PERMANYER

EXPERT'S CORNER

Retinoblastoma

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The types of cancers that occur most often in children are different from those seen in adults. According to the most recent information published by the American Cancer Society, the most common cancers of children are leukemia, brain and spinal cord tumors, Wilms' tumor, lymphoma (both Hodgkin and non-Hodgkin), rhabdomyosarcoma, retinoblastoma (RB), and bone cancer (including osteosarcoma and Ewing sarcoma).

RB is the most common primary intraocular tumor in childhood and represents 2.5-4% of all pediatric cancers. Its incidence is roughly 1:14,000-1:20,000, it is equally prevalent in both sexes, and it has no racial predilection. It usually occurs in children around the age of 1-3, 90% of the time, and it is seldom found in children older than 6, although it is worth mentioning that there have been case reports of adults with RB. This is believed to be a reactivation of a retinoma, meaning a RB that involutes in infancy.

RBs are usually found by the pediatrician or by the parents of the child who notices an unusual shine or reflex in one or both eyes. RB can debut with strabismus or glaucoma; however, the most common presentation is leukocoria (white pupil). It is important to remember the differential diagnoses of leukocoria, such as persistent fetal vasculature, retinopathy of prematurity, cataract, coloboma of the choroid and/or optic nerve, uveitis, toxocariasis, Coats' disease, familial exudative vitreoretinopathy, myelinated nerve fibers, Norrie disease, and retinal detachment.

RB was the first disease, for which a genetic etiology of cancer was described and the first tumor suppressor gene identified. In 1971, Knudson developed the hypothesis that RB is cancer caused by two mutational events. Loss or mutation of both alleles of the RB1 gene, localized to chromosome 13q14, is required to develop the disease. It is also important to clarify that not all cases of RB are related to a mutation in the RB1 gene. Rushlow et al. described that the amplification of the MYCN oncogene might initiate RB in the presence of non-mutated RB1 genes. These unilateral tumors are characterized by distinct histological features, only a few of the genomic copy-number changes that are characteristic of RB, and a very early age of diagnosis[1].

There are different ways to think about RB; some refer to them as unilateral or bilateral, and some see them as sporadic (non-hereditary) or congenital (hereditary). Most cases (60-75%) are unilateral, and most unilateral cases are non-hereditary. The median age at diagnosis for this variant is 2 years' old. The rest (25-40%) are bilateral, and most bilateral cases are hereditary. The median age at diagnosis for bilateral cases is 1 year old. Patients with the RB1 gene mutation in all the cells of their body are at risk to develop other types of cancer during their lifetimes, such as osteogenic sarcomas of the skull and long bones, soft tissue sarcomas, cutaneous melanomas, brain tumors, and lung and brain neoplasms. The cumulative incidence of developing a new cancer 50 years after the diagnosis of RB is 36% for hereditary and 5.7% for non-hereditary variants.

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It is important to understand the genetics of the disease to be able to advise families about the possibility of having another affected child. An easy way to remember is if a parent is:

Bilateral = 45% chance of having a child with RB and 55% of having an unaffected child

Unilateral = 7-15% chance of having a child with RB and 85-93% of having an unaffected child

Unaffected = < 1% chance of having a child with RB and 99% chance of having an unaffected child.

Once diagnosed, the next step is to stage the tumor and plan for management. The patient should undergo an examination under anesthesia to adequately assess both eyes; fundus photographs and ultrasound for documentation are advisable. Every patient should have an magnetic resonance imaging of brain and orbits, both with and without contrast, to evaluate for brain tumors and extraocular extension. It is not recommended to order a computed tomography scan as this imaging modality exposes the patient to ionizing radiation, which can cause or predispose him to develop other malignancies in the orbit.

There are several classification systems for RB, but the most commonly used is the International Classification, which divides the disease into five groups:

- Group A: Small tumors away from fovea and disc
- Group B: All remaining tumors confined to the retina
- Group C: Local subretinal fluid or vitreous seeding
- Group D: Diffuse subretinal fluid or seeding
- Group E: The presence of one or more of the following: > 2/3 of the globe filled with tumor, a tumor on the anterior chamber or ciliary body, and/or iris neovascularization.

Recently, the new TNM classification is being advocated for use around the world, to standardize the terminology and characterization of the disease.

Tumors in Groups A and B can be treated and controlled with laser therapy and/or cryotherapy. Tumors in Groups C and D will most likely require systemic chemotherapy. In Group E tumors, where the visual prognosis of the eye is poor, enucleation is recommended.

Finally, there are new drugs and chemotherapy delivery techniques that provide better control and salvage of the eye. Chemotherapy can be injected intravitreally for the treatment of tumor seeds, and chemotherapy can now be delivered intra-arterially, directly to the ophthalmic artery to avoid systemic complications and side effects of the systemic chemotherapeutic agents. Recently, Zhao et al. published a report of their technique of vitrectomy for the treatment of selected cases of tumors with recurrent and resistant seeding, in an effort to debulk the tumor from the eye. This technique is new and needs more time for follow-up to demonstrate its safety, although the preliminary data look promising[2].

Conflicts of interest

The author has no conflicts of interest to report.

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