FAMILIAL RETINOBLASTOMA IN INDORE REGION: STUDY OF 3 CASES & FOLLOW UP

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ABSTRACT

Retinoblastoma is a primary malignant intraocular neoplasm that arises from immature retinoblasts within the developing retina. It is the most common intraocular malignancy of childhood in all racial groups. The neoplasm has strong tendencies to invade the brain via optic nerve and metastasize widely. Here we present a case of retinoblastoma in a 6 year old girl who presented with left eye leukocoria at MGM medical college in the department of ophthalmology indore, India. She had a family history of retinoblastoma which affected her father and brother. Urgent left eye enucleation with orbital implant under general anaesthesia was recommended. Histological examination of the left globe revealed small blue round cell tumour, optic nerve free from tumour invasion. Retinoblastoma is generally a sporadic condition (i.e. no previously affected family members). Small number of patients have prior family history of retinoblastoma, in which case one of the parents is probably a survivor of the disease.

INTRODUCTION

A retinoblastoma is a neuroblastoma. Retinoblastoma is the most common primary intraocular tumour in children and results from mutations in the tumour suppressor retinoblastoma gene (RB1) located on chromosome 13. As per Knudson’s Two Hit hypothesis, retinoblastoma only develops when both alleles of RB1 acquire mutations. In the inheritable form of retinoblastoma, the child inherits one altered allele of the RB1 gene from one parent, meaning retinoblastoma will develop if the normal allele becomes mutated1. Intraocular tumours may exhibit a variety of growth patterns and is commonly seen in advanced countries. Extraocular retinoblastoma is common in developing countries because of delay in diagnosis.

In 60% of cases, the disease is unilateral (non hereditary) and the median age at diagnosis is two years. Retinoblastoma is bilateral (hereditary) in about 40% of cases with a median age at diagnosis of one year2. Trilateral retinoblastoma is rare and refers to bilateral or unilateral retinoblastoma associated with an intracranial primitive neuroectodermal tumor in the pineal or suprasellar region3. Diagnosis is made by fundoscopy, ultrasound, magnetic resonance imaging (MRI) and computed tomography (CT) scans may contribute to diagnosis. Management of patients with retinoblastoma must take into account the various aspects of the disease: the visual risk, the possibly hereditary nature of the disease, the life-threatening risk. Enucleation is still often necessary in unilateral disease; the decision for adjuvant treatment is taken according to the histological risk factors4.

In more developed countries overall survival rates exceed 95%, a success attributable to both early detection and prompt access to enucleation services. As a result, ocular salvage has now become the main concern. However, in less developed countries, retinoblastoma is still a life-threatening disease. If left untreated, retinoblastoma will invade locally and metastasize, mostly causing death within 2 years. Survival rates are about 70% in low and middle income countries1.

Case Presentation

a 4 year old girl presented to the Ophthalmology department in the MGM Medical college & MYH Hospital, Indore, India with a shiny opacity in the left eye(fig. 1), first noticed by her mother when the girl was 4 months old.

She was previously diagnosed to have some intraocular tumour, at 4 months of age for which she had undergone laser photocoagulation at 6 months of age which was followed by 5 cycles of chemotherapy, which were done at private hospital in Gujrat. There were no other associated symptoms described by her mother, no past medical history of note, and no history of trauma or eye infection. No ocular complaints in right eye. She was not taking any regular medication and had no known drug allergies. Patient’s father (fig .2) and brother (fig. 3) had history of same type of tumour in right eye and at nearly same age and operated (enucleated) for the same.

She was born at term through a normal vaginal delivery and had no post-natal complications. Clinically, She was well oriented to time, place and person. She fixed and followed light when shone in her right eye, but did not respond when light was shone in her left eye. Red reflex was elicited in her right eye, but not in the left. Retinoscopy of the right eye revealed a refractive error of +2.50 dioptres spherical, but the refractive error of the left eye could not be determined. External eye inspection revealed gross leukocoria in her left eye. Slit lamp examination revealed quiet anterior chambers with normal depth, pupil was central circular and reactive to light, and clear lenses bilaterally. Fundus examination was within normal limits in the right eye, but revealed endophytic growth with vascularization in the left eye.

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Investigations

- Routine blood investigations were within normal limits.
- X-ray skull and orbit showed no soft tissue calcification and no bony involvement.
- B-Scan of the left eye demonstrated well defined isoechoic soft tissue mass lesion with irregular margins of 1.6 / 1.4 cm in size with tiny calcific foci with evidence of significant vascularity. A computed tomography (CT) scan of the orbit revealed poorly enhancing enplaque lesion with soft calcification in posterior wall of left eye ball (fig. 4).

MRI brain and orbit showed presence of inhomogenous signal abnormality consisting of hemorrhages and soft tissue involving the entire posterior segment of left eye ball (fig. 5).

Histology shows deep blue cells with little cytoplasm. Flexner Wintersteiner rosettes: clusters of cuboidal or short columnar cells arranged around a central lumen. The nuclei are displaced away from lumen with necrosis an areas of haemorrhage and necrosis. (fig 6)
Differential Diagnosis

The differential diagnoses of leukocoria include retinoblastoma, retinopathy of prematurity, congenital cataract, Coats’ disease, toxocariasis, and persistent hyperplastic primary vitreous (PHPV). The normal perinatal history rules out retinopathy of prematurity. Lack of inflammatory changes on slit lamp examination rules out toxocariasis. Slit lamp examination revealed clear lenses, ruling out congenital cataract. The characteristics of the mass on ultrasound and CT scan did not correlate with Coats’ disease or PHPV. Rather, these characteristic findings on examination and imaging led to a diagnosis of retinoblastoma being confirmed.

Outcome & Follow-up

An urgent left eye enucleation was done under general anesthesia with informed consent from parents. The procedure occurred without complications and the globe was sent for histological examination. There were no postoperative complications.

DISCUSSION

Retinoblastoma is a proliferation of neural cells which have failed to evolve normally. In developed countries, retinoblastoma is usually diagnosed in its early intraocular stages leading to high chances for preservation of vision, globe and disease free survival of the patient. However, in developing countries like ours, retinoblastoma is often diagnosed at a later stage with extraocular dissemination, thus leading to much lower rates of ocular salvage and patient survival\(^\text{5,6,7,8,9}\). Retinoblastoma has a cumulative life time incidence of approximately 1 in 15000-20000 individuals\(^\text{10}\). Its annual incidence is highest in first few months of life; thereafter the yearly incidence decreases steadily and is extremely low by 6 years of age. Inspite of its early onset in most children it is rarely diagnosed congenitally or even within the first 3 months of life, except in familial cases.

In 10% cases a relative may also have had a retinoblastoma and in such cases the disease is usually, but not always, bilateral. In India retinoblastoma has an incidence rate of three to five per million children, per year, and accounts for 2.5 to 4% of all childhood cancers in most developed countries. Barshi, Chennai, and Delhi report a 2-3 fold higher incidence of tumors of the eye (majority of which will be retinoblastoma in children <15 years of age), a finding that has also been previously reported\(^\text{11,12}\). q14 band of the chromosome 13 is responsible for controlling retinal cell division, and in children with retinoblastoma, retinal cell division continues unchecked causing retinal tumour. It may grow mainly outwards, separating retina from choroid (glioma exophytum) or inwards towards the vitreous (glioma endophytum)\(^\text{13}\). A small proportion of eyes with retinoblastoma exhibit generalized thickening of retina by the tumour referred to as diffuse infiltrating retinoblastoma\(^\text{14}\). This form is commonly associated with diffuse vitreous seeding and is sometimes associated with extension of tumour cells into the anterior chamber aqueous. If this tumour is left untreated, it metastasizes to preauricular and neighbouring lymph nodes, and later in the cranium and other bones. Direct extension by continuity to the optic nerve and brain is more common while metastasis to other organs usually the liver is rare.

CONCLUSION

There are very few human malignancies where definitive treatment is started without any confirmed histopathological diagnosis and imaging plays an important role in diagnosis and staging of the disease. Imaging (preferably magnetic resonance imaging) is required to confirm the diagnosis, access for local spread into the orbit through the sclera or into the optic nerve, metastasis into the central nervous system and for trilateral retinoblastoma\(^\text{13}\). Untreated children who have retinoblastoma almost always die of intracranial extension or widely disseminated disease within approximately 2-4 years of initial tumour detection recognized adverse clinical prognostic factors include large size of the intraocular tumour, older age of the child at detection and diagnosis and, most important, evidence of retro bulbar optic nerve expansion on MRI or other imaging studies.

References


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