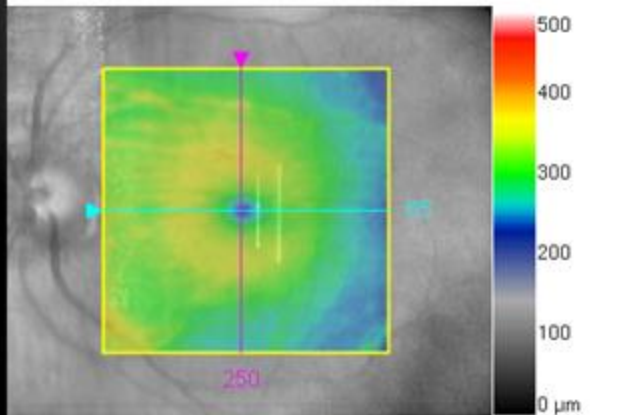
ILM-RPE Thickness ( $\mu\text{m}$ )



Fovea: Not found



Signal Strength 9/10

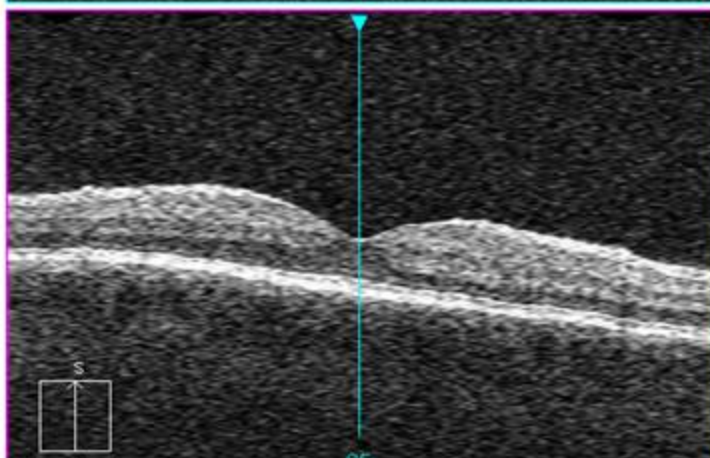
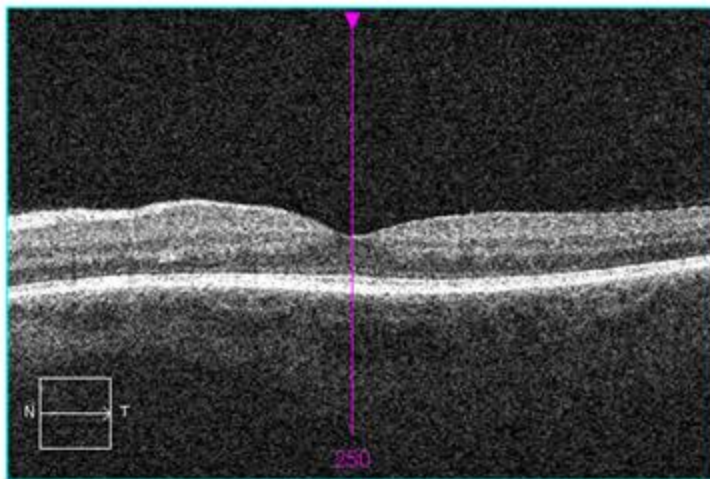
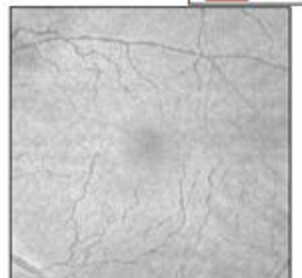
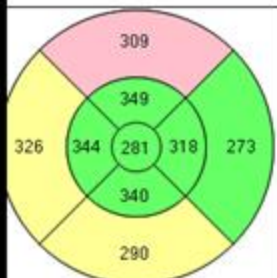


Overlay: ILM - RPE  
Transparency: 50%

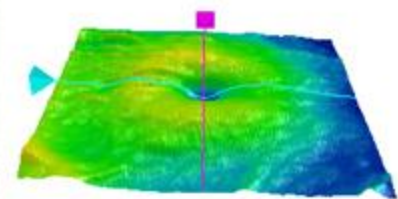
	Thickness Central Subfield (µm)	Volume Cube (mm³)	Thickness Avg Cube (µm)
ILM - RPE	281	10.8	301

Diversified Distribution of Normals

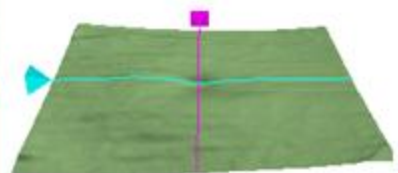
- 99%
- 95%
- 5%
- 1%



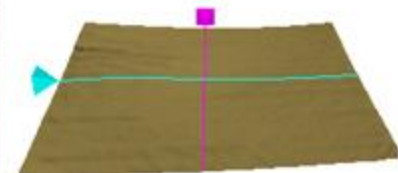
ILM - RPE



ILM

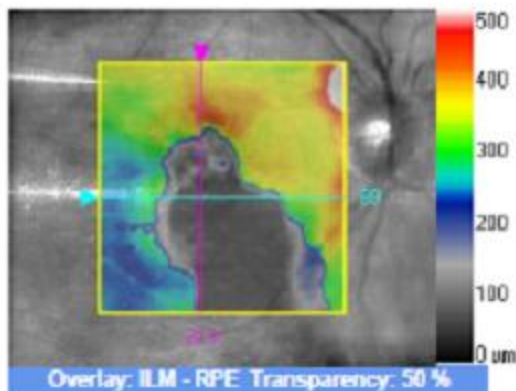


RPE

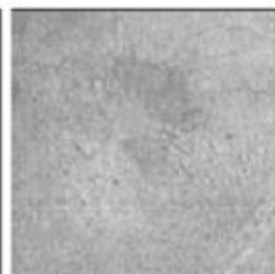


## THE CASE – MRS D.A.

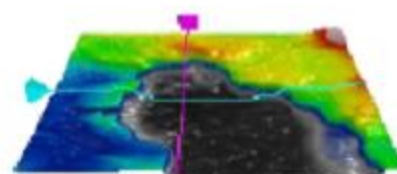
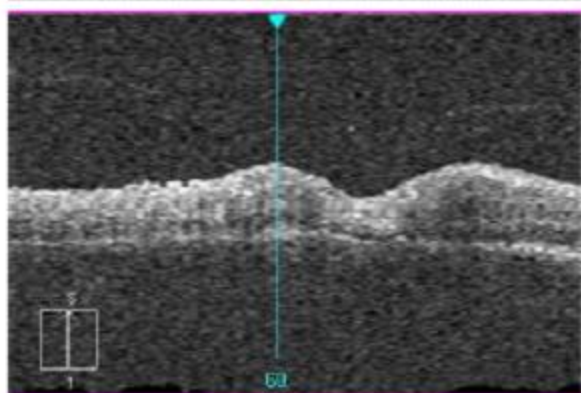
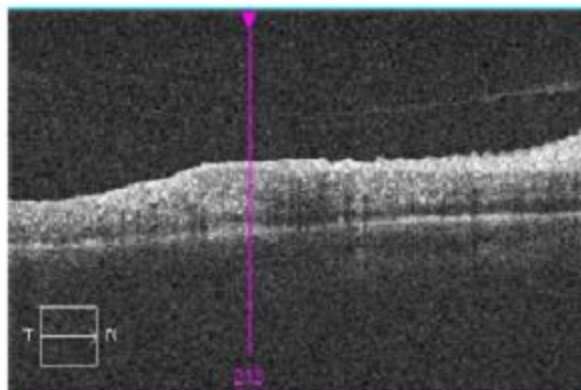
- Referred back to haem-oncologists for further management → ?relapse ?refractory
- No active ophthalmic management required
- Review in medical retina clinic 1/12



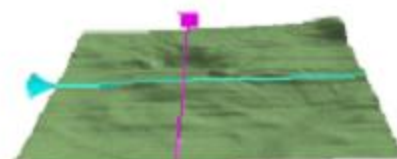
ILM-RPE Thickness ( $\mu\text{m}$ )



Fovea: 213, 69



ILM - RPE

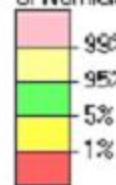


ILM



RPE

Diversified:  
Distribution  
of Normals



	Central Subfield Thickness ( $\mu\text{m}$ )	Cube Volume ( $\text{mm}^3$ )	Cube Average Thickness ( $\mu\text{m}$ )
ILM - RPE	32	8.7	242

# CHRONIC MYELOID LEUKEMIA

## KEY FACTS:

- Uncontrolled clonal proliferation of myeloid cells
  - Classified as a **myeloproliferative disorder** → cells proliferate yet retain ability to differentiate
- **15%** of leukemias
- **Philadelphia Chromosome**
  - Present in >80%
  - Hybrid chromosome- reciprocal translocation between long arm chr 9 + long arm chr 22- **t(9;22)**
  - Forms a fusion oncogene **BCR/ABL on chr 22- tyrosine kinase**
  - Without Ph chromosome worse prognosis.

# CHRONIC MYELOID LEUKEMIA

## NATURAL HISTORY:

- Median survival **5-6 years**
- 3 phases:
  - **CHRONIC** → last months/years, few symptoms
  - **ACCELERATED** → increasing symptoms, spleen size and difficulty in controlling counts
  - **BLAST TRANSFORMATION** → features of acute leukemia

## SYMPTOMS:

- WL, tiredness, fever, sweats
- Gout (from purine breakdown)
- Bleeding (platelet dysfunction)
- Abdo discomfort (splenomegaly)

**30% detected by chance**



# CHRONIC MYELOID LEUKEMIA

## SIGNS

- Splenomegaly (>75%) – massive
- Hepatomegaly
- Anaemia
- Bruising

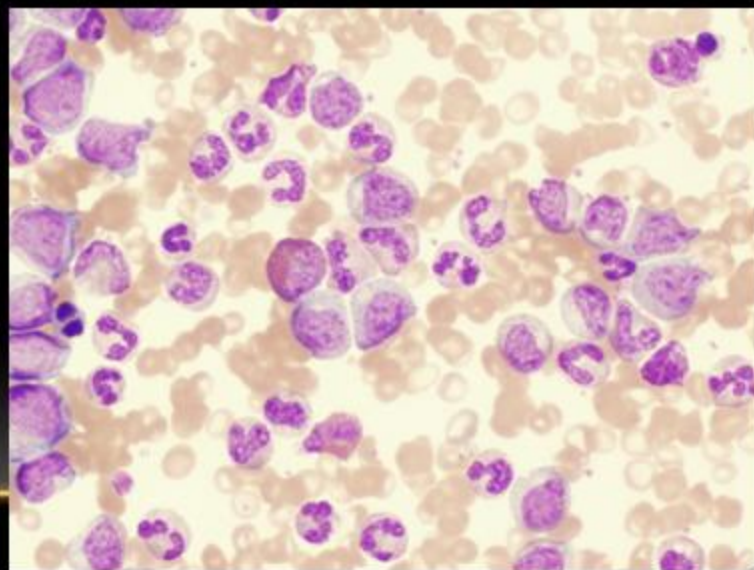
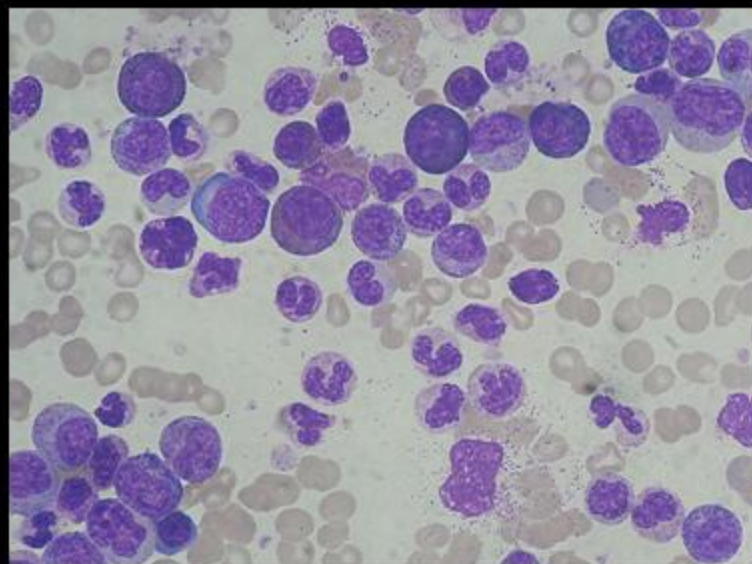
## INVESTIGATIONS

1. Blood picture → **WBC** ↑↑↑ ( $>100 \times 10^9/L$ )- with whole spectrum of myeloid cells
2. **Hb** ↓/N
3. Plt – variable
4. **Urate, vit B12** ↑
5. Ph on cytogenic analysis of blood or BM aspirate

# CHRONIC MYELOID LEUKEMIA

## TREATMENT:

- **Imatinib** – a specific BCR/ABL tyrosine kinase inhibitor
- **Hydroxycarbimide** – used in patients intolerant to imatinib
- **Stem cell transplantation** – allogenic HLA matched sibling/unrelated donor
  - Long term survival advantage

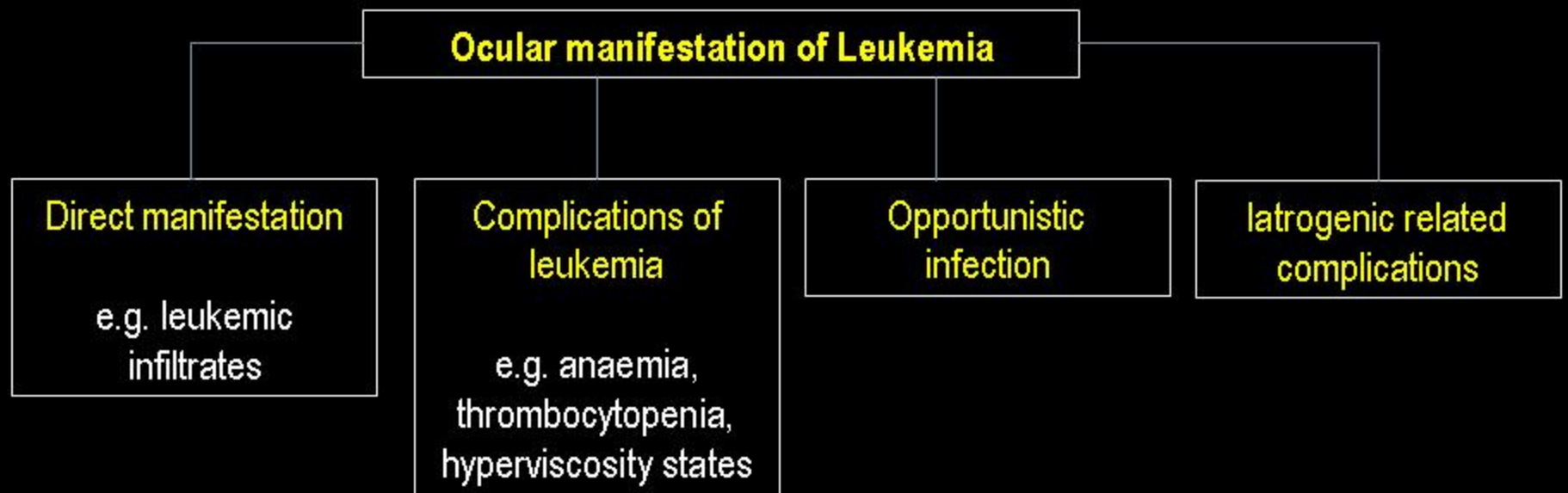


# LEUKEMIC RETINOPATHY

- Ophthalmic symptoms and findings may be **the initial manifestation** of systemic disease
  - Frequency of intraocular involvement range from **9-90% of cases**.
  - Intraocular manifestation of haematological malignancies **commonest cause of secondary or metastatic neoplastic** disease
  - **All structures** can be involved- wide spectrum of presentation
-

# LEUKEMIC RETINOPATHY

## CLINICAL MANIFESTATION



# LEUKEMIC RETINOPATHY

## Leukemic infiltrates

- Kawabara and Aiello – CML patient with **large grey-white nodules of varying sizes** in retina<sup>1</sup>
  - “ominous” prognostic sign, associated with high blood counts, early demise.
- Merle et al – **subretinal infiltrates with venous vasculitis** in T-cell leukemia<sup>2</sup>
- Grey-white streaks along blood vessels – **local perivascular leukemic infiltrates**<sup>3</sup>

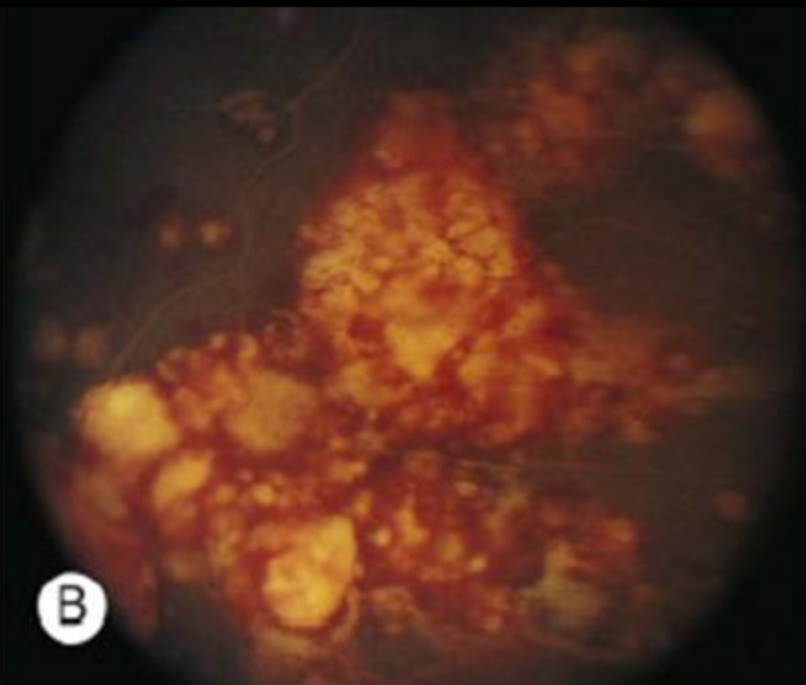
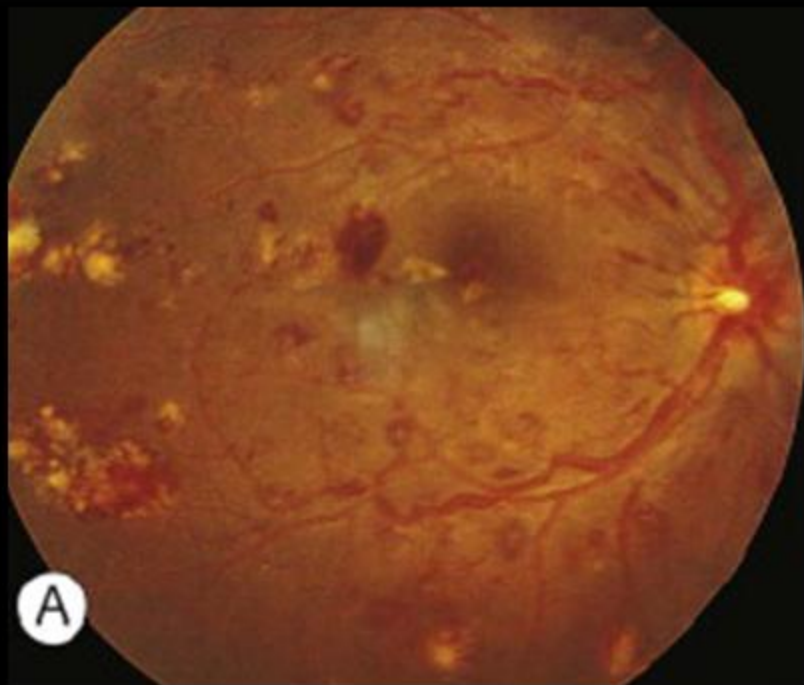
<sup>1</sup> Kawabara T, Aiello L. Leukemic military nodules in the retina. Arch Ophthalmol 1964; 72: 494-7

<sup>2</sup> Merle H, Donnio A, Gonin C et al. Retinal vasculitis caused by adult T-cell leukemia/lymphoma. Jpn J Ophthalmol, 2005; 49: 41-45

<sup>3</sup> Kim TS, Ducker JS, Hedges TR. Retinal angiopathy resembling unilateral frosted branch angiitis in a patient with relapsing acute lymphoblastic leukemia. Am J Ophthalmol 1994; 117: 806-808

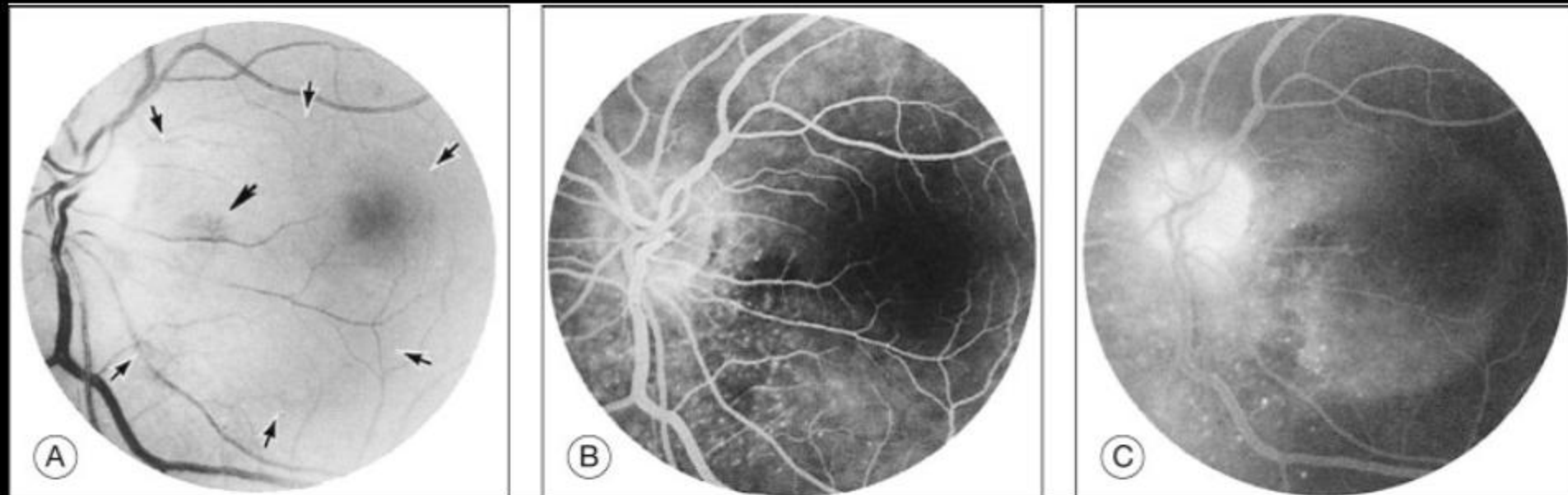
# LEUKEMIC RETINOPATHY

## Leukemic infiltrates



# LEUKEMIC RETINOPATHY

## Choroidal infiltrates



# LEUKEMIC RETINOPATHY

## Vitreous Infiltrates:

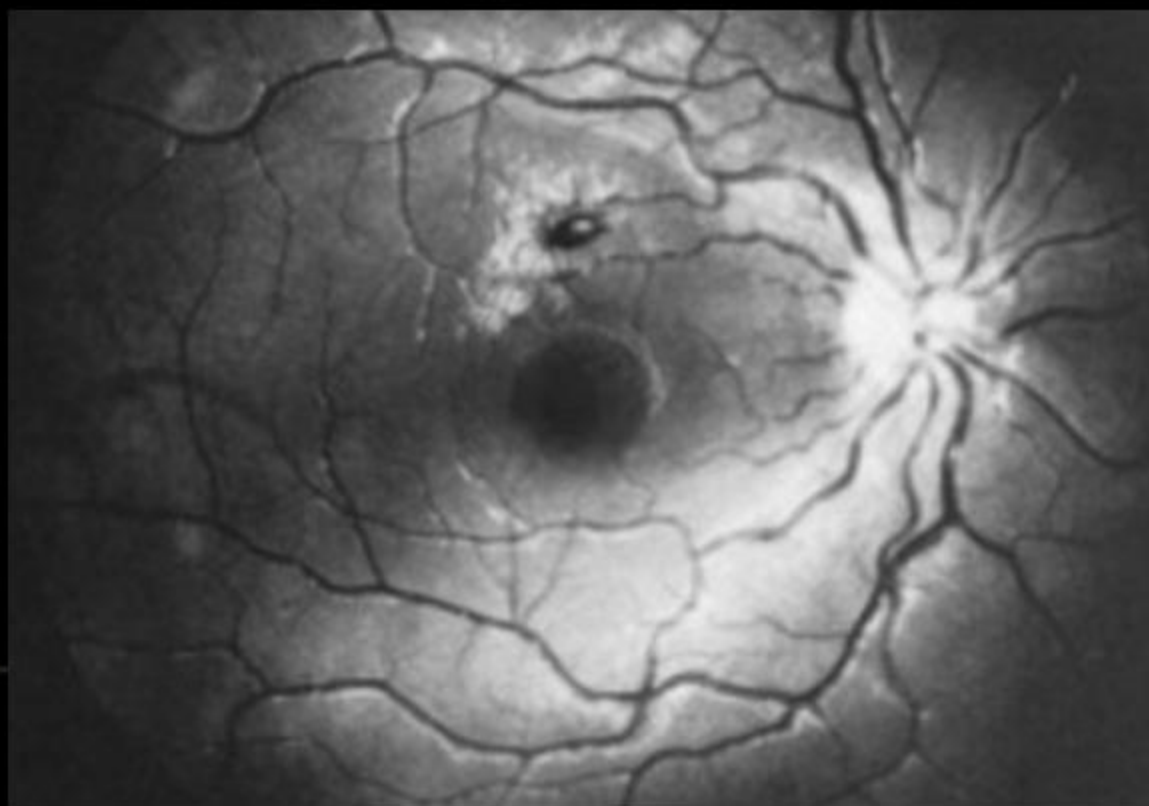




# LEUKEMIC RETINOPATHY

? Leukemic infiltrates → White-centred haemorrhages (NOT PATHOGNOMONIC)

- Aggregates of leucocytes
- DD: fibrin-platelet aggregates

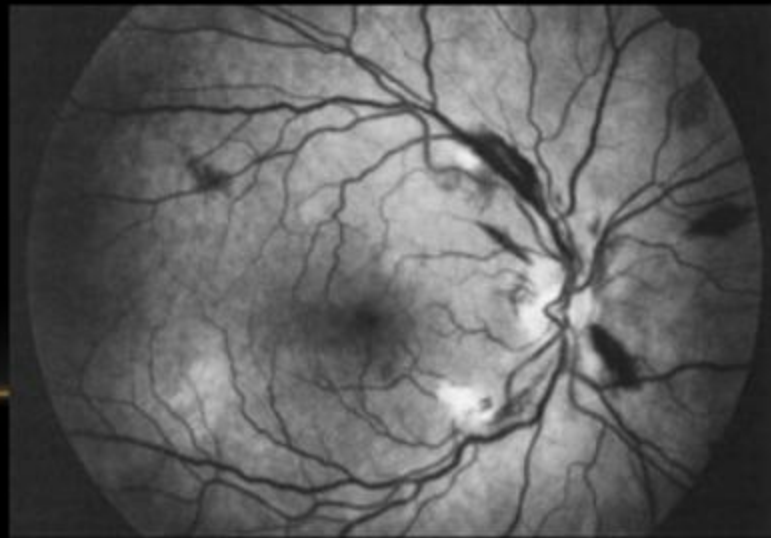
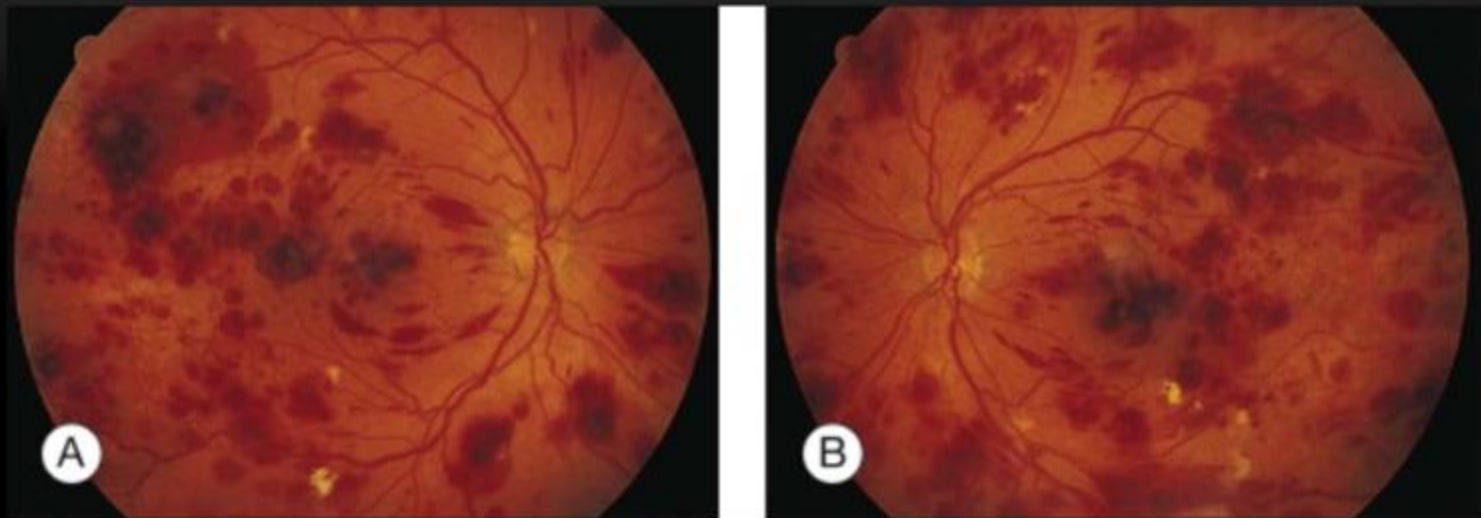


# LEUKEMIC RETINOPATHY

## Manifestations of anaemia and thrombocytopenia

- “Leukemic retinopathy” – classically denotes fundus manifestation of **anaemia, thrombocytopenia, increase blood viscosity**.
- Commonly **acute** leukemias
- Features:
  - **Perivascular sheathing** b/c perivascular infiltrates
  - Veins, arteries → **yellowish tinge** b/c anaemia and leukemia
  - Retina **haemorrhages**
    - Subretinal, deep retinal, superficial retina or pre-retinal → breakthrough into vitreous
  - **Cotton wool spots** → abnormally large cell or cluster of cells occluding retinal arterioles

# LEUKEMIC RETINOPATHY

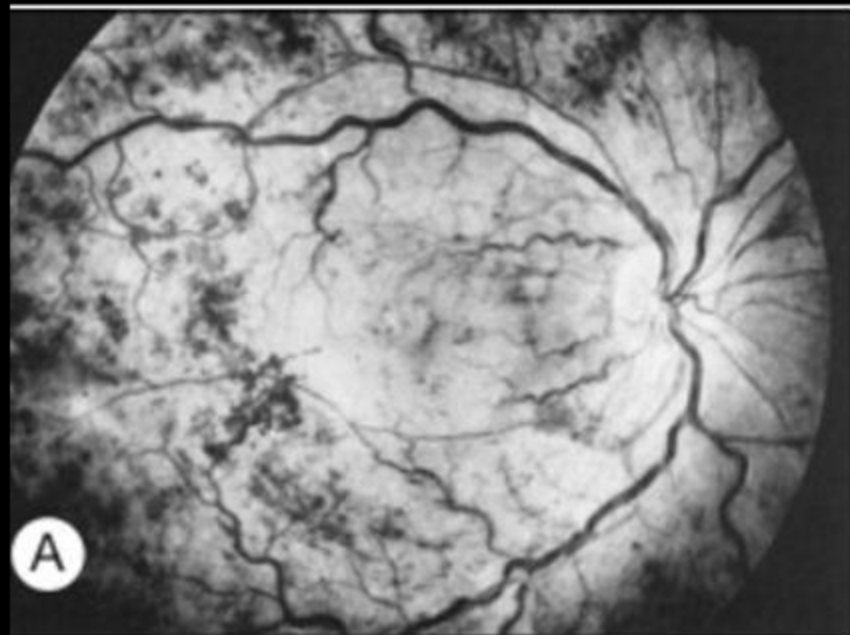


# LEUKEMIC RETINOPATHY

## Manifestations of hyperviscosity

- Veno-occlusive disease → microaneurysm formation, retinal haemorrhages, retinal neovascularisation
- Mild or “hyperpermeable” CRVO
  - Suspect systemic hyperviscosity if bilateral retinal vein occlusion.
- High WCC may lead to poor CSF absorption → bilateral disc swelling (akin to BIH)

# LEUKEMIC RETINOPATHY



# LEUKEMIC RETINOPATHY

## Opportunistic Infections

- Common in immunosuppressed patients.
- Literature:
  - CMV retinitis
  - HTLV-1 associated adult T-cell leukemia can present with necrotizing retinal vasculitis.
  - Herpes virus related retinitis
  - Mumps uveitis in a patient with ALL
  - Progressive outer retinal necrosis (PORN) after BM transplantation in AML.
  - Parasites → ocular toxoplasmosis
  - Fungal intraocular involvement → haem malignancy is a common predisposing systemic factor for fungal infection.
- If diagnostic dilemma → vitreous bx

# LEUKEMIC RETINOPATHY

## Prognosis

- Relationship between leukemic retinopathy to patient survival??
  - *Abu el-Asrar et al* prospectively reviewed 54 patients
  - Among the 35% of patients with leukemic retinopathy, mean survival time was shorter in patients with cotton wool spots than without.
  - 169 days vs 609 days
- *Ohkoshi and Tsiaras* reviewed prognostic significance of leukemic retinopathy in childhood leukemia
- 5 year survival was ↓ in leukemic retinopathy (21.4% vs 45.7%)
- Retinal infiltrates defined as whitish irregular patches near/around retinal vessels associated with leukemia with worse prognosis.

# LEUKEMIC RETINOPATHY

## Treatment

- 1<sup>st</sup> line → Intraocular manifestations treated with systemic chemotherapy
  - If CNS involvement → intrathecal chemotherapy
  - Supportive measures eg blood transfusions → anaemia, thrombocytopenia.
- If leukemic infiltrates fail to respond to systemic CTx → ocular radiation
  - Susceptible to radiation retinopathy with HIGH dose chemotherapy
- If severe hyperviscosity and leukemic retinopathy → ?leukapheresis



# LEUKEMIC RETINOPATHY

## Summary

- Wide spectrum of clinical presentation
  - Leukemic infiltrates
  - Opportunistic infections
  - Complications of leukemia- anaemia, thrombocytopenia, hyperviscosity
- Presence of leukemic retinopathy linked with higher mortality
- Masquerade condition → be aware!
- Refer to haem-oncologists for systemic management