GLOBAL JOURNAL OF BIOLOGY, AGRICULTURE & HEALTH SCIENCES
(**Published By**: Global Institute for Research & Education)
www.gifre.org

MULTIMODALITY APPROACH IN MANAGEMENT OF RETINOBLASTOMA A CASE REPORT AND REVIEW OF LITERATURE

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Abstract
We Report a case of retinoblastoma, which was treated by multidisciplinary approach, completed 13 yrs of follow-up, with no complication and good cosmesis.

Key words: Retinoblastoma, multimodality treatment.

1. Introduction
Retinoblastoma is most common primary intra-ocular solid tumour of childhood [1]. The incidence is approximately one in 15000 to 18,000 live births. [2] Boys are more affected than girls. More than 90% of retinoblastoma cases present before the age of 5years. Approximately 60-70% of patients have unilateral disease, rest have bilateral and 10% have a family history of Retinoblastoma. [3, 4]

Retinoblastoma is broadly divided into hereditary and sporadic in their presentation. The etiology of retinoblastoma is yet unknown, but deletion of long arm of Chromosome 13 is associated with most of the tumors. [3]

The presence of retinoblastoma may come to attention by mother. Pupillary white reflex, leukokoria or squint in older children or complete loss of vision. Extra-occular invasion and orbital proptosis and even clinically palpable node presents in advanced stage.

The primary objectives of therapy are first to save the life of the child, and secondary to preserve the eye and finally to maintain the vision. Currently the Oncologist utilizes surgery, radiation therapy, cryotherapy, photocoagulation and chemotherapy in the management of retinoblastoma to increasingly accomplish these goals with high degree of success.

2. Case Report
A 4 ½ years old female child presented as postoperative case with history of loss of vision in right eye since 2 months duration. She was operated 1 ½ month back. Enucleation was done under general anaesthesia. On examination her vitals was stable with intact higher mental functions. On ophthalmological examination her vision 6/6 in left eye. Her other systems and cranial nerves were normal.

Her routine blood count, liver function tests, renal function tests were within normal limits. USG of both orbits done, suggestive of detached retina in right orbit. CT scan showed right orbital calcification (intraconal) suggestive of retinoblastoma. Brain is normal. CSF cytology was negative for malignant cells. With this information Enucleation was done under general anaesthesia. Postoperative specimen shows tumour mass composed of dense masses of undifferentiated small round cells with hyperchromatic nuclei and scanty amount of cytoplasm. The cells are at places arranged in rosettes. These rosettes are composed of cluster of cuboidal cells arranged around a central lumen, thus pointing diagnosis of retinoblastoma with optic nerve involvement. She was planned for radiotherapy using anterior and lateral field with wedge to right orbit at depth of 2.25cm. A dose of 4500cGy was delivered in 13 fractions over 4 weeks. The course of radiotherapy was uneventful. After completion of radiotherapy patient was advised for prosthesis. She completed 13 years of follow-up. She is presently under observation of both Radiation Oncologists as well as Ophthalmologist.

3. Discussion
Retinoblastoma is one of the tumours, which is curable. It requires careful patient's evaluation, good planning and team approach in managements of patient. Many modalities come into play which includes Pediatrician, Ophthalmologist, Radiation oncologist and Prosthodontist. Thus whole treatment is multimodality and outcome totally depends upon good coordination among different doctors.

Radiotherapy and surgery were the mainstays of treatment, but platinum based chemotherapy regimens have shown very good response and commonly incorporated for tumour reduction prior to local treatment. [5] For unilateral advanced tumor, enucleation is considered standard, although radiotherapy is a reasonable organ-sparing alternative. [6], [7], [8] for small tumour away from optic disc, local vision sparing procedures such as cryotherapy and laser therapy may be used.

Although radiation therapy of retinoblastoma has minimal acute morbidity, long term radiation effects on the orbital bone growth and increased rate of second malignancy, other potentially serious side effects such as retinopathy, vitreous hemorrhage, Keratopathy and cataracts all of which effect vision.

Nowadays, newer treatment modalities like 3D Conformal Radiotherapy, Intensity modulated radiation therapy (IMRT) and proton radiotherapy dramatically reduce dose to non-target tissues (optic chiasma, pituitary gland, brain stem, upper cervical spine) and morbidity. The side effects from retinal brachytherapy are similar but more localized.

We reported a case which is unique in presentation because it completed 13 years of follow-up without any significant morbidity and good cosmoses (as shown in Figure No.1&2,).

FIG - 1

FIG - 2

Figure 1 - Photograph of patient taken at last follow-up before prosthesis, Figure 2 – Photograph of patient taken at last follow-up after prosthesis

3.1 Focal therapies for retinoblastoma- a novel approach to salvage eyes

With recent advancement in the field of management, local therapies for treating intraocular retinoblastoma have become an indispensable mode of management avoiding enucleation, the previously known as the only treatment of retinoblastoma.

3.2 Focal therapy includes

• Laser photocoagulation
• Cryotherapy
• Thermochemotherapy
• Plaque brachytherapy

3.3Indications for focal therapy (focal consolidation)

1. Group A – primary focal therapy
2. Group B – three to four cycles of chemotherapy followed by focal consolidation
3. Group C – six cycles of chemotherapy plus focal consolidation

3.4 Laser Photocoagulation

Commonly used lasers:
• 532 nm argon green
• 810 nm diode infrared

Indications for laser therapy
• Group A: primary laser photocoagulation
• Group B –D: primary chemotherapy followed by laser photocoagulation

3.4.1Timing of treatment: start concurrently with the beginning of the 2nd or 3rd cycle of systemic chemotherapy.

Goal of therapy: completely cover each lesion with 30% overlap during at least three different sessions Power settings:
• 532 argon –> 250 -300 mW (not > 500-600 mW) with a duration of 300-500 ms (not > 700 ms)
• 810 diode –> 400-600 mW (not > 700-800 mW) with a duration of 500 ms

3.4.2Complications of focal laser consolidation

• Iris burns at pupillary margin
• Focal lens opacities
• Subhyaloid and vitreous hemorrhage
• Decreased vision from RPE scar migration or “creep”
• Rarely tumor disruption and vitreous seedings

3.5Cryotherapy

Cryotherapy produces ice crystals which directly destroy tumor cells by rupturing the cellular membranes. It is useful in controlling local group A disease anterior to the equator when the tumor is confined to the sensory retina. It is useful in tumors up to 3.5 mm in diameter and 2.0 mm in thickness.

3.5.1Technique of Cryotherapy

Tumor is localized and it is elevated on the tip of the cryoprobe. Once the probe is directly beneath the tumor, freezing is begun, and the ice ball is allowed to thaw, and this freeze-thaw cycle is repeated for a total of two or three applications.

3.5.2 Complications of cryotherapy

• Vitreous hemorrhage
• Subretinal fluid
• Retinal holes and rhegmatogenous retinal detachment.

3.6 Brachytherapy

Plaque brachytherapy may be the treatment of choice in isolated group B intraocular retinoblastoma located at or anterior to the equator.

Radioactive isotopes used

• Iodine125 isotope
• Ruthenium106 isotope – a beta emitter, longer t1/2

Isotopes iodine125 seeds are secured in a gold carrier which prevents radiation from penetrating the substance of the plaque and shields normal bone and tissue from most of the radiation. Dosimetry planning is carried out with the help of sophisticated software. The calculated dose to the apex of the tumor is generally in the range of 40 Gy. The advantage of ruthenium is that the half-life is much longer than iodine so that a single plaque may be reused for up to one year. There are two major disadvantages. Because ruthenium is a beta emitter, a retinoblastoma lesion higher than 5 mm cannot be treated easily. Secondly, in ruthenium plaques the plaque itself contains the radiation sources. Therefore the possibility of differentially loading radiation seeds in the plaque to conform to the shape of the tumor is not possible, thus one plaque size may be necessary with ruthenium.

3.6.1Technique of plaque placement

Tumor is localized and 3600 peritomy is performed and traction is placed on appropriate rectus muscles by 4-0 silk sutures passed behind the muscles without needles. A generous margin of at least 2 mm is incorporated into the treatment plan. In the computer-regenerated model, the exact meridian and the distance in millimeters to the centre of the anterior edge of the plaque are available to the surgeon. Once the tumor is localized, a "cold" plaque (not containing radioactive seeds) is secured with temporary non absorbable sutures and its location verified by sclera depression along the edges. Once the correct position of the plaque is verified, the "cold" plaque is replaced by the "hot" plaque containing the radioactive seeds. The conjunctiva is closed with interrupted absorbable sutures.

The dose of radiation to the tumor apex ranges from 40-45 Gy. The plaque is left in situ for the duration of exposure, generally ranging from 36-72 hours.

3.6.2Complications of brachytherapy

• Radiation retinopathy
• Radiation papillopathy

3.7Thermotherapy

Thermotherapy involves focal heat generation using infrared diode laser to a subphotocoagulation level to induce tumor necrosis. Thermotherapy via infrared radiation can be delivered through an operating microscope, indirect ophthalmoscope, or transscleral probe. Hyperthermia is achieved by either the more classic low temperature (40-460 C) long time period (5-30 min) or by intense short bursts of heat. The delivery is time-intensive and tedious; it involves a continuous period of tumor monitoring by the ocular oncologist as the temperature in the tumor is elevated and maintained. Often, a gray white discoloration in the tumor is seen, indicating a successful take. Retinal vessels generally maintain their caliber during treatment, but retinal hemorrhage can occur. Thermotherapy may be used alone for very small tumors, or along with chemotherapy for larger tumors, where the combination may have a more potent effect (thermochemotherapy).

Complications of thermotherapy for retinoblastoma are focal iris atrophy, peripheral focal lens opacity, retinal traction and retinal vascular obstruction.

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