Chemotherapy For Retinoblastoma
A Current Topic

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Abstract

Retinoblastoma is the most common primary intraocular tumour in children, with an incidence of 1 in 15 000 live births. Treatment strategies for retinoblastoma have gradually evolved over the past few decades. There has been a trend away from enucleation (removal of the eye) and external beam radiation therapy toward focal ‘conservative’ treatments. Every effort has been made to save the child’s life with preservation of eye and sight, if possible.

Primary enucleation continues to be the commonly used method of treatment for retinoblastoma. It is employed in situations where eyes contain large tumours, long standing retinal detachments, neovascular glaucoma and suspicion of optic nerve invasion or extrascleral extension. Most of these eyes either have or are expected to have no useful vision. Radiation therapy continues to be an effective treatment option for retinoblastoma. However, external beam radiotherapy has unfortunately been associated with secondary non-ocular cancers in the field of radiation (primarily in children carrying the RB-1 germline mutation). Ophthal-
mic plaque brachytherapy has a more focal and shielded radiation field, and may carry less risk. Unfortunately, its applicability is limited to small to medium-sized retinoblastomas in accessible locations. Cryotherapy and transpupillary thermotherapy (TTT) have been used to provide control of selected small tumours. TTT is an advanced laser system adapted to the indirect ophthalmoscope which provides flexible nonsurgical treatment for small retinoblastomas.

Recent research in the treatment of retinoblastoma has concentrated on methods of combining chemotherapy with other local treatment modalities (TTT, radiotherapy, cryotherapy). This approach combines the principle of chemotherapeutic debulking in paediatric oncology with conservative focal therapies in ophthalmology. Termed chemoreduction, intravenous or subconjunctival chemotherapy is used to debulk the initial tumour volume and allow for focal treatment with TTT, cryotherapy and plaque radiotherapy. Cyclosporin has been added to the chemotherapy regimen in several centres.

Other clinical settings where chemotherapy is considered are situations where the histopathology suggests a high risk for metastatic disease and where there is extraocular extension. There is no consensus that chemotherapy is needed when choroidal invasion is observed on histopathology. However, in patients where the retinoblastoma is noted beyond the cut end of the optic nerve or if there is disruption of the sclera with microscopic invasion of the orbital tissue, treatment has been helpful. Systemic and intrathecal chemotherapy with local and cranial radiotherapy has improved the survival of these patients. Most recently, the use of new chemotherapy modalities with haematopoietic stem cell rescue or local radiotherapy has increased the survival of patients with distant metastasis. Nevertheless, the prognosis of patients with central nervous system involvement is still poor.

1. Current Treatment Options for Retinoblastoma

Although retinoblastoma is the most common primary intraocular tumour in children, the treatment of this disease is a complex topic. Therapeutic plans usually require a multidisciplinary approach by a team consisting of ocular oncologists, paediatric oncologists and radiation oncologists. The most important goal is to save the child’s life, followed by preservation of vision and the cosmetic use of the eye. Therapy is tailored to each patient, considering the size, location, number, laterality of tumour(s), the condition of the other eye, risk for metastasis and secondary cancers, and systemic status of the patient.[1-11] Treatment options include enucleation, external beam radiotherapy (EBRT), brachytherapy, laser photocoagulation, cryotherapy, thermotherapy, chemothermotherapy, intravenous chemoreduction, and systemic chemotherapy for metastasis.[1-11]

Primary enucleation is the commonly used method of treatment for retinoblastoma. We recommend primary enucleation for patients with unilateral retinoblastoma in the following situations: eyes containing large tumours (20mm in base, 10mm in height), long standing retinal detachment, neovascular glaucoma, iris neovascularisation or seeding, suspicion of optic nerve or choroid invasion or extrascleral extension, and no expectation for useful vision.[12] Primary enucleation allows cure rates of 92% in most patients with unilateral retinoblastoma.[12,13] In bilateral retinoblastoma, standard therapy was enucleation in the advanced eye and EBRT in the less advanced eye.[14] However, in recent years this standard has changed with the advent of new investigational eye preserving treatment modalities.[1-3,14]