



Case report

Bilateral retinoblastoma in early infancy

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Abstract

Introduction: Retinoblastoma is the most common primary intraocular malignancy of childhood. It is usually diagnosed before the age of 5 years. In spite of its early onset in most children, retinoblastoma is rarely diagnosed congenitally or even within the first 3 months of life. **Objective:** To report a case of retinoblastoma in early infancy. **Case:** This was a case of the earliest presentation of retinoblastoma in a female child 20 days after birth. The presenting complaint was of leukokoria noticed by the mother 13 days after birth. The father of the child was also found to have a suspicious lesion of retinocytoma in one eye and regressed retinoblastoma in the other eye. **Conclusion:** For early diagnosis of the disease, awareness and knowledge about the modes of presentation of the disease are very important. Similarly, the ophthalmic examination of the parents and siblings with retinoblastoma should always be done to exclude the disease.

Key-words: retinoblastoma, retinocytoma, phthisis bulbi

Introduction

Retinoblastoma is the most common primary intraocular malignancy of childhood and accounts for about 3 % of all childhood cancer (Kanski, 2007; American Academy of Ophthalmology, 2008-2009). The median age at diagnosis is approximately 12 months in children who have bilateral retinoblastoma and 24 months in those who have unilateral disease. It affects boys and girls with equal frequency and has no known racial predilection. Approximately 60-70% of cases are unilateral and 30-40% of those are bilateral (American Academy of Ophthalmology, 2008-2009). It is usually a sporadic condition. Only 6% have positive family history (American Academy of Ophthalmology, 2008-2009). In hereditary cases, the affected child usually, but not always, has multiple tumors in both eyes. Transmission of the disease in

such families follows the rules of autosomal dominant inheritance (Yanoff et al, 2009).

Retinoblastoma is caused by a mutation in the *RB1* gene, located on the long arm of chromosome 13 at locus 14 (13q14). Both copies of the *RB1* gene must be mutated in order for a tumor to form.

We here report a case of bilateral retinoblastoma with an early presentation, at the age of 20 days. To the best of our knowledge, this is probably the earliest diagnosed case of retinoblastoma in Nepal.

Case report

A 20-day-old female child from the south eastern part of Nepal was brought to our institute with the complaints of whitish pupillary reflex in the right eye (RE), which her mother first noticed when the baby was 13 days of age. There were no other ocular complaints. The baby was born full term via spontaneous vaginal delivery in a hospital to a 26-year-old mother. Further inquiry revealed that her elder brother was diagnosed as a case of

Received on: 01.08.2012 Accepted on: 13.12.2012

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retinoblastoma and died at the age of 28 months after the 2nd cycle of chemotherapy.

On examination, the baby could fix light with both eyes (BE). The anterior segment was within normal limits on both sides. Indirect ophthalmoscopy revealed a whitish mass in BE. Intraocular pressure (IOP) was digitally normal in both the eyes. The ultrasonography B scan showed a dome-shaped echogenic mass in BE, arising from the retina extending into the vitreous cavity. In the right eye, the mass occupied almost the whole of the vitreous cavity. The A Scan showed a characteristic V-Y pattern with alternating high and low spikes. The CT scan of the orbit showed a hyperdense mass with flecks of calcification in the posterior aspect of the vitreous of both globes.



Figure 1: Ultrasonography of the right eye

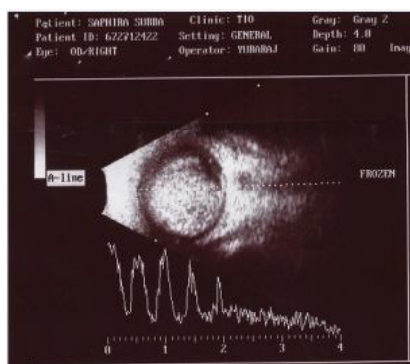


Figure 2: Ultrasonography of the left eye

B-scan showing echogenic mass in the vitreous cavity. A-scan showing V-Y pattern with alternating high and low spikes.

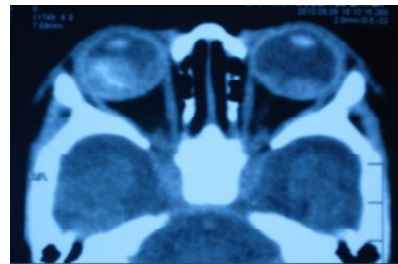


Figure 3: CT Scan of orbit showing hyperdense mass with flecks of calcification in posterior aspect of the vitreous of both globes

A detailed examination under general anesthesia revealed a corneal diameter of 11mm X 11.5 mm and IOP of 12 mmHg in both the eyes.

The anterior segment was within normal limits in both eyes. On posterior segment examination, no vitreous seeding was seen. In RE, a whitish tumor mass occupying whole of the fundus was seen with dilated overlying vessels. In the left eye (LE), the optic disc was pink and round with a well-defined margin with the CDR 0.3:1. Multifocal elevated whitish tumors confluent to each other, measuring about 6 X 7 disc diameter temporal to the disc involving the macular area with overlying dilated vessels, were also seen in the left eye.

Enucleation of the right eye with 14 mm Acrylic ball implant was done and in left eye photocoagulation with a diode laser around the tumor was tried.

The histopathological examination of the enucleated eye showed a diffusely growing tumor, composed of small round cells with scant cytoplasm and oval hyperchromatic moulded nuclei with the presence of frequent true and pseudo-rosettes and focal areas of necrosis. The choroid, sclera, cornea and optic nerve were free of tumor. With this information, a diagnosis of “well-differentiated retinoblastoma” was made.

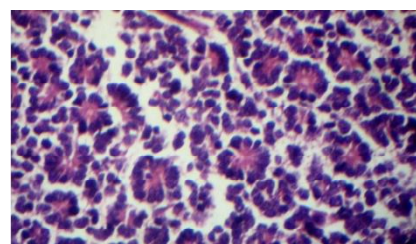


Figure 4: Photomicrograph showing multiple Flexner-Wintersteiner rosettes (true rosettes). The

halo-like cluster of cells in each rosette surrounds a nearly empty appearing central lumen containing fine cytoplasmic processes (Hematoxylin and Eosin stain, magnification 10x, low power).

Chemotherapy was then started. After completion of two cycles, the patient was again examined under general anesthesia. The tumor mass in the left eye had increased in size to occupy almost the whole of the fundus. As the tumor size was growing rapidly and was not regressing despite chemotherapy, the second eye of the patient was also enucleated after discussing with the parents as the life of the patient was deemed more important. The patient also underwent a total of 6 cycles of chemotherapy.



Figure 5: after enucleation of RE and 2nd cycle of chemotherapy

RE- Anophthalmic socket. LE- tumor mass with overlying vessels, seen with naked eyes.

The parents were also examined and it was found that the father had a best corrected visual acuity of 6/6 in the left eye and in the right eye there was no perception of light. He was on prosthesis of the right eye. He told us that according to his parents, his right eye started to decrease in size at the age of 2 years. On further examining the father, we found a whitish lesion measuring about the size of 4 - 5 disc diameters in supero-nasal quadrant of the left eye with an area of some calcification in the central portion of the tumor and areas of some chorioretinal atrophy surrounding the lesion. With these clinical findings, we assumed that the phthisis bulbi was perhaps the result of spontaneous regression of retinoblastoma and that the lesion of the left eye was retinocytoma.



Figure 6: Fundus photograph of patient's father showing superonasal quadrant of LE indicating whitish lesion measuring about the size of 4-5 disc diameters with area of some calcification in the central portion of the tumor and areas of some chorioretinal atrophy surrounding the lesion.

Both the baby and the father were kept on regular follow up. The parents were explained about the disease and the risk of the other child developing retinoblastoma was explained.

Discussion

In spite of its early onset in most children, retinoblastoma is rarely diagnosed congenitally or even within the first three months of life (Kanski, 2007).

Here, we diagnosed retinoblastoma in a 20-day-old female which is probably the earliest diagnosed case in Nepal.

Abramson et al stated that the most common manifesting sign of children with retinoblastoma diagnosed in the first month of life is family history (Abramson et al, 2002). Similarly, in our case, though the patient was brought to us due to white pupillary reflex, the positive family history of her brother, who died at the age of 28 months due to the same cause, made the parents seek medical help soon after detecting leukokoria.

If the parents were aware of the disease, they would have taken the first child to the hospital in early stage of the disease. However, very early diagnosis does not always guarantee vision, salvage of the globe,



or patient survival since the diagnosis may not reflect an early stage of the disease. We could not save both the eyes of our patient as the tumor was very advanced and aggressive.

A family history of retinoblastoma is very important. Retinoblastoma was the first cancer to be directly associated with a genetic abnormality. So, the parents and siblings of patients with retinoblastoma should have screening ophthalmic examinations to exclude an unknown familial disease. On screening ophthalmic examination, we found the father of the patient to have a phthisis bulbi (RE), which might be a regressed retinoblastoma, and also a suspicious lesion of retinocytoma in the fellow eye.

Spontaneous regression in a retinoblastoma, though a rare phenomenon, is also well documented in the literature. Regression of retinoblastoma usually leads to a phthisical eye. A study by Das has reported three cases of spontaneously regressed retinoblastomas in 140 eyes removed for retino-blastoma (Das, 1964). Isolated cases of phthisical eyes showing regressed retinoblastoma have been reported by other researchers too (Jain et al, 1968; Mehra et al 1965).

In the literature, retinocytoma and retinoblastoma have also been reported in different forms and associations: in the same family, in a case with retinoblastoma in one eye and retinocytoma in the fellow eye, as two separate foci in the same eye and in the parents of a child with retinoblastoma (Gallie et al, 1982; Singh et al, 2000; Balmer et al, 1991; Lueder et al, 1995).

Based on the evidence documented in the literature, the father in our case was diagnosed with regressed retinoblastoma in the right eye and retinocytoma in the left eye on the following grounds: presence of phthisical eye, presence of calcified tumour in the fundus with a characteristic clinical picture, presence of retinoblastoma in two children.

Management of retinoblastoma should be guided by the objectives to save life, to retain anatomical integrity of the eye, to preserve vision, and to obtain

good cosmetic results (Goddara et al, 1999). In our case we tried all possible measures to preserve at least the left eye but as the tumor size was increasing aggressively and could have threatened the life of the patient, the second eye too had to be enucleated without delay.

Genetic counseling is another important thing to be considered while treating retinoblastoma. The parents of a child with retinoblastoma should have an ocular examination and genetic counseling and the risk of the child's siblings developing retinoblastoma should be clearly explained.

A child who has hereditary retinoblastoma is at risk for developing trilateral retinoblastoma and other cancers. Similarly, most retinocytomas are stable and demonstrate no tendency to grow or metastasize (Singh et al, 2000). However, there is still a possible chance of malignant transformation which stresses the importance of close follow-up of the patient with a presumed diagnosis of retinocytoma. Hence, in this case, both the father and the child should be kept in a long-term follow-up.

Conclusion

Awareness and knowledge about the disease is very important as it may lead to early diagnosis, which may save eyes and lives, though this is not always possible as the earlier diagnosis does not always reflect an early stage of the disease. Also, screening ophthalmic examination of the parents and siblings with retinoblastoma should always be done to exclude the disease.

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Source of support: nil. Conflict of interest: none declared