INTRODUCTION

- Field details away from our knowledge.
- Curable if treated Vs Lethal disease.
- Many Advances in Staging & Management.
- Privileged experience.
WHAT IS RETINOBLASTOMA?

Malignant tumor of the Embryonic neural retina (fetal Retinoblasts) that normally differentiate into post-mitotic retinal photoreceptor cells and neurons.

INCIDENCE

- 11% of Ped. Cancer in the 1st year but only 3% of all Ped. Cancers up to 15 years.
- 1/13000 birth.
- Nearly 120 new case/year in Egypt.
- 250 case/year in USA.
  • Increased in Africa – South America.
RETINOBLASTOMA IN DEVELOPING COUNTRIES

Incidence may be higher
- Delayed diagnosis
- Advanced intraocular disease at presentation
- Extraocular disease at presentation
- Existence of several barriers to optimal delivery of care
- Poor survival rate

CLASSIFICATION

There are three overlapping parameters for classifying retinoblastoma:

1. Laterality: Tumours may be unilateral or bilateral
2. Focality: Tumours may be unifocal or multifocal
3. Genetics: Tumours may be hereditary (40%) or nonhereditary (sporadic 60%)
Other Method to Classify RB according to pattern of growth:
1- Endophytic
2- Exophytic
3- Surface infiltration
4- Combined
ENDOPHYTIC  

EXOPHYTIC  

AETIOLOGY

Genetic determined (2 Hits Hypothesis)

1st Step: Mutation of RB1 gene (13q14)

Tumour suppressor gene that regulates Cellular proliferation

2nd Step: Anti Apoptotic Changes Resulting in Decreased Cell Death
PATHOLOGY

- The tumour is composed mainly of undifferentiated Anaplastic cells that arise from the nuclear layers of the retina.
- Aggregation around blood vessels, necrosis, calcification, and Flexner-Wintersteiner rosettes.
- Retinoblastomas are characterized by marked cell proliferations evidenced by high mitosis counts.

PATTERNS OF SPREAD

1- Direct: Retinoblastoma invades the optic nerve. From there it can spread directly along the axons to the brain or may cross into the subarachnoid space and spread via the cerebrospinal fluid to the brain.

2- Hematogenous spread leads to metastatic disease, most commonly to brain, bone marrow, or bone.

3- Lymphatic spread is rare (preauricular and submandibular).
CLINICAL PRESENTATION

- Leukocoria
- Squint
- Impaired vision
- Others:
  - Glaucoma
  - Hyphema
  - Uveitis
  - Orbital

Presentations of retinoblastoma

- Leukocoria - 60%
- Strabismus - 20%
- Secondary glaucoma
- Anterior segment invasion
- Orbital inflammation
- Orbital invasion
LEUKOCORIA

AIM OF MANAGEMENT

1- Save Life
2- Save Vision
3- Preserve the Eye globe
**MANAGEMENT**

1. Group Work in Multidisciplinary Centers
   - Ped. Ophthalmologist
   - Ped. Onchologist
   - Radiodiagnosis
   - Radiotherapist
   - Pathology
   - Psychiatrist (Pediatric)

**OR SETUP**

![OR Setup Images]
MANAGEMENT
2- PROPER DIAGNOSIS & STAGING:

Compulsory

- Initial Evaluation
- EUA + RetCam
- B Scan US
- FA
- Full physical exam
- CBC, Electrolytes,
- CT/MRI for brain & orbit

Optional

- Lumbar puncture
- Bone Scan
- Audiometry

STAGING
Reese-Ellsworth Classification

- 1a  Solitary tumor  Less than 4 disk diameters
  At or behind the equator
- 1b  Multiple tumors  None more than 4 disk
  All at or behind the equator
- 2a  Solitary tumor  4–10 disk diameters in size
  At or behind the equator
- 2b  Multiple tumors  4–10 disk diameters in size
  At or behind the equator
- 3a  Tumor anterior to the equator
- 3b  Solitary tumor  More than 10 disk diameters
  At or behind the equator
- 4a  Multiple tumors  More than 10 disk diameters
- 4b  Tumor anterior to the ora serrata
- 5a  Massive tumors involving more than half the retina
- 5b  Vitreous seeding

International Classification

GROUP I: Small intraretinal tumors away from foveola and disc
- GROUP II: All remaining discrete tumors confined to the retina
- GROUP III: Discrete local disease with minimal subretinal or vitreous seeding
- GROUP IV: Diffuse disease with significant vitreous or subretinal seeding
- GROUP V: Presence of any one or more of these poor prognostic features:
  - Tumor touching the lens
  - Tumor anterior to the anterior vitreous face
  - involving ciliary body or anterior segment
  - Diffuse infiltrating retinoblastoma
    - Neovascular glaucoma
    - Opaque media from hemorrhage
  - Tumor necrosis with aseptic orbital cellulites
    - Phthisis bulbii
GROUP A

GROUP B

GROUP C

GROUP D
GROUP E

Fluorescin Angiogram

INTENSE HYPERFLUORESCENCE AND A FINE VASCULAR NET - WORK WITHIN MODERATELY SIZED TUMORS. LATE PHASES OF THE ANGIOGRAM SHOW MARKED STAINING AND LEAKAGE.
TREATMENT OPTIONS

1- Chemotherapy
2- Local treatment
3-Intrarterial Melphalan
4-Intravitreal Melphalan
5- Combined approaches
6- Radiotherapy
7- Combined approaches
8- Enucleation

MANAGEMENT

Unilateral Retinoblastoma

Gr A: Local
Gr B: 2 cycles of Low Chemo then local
Gr C: 2-6 cycles of Low Chemo and local
Gr D: chemo trial (intrarterial) Vs primary Enucleation
Gr E: Enucleation
MANAGEMENT

Bilateral Retinoblastoma

6 cycles of Low/High dose VEC with follow up every 2 cycles for local ttt

Failure:
Radiotherapy/ Enucleation / Combined Chemo-Radio

ROLE OF CHEMOTHERAPY

Chemoreduction
Thermochemotherapy
Neoadjuvant ttt
Chemoprevention in High risk (Adjuvant)
Palliative ttt in Metastatic & Extraocular
RADIOTHERAPY

External Beam Radiotherapy (ERBT)
- Radiosensitive
- Major Complications
  - Dry eye
  - Retinopathy
  - Retarded orbital development
  - Restrictive motility
  - Secondary malignancy (Orbital Sarcoma)

LASER THERAPY

Diode laser IQ 810
- CW-Pulse Mode
- Long pulse mode induce photoagulation

Diode Laser IQ 810
TTT Modality
Using Long pulse mode with low power to give thermal effect by increasing the temperature of tissue to 40-60 °C
LOCAL THERAPY

1- Lasers
2- Cryotherapy
3- Brachytherapy
4- Transpupillary Thermo Therapy TTT
5- Enucleation

Local Laser treatment

- Local primary treatment
- Local consolidation treatment
Consolidation by laser

DIODE LASER ( TTT )
CRYOTHERAPY

• Cryotherapy is the technique of precise freezing and thawing of undesirable tissue, resulting in cell death and regression.
• It produces intracellular crystal formation which destroy the tumour by interrupting microcirculation.
Scleral implantation of radioactive seeds transiently with 40-Gy

**SELECTION OF FOCAL THERAPY**

Selection is based on size and location of the tumor according to the following:

<table>
<thead>
<tr>
<th>Tumor location</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posterior tumors</td>
<td>Laser</td>
</tr>
<tr>
<td>Anterior tumors</td>
<td>Cryotherapy</td>
</tr>
<tr>
<td>Minimal vitreous seeds</td>
<td>Intravitreal chemotherapy</td>
</tr>
<tr>
<td>Tumors that cannot be consolidated with laser or cryotherapy and are not in need of external beam radiotherapy</td>
<td>Brachytherapy</td>
</tr>
</tbody>
</table>
SIGNS OF REGRESSION

FISH FLESH SIGN
FLAT SCAR

FRAGMENTATION
ENUCLEATION

- Excellent-Efficient-Cost effective Option
- Primary
  Unilateral advanced
  In Bilateral for more advanced eye
- Post Chemoth. Failure
- Strict measures for intraoperative hemostasis
- +/- Orbital Implant

POST TREATMENT FOLLOW UP

- Regular Ophthalmologic Exam every 1-3 Months

- Systemic Evaluation every 3 Months

- For 3-5 years from End of treatment
PLAN OF FOLLOW UP

Phase 1: During the course of treatment according to the roadmap
- To evaluate the response to chemotherapy
- Apply local treatment
- To trace any complications
- Failure of treatment and risk factor
RESPONSE TO CHEMOTHERAPY

OCT EVALUATION
OCT EVALUATION

INITIAL

AFTER 2 CYCLES
Phase 2: Regular follow up 1-3 ms increasing to every 6ms up to 5 years following the stability of the condition

- To ensure stability
- Detection of local recurrences in old tumours
- Detection of new lesions
- Detection of risk factor
- Tracing any complications
APPLICATION OF LOCAL TREATMENT

NEW LESION IN OTHER EYE
ACTIVATION OF OLD LESIONS

FAILURE OF TREATMENT AND RISK FACTOR
WHAT ARE THE OPTIONS OF TREATMENT OF RECURRENT CASES

- Local treatment with laser and cryo (size and accessibility)
- If it is unilateral and aggressive — enucleation
- If it is one eyed or eye with vision potential

**3 EBR????????**
1. Inrarterial chemotherapy
2. Intravitreal Melphalan
4. Enucleation
Cases can answer this question

ONE EYED PATIENT SEQUELE OF TTT
INITIAL STAGING
11/2015------12/2016

2017 STARTING FOLLOW UP EVERY 2 WEEKS AND 1ST INTRAVITREAL 4/2017
AGGRESSIVE SEEDS IN 8/2017 LASER AND REINJECTION WITH GOOD RESPONSE TILL THE LAST VISIT 29-10-2017

OTHER CASE READY AT DAY OF INTRAVITREAL MELPHALAN
CASE UNILATERAL C
25/6/2014 TO 12-2016 RECURRENCES TREATED WITH LASER

ON 14/5/2017 AGGRESSIVE RECURRENCE OF ORIGINAL TUMOUR
COMBINED DECISION ENUCLEATION # INTRARTERIAL
POST INTRARTERIAL MELPHALAN TO LAST FOLLOW UP 5-11-2017

VIDEO
OCULAR SURVIVAL: UNILATERAL DISEASE

OCULAR SURVIVAL BILATERAL DISEASE
CONCLUSIONS

• There is no doubt that the application of different treatment modalities among a multidisciplinary system in the treatment of retinoblastoma gives a very good percentage of success despite the relatively late presentation and the higher incidence of advanced cases.

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THANK YOU