RETINOBLASTOMA- NEWER CONCEPTS

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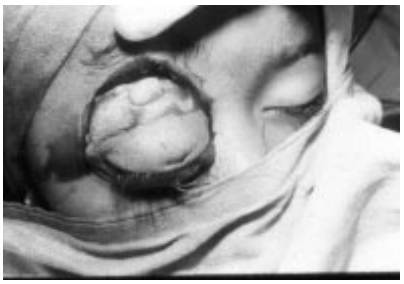
Introduction

Major advances in the diagnosis and clinical management of retinoblastoma have increased survival of retinoblastoma patients leading to new challenges including reduction in the second tumor rate association with current treatments and enhancements of visual outcome especially in patients with bilateral diseases. However trilateral retinoblastoma has a poor prognosis.

It is the most common intraocular tumor of childhood forming 1-3% of all pediatric tumors.

It is also the second most common primary intraocular tumor in humans after uveal melanoma. The incidence being 14000 to 34000 live births. The mortality reported was 87% in 1897, 41% in 1931, currently down to 8%.



REESE ELSEWORTH CLASSIFICATION (1950)

This was proposed to predict survivability after external beam radiotherapy but has drawbacks.

a. Anterior lesions classified into advanced stages IIIA, IVB.
b. Vitreous seeding classified as stage VB

DESUTTER HOPING CLASSIFICATION

It is based on the outcome of eye saving conservative treatment and globe salvage achieved.
Five parameter were identified and points are assigned to each of the following parameters

1. No of tumors
2. Size of tumor
3. Retinal detachment
4. Vitreous seedling and tumor site

Group assigned in Desutter Hoping classification

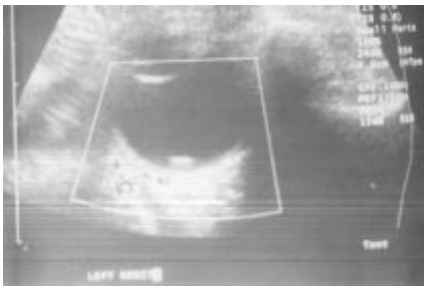
CLASSIFICATION	POINTS
PROGNOSIS	EYE SALVAGED
I	0-1
Very favourable	93%
II	2-6
Favourable	69%
III	7-13
Unfavourable	26%
IV	14-29
Very unfavourable	10%

HUNGER FORD MODIFICATION

I same
II II+ III of old and vitreous seeding
III IV + V of old

INVESTIGATIONS

A. Baseline hematological prior to therapy
B. USG B scan



C. Color Doppler for vascularity (to study response of treatment
D. CT scan and DTPA enhanced MRI scan
E. Fluorescein for vascularity
F. Aqueous tap for LDH levels
G. Carcinoembryonic antigen and alpha feto protein levels are elevated
H. Aqueous levels of alpha and gamma sub units of enolase are elevated

I. Esterase enzyme is used as a screening test

TREATMENT

Our aim of treatment is

1. preserve life
2. retain eye
3. retain vision
4. cosmesis

Various methods of treatment

1. external beam Radiotherapy
2. chemotherapy
3. laser
4. cryo
5. enucleation
6. exenteration

EXTERNAL BEAM RADIOTHERAPY

External beam radiotherapy has been employed as a standard therapy in patients with bilateral retinoblastoma

To treat the eye with less involvement

It is also used in cases with posterior tumors involving macula and near the disc.

Optic nerve invasions and intracranial extensions

It is used in the tumors of more than 3 disc diopters and more than 2.5 mm thick.

A 6 mev linear accelerator is utilized with anterior and lateral ports and a lens-sparing device. The total dose ranges from 3500 to 5000 cCy. distributed over 15 – 25 fractions with a daily dose of 200 rads over a period of 20-35 days. The complications have been eliminated by reducing the total dose and the number of fractions.

A more recent study showed significant tumor development in the radiation field in infants who received radiation therapy as a primary treatment before 12 months but not in patients irradiated after 12 months of age.

CHEMOTHERAPY

This is based on

1. St Judes experience.
2. Children cancer study group.

Indication

1. extraocular retinoblastoma – orbital spread
2. high risk for metastasis like choroidal invasion and optic nerve involvement
3. shrink the tumor away from the macula and the disk.
4. patients with intracranial metastasis are given inj methotrexate, arabinoside, hydrocortin

Chemotherapy is now being combined with serial aggressive local therapy (SALT).

RADIOACTIVE PLAQUE THERAPY (BRACHYTHERAPY)

To reduce the risk of second tumors and to restrict the orbital area exposed episcleral radiation plaques are employed. The plaques are iodine 125, cobalt 60, iridium 192, and ruthenium 106. The major role of brachytherapy is in treating unifocal tumors with basal diameters less than 16 mm and thickness less than 8 mm. It is also used in treating tumors that have failed prior therapy like external therapy and cryo. It is also used in treating vitreous seedlings.

CRYO AND LASER PHOTOCOAGULATION

Small tumors (< 3.5 mm in diameter and less than 2 mm thick) respond well to cryotherapy and tumors less than 4.5 mm diameter and 2.5 mm thick respond well to laser. Cryotherapy normally involves 2-3 sessions of triple freeze and thaw cycles. Laser photocoagulation involves the placement of a double row of confluent burns around the tumor to destroy the vasculature.

ENUCLEATION

It is done in advanced stages where other treatment has failed.

GENETIC COUNSELLING

Parents of all patients should be counselled keeping in mind the hereditary basis of retinoblastoma and 15% of unilateral sporadic retinoblastoma patients are gene carriers.

NEWER MODALITIES

A. Cyclosporin is given to prevent multidrug resistance due to overexpression of p-glucoprotiens. It improves long term response of retinoblastoma to chemotherapy.
B. Thermochemotherapy. This involves systemic carboplatin followed by continuous diode laser hyperthermia i.e heat which is synergestic with platimum is given to the eye.

The advantage is that the cytotoxicity of

carboplatin is enhanced. Carboplatin is given and within 1-4 hrs

Transpupillary laser hyperthermia is given for 15-30, min for 2-3 cycles over 4-7 days.

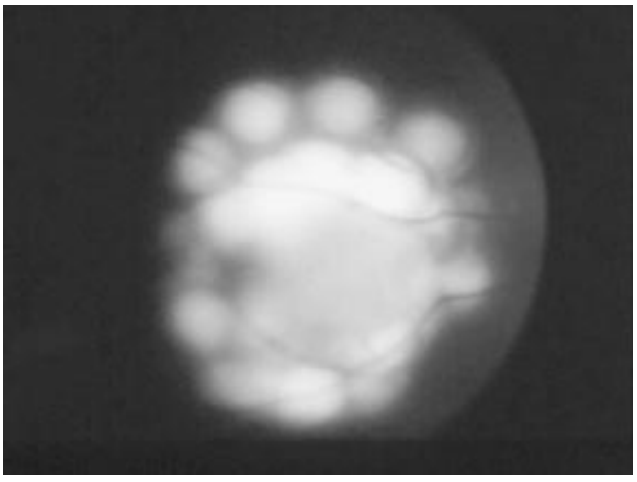
C. Photodynamic therapy is based on the principle of production of singlet oxygen by light activation of photo-sensitizer that is benzoporphyrin which is a derivative of a monoacid ring in 690 nm range (infrared) . This is retained in the choroidal neovasculature causing disruption of cellular structures and occlusion of vessels. Drug injecton is by IV pump over 10 min; 5 min is the waiting period. Drug accumulates in abnormal vessels, infrared laser applied through a slit for 83 seconds to activate photosensitizer, which activates vertiporfin. This causes production of active oxygen which results in cell death. This is repeated after 3 months.

D. Transpupillary thermotherapy. This employs a large spot size of 3 mm of modified diode laser that is directed over the lesion for several minutes. Long exposures to low level irradiations produces temperatures sufficient to produce hyperthermia but not coagulation of tissues. TTT penetrates to a depth of 4 mm and produces extensive vascular thrombosis.

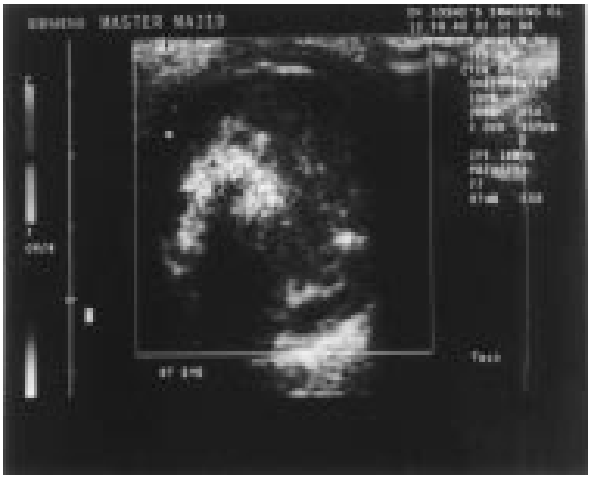
E. Other treatment modalities include vitamin D; differentiating agents like butyrate , retinoic acid and hexamethalenebis-acetamide; immunomodulation and radiosensitizers like misonidazole and SR-2508. monoclonal antibodies F(ab')2:ricin-A and interferon.

REFERENCES

1. Murphee,: retinoblastoma tumors of the retina Vol1, Stephan J. Ryan.1989
2. Shields J.A : Diagnosis and management of intraocular tumors 1983.
3. Marita Uusitalo, Sharon Wheeler and Joan M.O'Brien Ocular oncology Ophthalmology clinics of north America 0896-1549/99
4. Abramson DH: the focal treatment of retinoblastoma with emphysis on zenon arc photocoagulation. Acta Ophthalmol 194 (suppl) 3-63, 1989
5. Roarty JD, McLean IW, Zimmerman LE : incidence of second neoplasms in patients with bilateral retinoblastoma. Ophthalmology 95:1583-1587, 1988



Retinoblastoma treated by xenon arc photocoagulation



Colour doppler in retinoblastoma