ORIGINAL ARTICLE

A 10-year retrospective study of retinoblastoma in 2 regional hospitals in Hong Kong

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Abstract

Aim: To describe the clinical features and treatment outcomes for retinoblastoma in 2 regional hospitals in Hong Kong.

Patients and methods: The clinical records and histopathologic reports of patients with retinoblastoma at the Queen Mary Hospital and Pamela Youde Nethersole Eastern Hospital in Hong Kong from 1996 to 2005 were studied retrospectively.

Results: Eight eyes of 8 patients with retinoblastoma were reviewed. There were 5 boys (62.5%) and 3 girls (37.5%). The mean age at presentation was 16.6 months (range, 8-25 months). Data for staging, histopathology, and orbital implant were missing for 1 patient. Of the remaining 7 patients, 7 (100%) presented with Reese-Ellsworth stage V disease; 1 (14%) had optic nerve invasion and choroidal invasion; 7 (100%) had clear margins at the optic nerve resection ending; and 0 (0%) had scleral or extraocular invasion. All patients (100%) underwent enucleation. No patients received chemotherapy or radiotherapy. There was a 100% 5-year survival rate, 0% recurrence rate, and no patients developed secondary tumor.

Conclusion: Retinoblastoma is rare in Hong Kong. Most patients have unilateral involvement and present late in the course of the disease. Enucleation remains the treatment of choice for advanced retinoblastoma with poor visual potential. The prognosis is excellent in terms of 5-year survival and recurrence rates for patients without extraocular extension.

Key words: *Eye enucleation, Retinoblastoma, Treatment outcome*

Introduction

Retinoblastoma is the most common intraocular malignancy in childhood.[1] The condition can occur in one or both eyes, and may be either unifocal or multifocal. Retinoblastoma occurs in both sporadic and inherited forms. The inheritance is autosomal dominant with a high penetrance of 90%.[2] The retinoblastoma gene is identified in a segment of chromosome band 13q14, which is frequently deleted in patients with retinoblastoma. The presenting symptoms and signs include leukocoria, strabismus, decreased visual acuity, painful red eye, proptosis, and buphthalmos. Small tumors at early stages can be treated conservatively with chemoreduction followed by local treatment.[3] Advanced disease should be treated with external beam radiotherapy or enucleation.[3]

Despite the importance of retinoblastoma, there are no data detailing the presentation and treatment outcomes for this tumor in Hong Kong people. This study was performed to describe the clinical features and treatment outcomes for retinoblastoma in 2 regional hospitals in Hong Kong.

Patients and methods

In this 10-year retrospective series, data were retrieved from the clinical data analysis record system of the Hong Kong

Table 1. Clinical features and treatment outcomes of 8 patients with retinoblastoma in Hong Kong.

Patient number	Sex	Age at diagnosis (months)	Time (months)			Presenting signs	Staging	Mode of treatment	Recurrence	5-year survival	Secondary tumor
			Duration of symptoms	Time before treatment	Onset of symptoms to treatment						
1	M	8	1	1	6	Leukocoria	RE V	Enucleation	No	Yes	No
2	F	14	2	0.75	2.75	Leukocoria	RE V	Enucleation	No	Yes	No
3	F	16	6	0.5	6.5	Strabismus	NA	Enucleation	No	Yes	No
4	F	25	0.5	0.5	1	Leukocoria	RE V	Enucleation	No	Yes	No
5	M	18	12	0.75	12.75	Strabismus	RE V	Enucleation	No	Yes	No
6	M	8	3	0.5	3.5	Leukocoria	RE V	Enucleation	No	Yes	No
7	M	24	0.067 (2 days)	0.25	0.25	Leukocoria	RE V	Enucleation	No	Yes	No
8	M	20	0.25	0.5	0.75	Leukocoria	RE V	Enucleation	No	Yes	No

Abbreviation: RE V = Reese-Ellsworth stage V disease.

Table 2. Histology of patients with retinoblastoma in Hong Kong.

Patient number	Optic nerve invasion	Choroidal invasion	Optic nerve resection margin	Scleral invasion	Extraocular invasion
1	No	No	Clear	No	No
2	Yes	No	Clear	No	No
3	NA	NA	NA	NA	NA
4	No	No	Clear	No	No
5	No	No	Clear	No	No
6	No	No	Clear	No	No
7	No	Yes	Clear	No	No
8	No	No	Clear	No	No

Abbreviation: NA = not applicable.

Hospital Authority. Patients with retinoblastoma treated at the Queen Mary Hospital and the Pamela Youde Nethersole Eastern Hospital from 1996 to 2005 were included for analysis. Data for sex, laterality, age at diagnosis, presenting signs, duration of symptoms before diagnosis, time before treatment, interval between onset of symptoms and treatment, family history, presenting stage, histopathology, treatment mode, type of orbital implant, survival rate, recurrence rate, and occurrence of second tumor were collected.

Duration of symptoms was defined as the interval between onset of the initial symptom, as recalled by the patients' parents, and the time of diagnosis. The time before treatment was defined as the interval between diagnosis and treatment. The interval between onset of symptoms and treatment is equal to the sum of the duration of symptoms and the time before treatment.

Results

Eight eyes of 8 patients were diagnosed with retinoblastoma during the 10-year study period (**Tables 1 and 2**). One patient was born in Macau, 1 in China, and 6 in Hong Kong.

There were 5 boys (62.5%) and 3 girls (37.5%). Tumor involvement was unilateral in all 8 patients; 4 right eyes (50%) and 4 left eyes (50%) were involved. None of the patients had a family history of retinoblastoma.

The mean age at presentation was 16.6 months (range, 8 to 25 months). The average duration of symptoms before diagnosis was 3.1 months (range, 2 days to 12 months). The average time before treatment was 0.59 months (range, 1 week to 1 month). The average interval between onset of symptoms and treatment was 4.19 months (range, 1 week to 12.7 months).

The most common presenting sign was leukocoria, occurring in 6 patients (75%). The remaining 2 patients (25%) presented with strabismus. There were no data about the staging, histopathology, and type of orbital implant for 1 patient. Of the remaining 7 patients, 7 (100%) presented with Reese-Ellsworth stage V disease. One patient (14%) had optic nerve invasion and choroidal invasion; all patients (100%) had clear margins at the optic nerve end resected; and no patients (0%) had scleral or extraocular invasion.

All patients underwent enucleation. No patients received chemotherapy or radiotherapy. All patients had placement of an orbital implant. Among the 7 patients for whom data were available, 3 (42.9%) had a hydroxyapatite implant and 4 (57.1%) had a polyethylene implant. There was a 100%

5-year survival rate, and 0% recurrence rate; no patients developed secondary tumor.

Discussion

The crude incidence of retinoblastoma in Hong Kong Island was able to be estimated by this study. According to the Hong Kong Government Census of 2005,[4] the population of Hong Kong Island was approximately 1,305,000 between 1996 and 2005. The average crude birth rate during this period was 8.3/1000, resulting in approximately 108,356 births in Hong Kong Island. Thus, the 10-year incidence of retinoblastoma in Hong Kong Island from 1996 to 2005 was 1/18000 births.

According to the public health care system in Hong Kong, people tend to be referred to hospitals located in the district where they live. Queen Mary Hospital and Pamela Youde Nethersole Eastern Hospital together provide the public ophthalmology service for the population of Hong Kong Island. This makes the estimation of the incidence of retinoblastoma in Hong Kong Island possible. However, any patients who sought private treatment or were referred to a hospital outside Hong Kong Island would not be listed in the database.

All patients in this series had unilateral involvement and none had a family history. This suggested that all patients in this series were likely to have sporadic rather than hereditary retinoblastoma, which can be bilateral and often presents at an earlier stage. Choy et al found that 19% of patients with retinoblastoma in Hong Kong carried a germ line RB1 mutation.[5] The identification of genetically susceptible family members can lead to early diagnosis. Genetic analysis also provides important information about the risk for parents and long-term survivors of retinoblastoma to have children with the condition. Unfortunately, genetic study was only available for some of the patients in this series.

The mean age at diagnosis of retinoblastoma reported in the Western population is 18 months.[6] The mean age has been reported to be higher in Asia, at 20.7 months in Japan[7] and 26.3 months in Taiwan.[8] In this series, the mean age at diagnosis was 16.6 months.

Duration of symptoms for longer than 6 months has been shown to be associated with extraocular extension and a poor prognosis.[9] In this series, only 2 patients had duration of symptoms longer than 6 months, while the other patients had symptoms for less than 3 months. The 2 patients with a long duration of symptoms lived in China and were referred to Hong Kong for management of the disease. The lower parental alertness to the condition in China and longer referral process may account for the longer duration of symptoms. However, in this series, neither the duration of symptoms nor an interval between onset of symptoms and treatment of up to 1 year were associated with extraocular disease. A 5-year disease-free treatment outcome was also achieved.

The time before treatment of greater than 2.5 months has been identified as a factor for poor prognosis in a Taiwanese series, in which the refusal rate for treatment was 13.7%.[8] The causes of refusal of treatment or delay in starting treatment included cultural factors, refusal of enucleation, and desire to use traditional Chinese medicine or to seek a second opinion, all of which were driven by a strong fear of the loss of the eye.[8] Although Hong Kong people share a similar Chinese background, this phenomenon was not observed in this series. The time to treatment in this study was 0.59 months. None of the patients' families refused enucleation after information was provided.

Consistent with other reports, the most common presenting sign was leukocoria, followed by strabismus.[8,10] All patients in this series presented late, with Reese-Ellsworth stage V disease. Currently, retinoblastoma at Reese-Ellsworth stages I to III can be managed with chemotherapy and local treatment of thermotherapy, laser therapy, cryotherapy, or brachytherapy.[3] However, for patients with unilateral Reese-Ellsworth stage IV to V disease, with no hope for useful vision, enucleation remains the treatment of choice.[3] In this series, all 8 patients underwent enucleation, and none received chemotherapy or radiotherapy. This was primarily because all patients had unilateral intraocular tumors at an advanced stage and the fellow eyes were tumor-free.

Extraocular retinoblastoma has been identified as a poor prognostic factor, and involvement of the central nervous system results in the worst outcome.[11] The rate of extraocular tumor extension is 30% in Taiwan.[8] However, none of the patients in this series had extraocular invasion. According to the literature, the 5-year survival rate for retinoblastoma in Japan is the highest in Asia, at 93%.[7] The 5-year survival rate in Taiwan is 80.9%,[7] while the 3-year survival rate in Singapore is 83%.[12] The prognosis after enucleation in this series was excellent with a 0% recurrence rate and 100% 5-year survival rate. This can be attributed to the fact that none of these patients had extraocular extension.

There were limitations to this study. With regard to the patient recruitment process, those who declined the first examination-under-anesthesia (EUA) appointments or those who were referred to other ophthalmic centers before the first EUA appointment would not appear in the database and the final outcome would be unknown. Patients with bilateral disease who would have benefited from globe-preserving chemoreduction therapy were referred to another retinoblastoma centre, which had greater experience at managing these patients. Moreover, the sample size of this series was small. A population-based study involving other ophthalmic centers in Hong Kong would reflect the incidence and clinical features of retinoblastoma in Hong Kong children more accurately.

Retinoblastoma is rare in Hong Kong. Most patients have unilateral involvement and present at a late stage of the disease. Enucleation remains the treatment of choice for

advanced stage retinoblastoma with poor visual potential. The prognosis is excellent in terms of the 5-year survival rate and recurrence in patients without extraocular extension.

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