Taiwan Journal of Ophthalmology 6 (2016) 79–84

Contents lists available at ScienceDirect

Taiwan Journal of Ophthalmology

journal homepage: www.e-tjo.com

Original article

Retinoblastoma in Mongolia: Clinical characteristics and survival from 1987 to 2014

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ARTICLE INFO

Article history:
Received 21 December 2015
Received in revised form
7 April 2016
Accepted 9 April 2016
Available online 20 May 2016

Keywords:
leukocoria
retinoblastoma
Rb protein

ABSTRACT

Background/Purpose: This study aims to describe the clinical characteristics and treatment outcome of retinoblastoma in Mongolian children.
Methods: Data of all children diagnosed with retinoblastoma at the National Center for Maternal and Child Health of Mongolia from 1987 to January 2014 were reviewed retrospectively. The ICRB classification was used. Survival characteristics of the cohort were analyzed.
Results: Retinoblastoma was diagnosed in 79 eyes of 64 cases during the study period. Median age of diagnosis was 24.5 ± 15.8 months. There were no differences in sex ratio, and 15 cases (23%) were bilateral. Forty-three (67%) patients were from rural areas. The more frequent clinical presentations were leukocoria in 50 (78%) patients, strabismus in 24 (38%) patients, and glaucoma in 21 (33%) patients. Sixty-one (95%) patients were diagnosed with Classification D or worse when presented to us. Due to late diagnosis in the majority of cases, unilateral and bilateral enucleations were performed in 48 (61%) eyes and 24 (30%) eyes, respectively; exenteration was done in three (4%) eyes. Fifty-two (81%) patients received chemotherapy and 13 (8.3%) patients underwent external beam radiation after enucleation. At the time of last follow-up, 52 (81%) patients were alive, five (8%) patients were dead, and seven (11%) patients had lost to follow-up or unknown vital status. The mean follow-up period was 121.5 months (range, 12–360 months). In five cases with immunohistochemistry analysis in the eye specimen, neuron-specific enolase-, Ki-67 protein-, and B-cell lymphoma 2-positive cells were found in all five (100%) cases and Rb protein was detected in three (60%) cases.
Conclusion: Retinoblastoma in Mongolia is frequently diagnosed at late stages and has a poor outcome. These data show the importance of early pediatric eye examinations and better treatment of retinoblastoma in children younger than 3 years in Mongolia.

1. Introduction

Retinoblastoma (RB) is a cancer of the very young; two-thirds are diagnosed before 2 years of age and 95% before 5 years of age. For these reasons, therapeutic approaches need to consider not only the cure of the disease, but also the need to preserve vision with minimal long-term side effects. The estimated incidence of RB is one in 16,000–18,000 births per year worldwide.[1,2]

Although RB is very curable when diagnosed early and treated appropriately, the prognosis is poor when the basic elements in diagnosis and treatment are lacking. Survival rates in the developed world are very high, but the rates are much lower in developing nations due to poor medical infrastructure, low alertness of parents as well as pediatricians, and complex and deficient socioeconomic environments.[3]

In Mongolia, only three to four new cases of RB are estimated each year. However, RB is an emerging health issue with problems of late diagnosis and poor visual outcome.[4] Although the country

Conflicts of interest: No conflicting relationship exists for any author.

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http://dx.doi.org/10.1016/j.tjo.2016.04.004

has good systems of registration for reflecting the burden of illness, there is no system for collating such important data. There is a need to review these situations and study survival of patients. This study aims to describe the clinical characteristics and treatment outcome of RB in Mongolian children.

2. Methods

Data of all children diagnosed with RB from 1987 to 2014 at the National Center for Maternal and Child Health in Ulaanbaatar, Mongolia were reviewed retrospectively with approval from the Institutional Review Board of Mongolian National University of Medical Science, Ulaanbaatar, Mongolia. The National Center for Maternal and Child Health is the only referral tertiary-care level hospital with a pediatric ophthalmology department. This department is responsible for the whole country's pediatric eye care services.

The data recorded included jurisdiction, sex, date of birth, age at diagnosis, and information on laterality of tumor, family history of RB, clinical presentations, and mode of treatment. The diagnosis of RB was based on the results of slit-lamp examination, indirect ophthalmoscopy, echography, computerized tomography, or magnetic resonance imaging, depending on the availability of the tools. The International Classification of RB was used.[5]

Enucleation and exenteration combined with systemic chemotherapy were treatments used for these patients. No other treatment modalities such as laser, cryotherapy, selective ophthalmic arterial chemotherapy, or intravitreal chemotherapy were available at our center.

The 1-, 5-, 10-, 15-, and > 25-year survival rates of the cohort were documented and analyzed.

2.1. Histologic and immunohistochemical assessments

With hematoxylin and eosin stain, the extent of tumor in optic nerve, choroid, and anterior chamber was scored and confirmed by pathologists. The immunohistochemistry of RB was performed at Beijing Tongren Hospital, Beijing, China. The expressed protein checked in this study included RB protein, neuron-specific enolase (NSE), s-100 protein, p53, vimentin, bcl-2, ki67, and glial fibrillary acidic protein.

2.2. Statistical analysis

The data of RB patients at our center from 1987 to 2014 were collected and analyzed. The data were presented as descriptive statistics. Patient survival was calculated and analyzed using the Kaplan–Meier method. Data were expressed as mean ± standard deviation.

3. Results

3.1. Patients

Seventy-nine eyes of 64 children were diagnosed with RB at the Department of Pediatric Ophthalmology in the National Center for Maternal and Child Health from January 1987 to January 2014. During this period, there were 2,081,930 newborns in Mongolia according to statistics of health indicators, the Ministry of Health of Mongolia. The incidence of RB was about one in 32,000–33,000 live births. Since the Pediatric Ophthalmology Department of the National Center for Maternal and Child Health treats and takes care of only RB patients in Mongolia, the estimation could represent the whole country's estimation. The annual RB incidence between 1987 and 2013 varied from zero to 0.98 per 10,000 live births (Figure 1). Among these 64 patients, 43 (68%) were from rural areas and 21 (32%) from the capital city Ulaanbaatar.

3.2. Sex and laterality

There was equal sex distribution in our study; 32 (50%) were boys and 32 (50%) were girls. In location, it was unilateral in 49 (77%) patients and bilateral in 15 (23%) patients. The disease was familial in one (2%) patient and sporadic in 63 (98%) (Table 1).

3.3. Age at diagnosis

The age of diagnosis ranged from 1 month to 72 months. The mean age of diagnosis was 24.5 ± 15.8 months. Fifty-three (83%) patients were diagnosed before the age of 3 years. The age at diagnosis was earlier in bilateral cases (mean age, 13.1 ± 12.8 months; range, 1–42 months) than in unilateral cases (mean age, 28.1 ± 15 months; range, 1–72 months) (Table 1).

3.4. Presenting signs and stage

The most prevalent clinical conditions were as follows: leukocoria in 50 (78%) patients, strabismus in 24 (38%) patients, secondary glaucoma in 21 (33%) patients, hyphema in seven (11%) patients, and orbital cellulitis in seven (11%) patients (Table 1). Three (5%) patients presented with late-stage, extraocular extension of RB (Figure 2). Sixty-one (95%) patients were diagnosed with Classification Group D or worse when presented to us. Out of all the eyes, 75 (95%) were diagnosed with Classification Groups D and E, two (2.5%) with Group B, and two (2.5%) with Group C.

3.5. Disease detection

Since there were no eye-screening programs in Mongolia, all (100%) patients were referred to ophthalmologists for further evaluation due to various presenting signs mentioned above. Thirty-nine (60%) patients were examined with B scan, 38 (59%) patients with computerized tomography, and 30 (46%) patients with magnetic resonance imaging.

3.6. Spread of tumor

One (2%) case had intracranial extension, three (5%) cases had extraocular extension, and one (2%) case developed orbital recurrence of RB 4 years after initial enucleation (Figure 3). The other 59 (92%) patients had intraocular RB without any extraocular extension.

3.7. Secondary tumor and metastasis

None of our cases developed a secondary malignant neoplasm before the cutoff date.

3.8. Mode of treatment

Enucleation of one eye was performed in 48 (61%) eyes, bilateral enucleation in 24 (30%) eyes, and exenteration in three (4%) eyes in the early years of this study. Additional exenteration was done in one eye due to orbital recurrence of RB after 4 years of initial enucleation. Two eyes (2.5%) received local laser treatment in Korea and China, and two (2.5%) cases received systemic intravenous chemotherapy only and the tumors were stable with partial regression (Table 2).