Developing Rb genetics and counselling

It was long believed that mutated RB1 genes are a prerequisite to develop Rb. Recently, however, researchers have found that Rb may arise even in the presence of non-mutated RB1 genes when the MYCN oncogene is amplified. These cases are relatively rare, occurring in <3% of unilateral Rb cases, and present earlier, at a median age of 4.5 months.

The field of Rb molecular genetics has evolved significantly since the RB1 gene was cloned in the mid-1980’s. Today, genetic laboratories are able to detect specific mutations and correlate them to the probability of developing Rb in an individual and her or his relatives. It has also set the basis for the development of screening programmes, which are discussed by Rosser et al in the current issue.

Knowledge of the genetic status has direct impact on the recommended screening frequency and also on the recommended screening protocol for siblings and offspring. Individuals harboring a germline mutation are also at risk of developing secondary non-Rb malignancies later in life, a risk that is further intensified if treated with external-beam radiotherapy, a treatment modality that used to be commonly used for Rb.

Genetic testing, however, is not available in all centres across the world, being particularly sparse in low-resource countries. Genetic testing and screening will depend on genetic services being developed in these settings. Until then, clinicians should use epidemiological and clinical signs, including the age of presentation, laterality, tumour focality, presence of retinoma in a parent and family history of Rb, to counsel patients and their families.

References


From the field

How we manage patients with retinoblastoma

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When a child with retinoblastoma reports to our centre, a message is immediately passed on to a physician who treats retinoblastoma.

The child is then expedited to reach the physician, where a proper history is taken. After initial evaluation, drops are applied for pupillary dilatation. After the dilatation, the fundi are examined and a quick assessment of tumor volume and initial staging and grouping of the tumour in the eyes is made.

The child then undergoes ultrasound of both eyes, irrespective of it being unilateral presentation. An MRI of the orbits and brain is then advised. The MRI usually happens the same day and reporting takes place within a few hours. Once this information is available, the child is scheduled for an examination under general anaesthesia. Following this, the treatment plan is discussed with the parents.

In case of an orbital presentation, or an MRI showing optic nerve involvement, additional testing in the form of cerebrospinal fluid (CSF) analysis and a bone marrow aspirate is conducted and evaluated. Staging of the tumour is then performed as per the tests.

If enucleation is planned, we always ask for an opinion from another retinoblastoma expert.

The option of performing genetic testing is also discussed with the parents; however, this is not routinely done as a standard of care as the testing is often expensive and not many parents can afford it. Our aim therefore shifts to the management of the child.

We have an ocular oncologist in the team who visits our hospital to examine these children in case they require chemotherapy. We are also equipped to perform brachytherapy when needed.

“If enucleation is planned, we always ask for an opinion from another retinoblastoma expert.”