LEUKEMIC RETINOPATHY

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OST1
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- Chronic Myeloid Leukemia
- Leukemic Retinopathy
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
  - Ciprifloxacin
  - Voriconazole
### THE CASE – MRS. D.A.

**Examination:**

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>VA</td>
<td>6/4</td>
</tr>
<tr>
<td>Ishihara</td>
<td>17/17</td>
</tr>
<tr>
<td>Upper nasal quadrant defect</td>
<td>Confrontational VF</td>
</tr>
<tr>
<td>RAPD</td>
<td>no</td>
</tr>
<tr>
<td>Lids</td>
<td>N</td>
</tr>
<tr>
<td>Conj</td>
<td>white</td>
</tr>
<tr>
<td>Cornea</td>
<td>Clear, no staining</td>
</tr>
<tr>
<td>A/C</td>
<td>d+ q</td>
</tr>
<tr>
<td>Iris/Lens</td>
<td>N</td>
</tr>
<tr>
<td>IOP</td>
<td>13</td>
</tr>
</tbody>
</table>
THE CASE – MRS. D.A.

- Examination:

<table>
<thead>
<tr>
<th>pigment</th>
<th>Vitreous</th>
<th>Retina</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>syneresis</td>
<td>NAD</td>
</tr>
</tbody>
</table>

- Swollen elevated pale lesion with overlying haemorrhage
- No signs of vitritis, retinitis

**Blood Count (18/2/2013)**

- WCC: 1.4 (4.1-11 x 10⁹/L)
- Hb: 90 g/l (140-180 g/L)
- Plt: 13 (150-400 x 10⁹/L)
- Neu: 0.9 (2.5-7.5 x 10⁹/L)
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
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 x 10⁹/L) - with whole spectrum of myeloid cells
2. Hb ↓/N
3. Plt – variable
4. Urate, vit B12 ↑
5. Ph on cytogenetic analysis of blood or BM aspirate
CHRONIC MYELOID LEUKEMIA

TREATMENT:

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

Ocular manifestation of Leukemia

Direct manifestation
- e.g. leukemic infiltrates

Complications of leukemia
- e.g. anaemia, thrombocytopenia, hyperviscosity states

Opportunistic infection

Iatrogenic related complications
LEUKEMIC RETINOPATHY

Leukemic infiltrates

• Kawabara and Aiello – CML patient with large grey-white nodules of varying sizes in retina¹
  • “ominous” prognostic sign, associated with high blood counts, early demise.

• Merle et al – subretinal infiltrates with venous vasculitis in T-cell leukemia²

• Grey-white streaks along blood vessels – local perivascular leukemic infiltrates³

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Leukemic infiltrates
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Choroidal infiltrates

1 Gass JDM. Stereoscopic atlas of macular diseases: diagnosis and treatment., 4th Edn. St Louis; Mosby; 1997
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Vitreous Infiltrates:
LEUKEMIC RETINOPATHY

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

• Aggregates of leucocytes
• DD: fibrin-platelet aggregates
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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
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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 BlH)
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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
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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.
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**Treatment**

- 1st line \( \rightarrow \) Intraocular manifestations treated with systemic chemotherapy
  - If CNS involvement \( \rightarrow \) intrathecal chemotherapy
  - Supportive measures eg blood transfusions \( \rightarrow \) anaemia, thrombocytopenia.

- If leukemic infiltrates fail to respond to systemic CTx \( \rightarrow \) ocular radiation
  - Susceptible to radiation retinopathy with HIGH dose chemotherapy

- If severe hyperviscosity and leukemic retinopathy \( \rightarrow \) ?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