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Retinoblastoma in Southwest Iran

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Abstract

Background: Retinoblastoma is the most common embryonic tumor of retina of children. This tumor include 3-4% of all children malignancies during the age range 0-14 years. In this study, we reported the incidence, therapeutic protocols, and treatment outcome of children with RB in South west Iran.

Methods: We retrospectively investigated the medical reports clinical and pathological features of RB cases at referral Shafa Hospital of Ahvaz city located in Southwest Iran, between 1994 and 2014.

Results: Our results showed leukocoria, white discoloration in the pupil, as the most common primary symptom in retinoblastoma patients. Forty-two percent of our patients had bilateral neoplasms. Based on histological investigations, stage IV was most common stage in our patients (79.1%).

Conclusion: In conclusion, our study showed that leukocoria, stage IV and Choroid involvement as most common symptom, stage and organ involvement, respectively and inherited cases is rare in our population. The results of our study can be as a base for further researches in future.

Keywords: Retinoblastoma, clinical manifestation, incidence, heritable, staging, treatment modality

Introduction

Retinoblastoma is the most common embryonic tumor of retina in children under 5 years of age with an incidence of 1 in 15000-20000 live births [1,2]. Retinoblastoma accounts for 3-4% of all malignancies in children younger than 15 years[3]. Approximately 60% of the Rb cases present as unilateral[4]. Retinoblastoma occurs in both heritable and nonheritable forms. About 15% of the children with unilateral disease and almost all bilateral cases are assumed to have the heritable form [5]. Mutation of RB1 gene is one of the most important risk factors for developing the hereditary cases and contribute to the poor prognosis of the disease [6]. Since the 1970s, the survival rate and treatment outcome of retinoblastoma has improved [7-9]. Treatment protocols consist of enucleation, cryotherapy, radiotherapy, exenteration, and laser photocoagulation. Among treatment protocols, enucleation (removal of the eye) is accompanied by excellent survival in most unilateral cases. However, complementary chemotherapy is necessary for those patients with adverse histological results [9,10]. For bilateral patients the goal of treatment is saving vision. According to the size and location of the tumor, this goal can be often obtained by chemotherapy or by combination of chemotherapy and local therapies [10, 11]. In heritable retinoblastoma long follow-up period is necessary since the mutant RB1 gene acts as a cancer susceptibility gene predisposing the patient to second malignancies[12]. This is a report on incidence, therapeutic protocols, and treatment outcome of children with retinoblastoma in a referral center in southwest Iran.

Patients and Methods

We retrospectively reviewed the medical reports of patients with retinoblastoma referring to Shafa Hospital, Ahvaz, southwest Iran, during 1994-2014. Demographic data including age, sex, family history and other parameters such as duration of symptoms, laterality of the disease, histopathology, stage of the disease, treatment protocols and outcome were analyzed. Tumor stage (Reese-Ellsworth classification system) was determined by an ophthalmologist under general anesthesia upon initial examination. In bilateral cases all the data were applied for each eye, respectively. SPSS software, version 16 was used for statistical analysis.

Results

Medical records of 43 patients, including 22 women, were studied. The mean±SD age at diagnosis was 24.49±22 months. There were 33 (76.7%) unilateral (18 involving the right eye) and 10 (23.3%) bilateral cases (Table 1). Positive family history was observed in 2.3 % of the patients.

Table 1: General characteristics of the patients with retinoblastoma

Variables	Patients (n=43)
Age at diagnosis (month):	24.49 ± 22.64
Duration of symptoms (month):	18.51 ± 17.36
Gender	
Female, No (%)	22(51.2)
Male, No (%)	21(48.8)
Family history	
Yes, No (%)	1(2.3)
No, No (%)	42(97.7)
Laterality	
Unilateral (left), No (%)	15(34.9)
Unilateral (right), No (%)	18(41.9)
Bilateral, No (%)	10(23.2)
Main primary symptom	
Leukocoria, No (%)	19(44.2)
Strabismus, No (%)	3(7)
Red eye, No (%)	5(11.6)
Decreased vision, No (%)	1(2.3)
Proptosis, No (%)	3(7)
Leukocoria and strabismus, No (%)	1(2.3)
Leukocoria and inflammation, No (%)	1(2.3)
Leukocoria and Red eye, No (%)	9(20.9)
Parent consanguinity	
Yes, No (%).	17(39.5)
No, No (%).	26(60.5)

Table 2: Pathological data in patients with retinoblastoma

Variables	Number of patients (%) (Total=43)
Positive evidence of organ involvement	
Optic nerve	3(7)
Choroid	5(11.6)
None	35(81.4)
Distant Metastasis	
Yes, No (%)	4(9.3)
No, No (%)	39(90.7)
Disease stage	
I	1(2.3)
II a	2(4.6)
II b	1(2.3)
III	3(7)
IV	34(79.1)
V	1(2.3)
Unknown	1(2.3)

Table 3: Different modality of treatments and outcomes in patients with retinoblastoma:

Treatment protocol	
• Uni-enucleation and chemotherapy, No (%)	34(79.1)
• Bi-enucleation and chemotherapy, No (%)	9(20.9)
Chemotherapy protocol	
• Vincristine-Adriamycin-Cyclophosphamide, No (%)	19(44.2)
• Vincristin-Etoposide-Carboplatin, No (%)	7(16.3)
• Vincristine-Cisplatin-Etoposide-cyclophosfamide, No (%)	13(30.2)
• Vincristine-Etoposide-Cisplatin, No (%)	4(9.3)
Outcome	
• Remission	37(86.0)
• Death	5(11.6)
• Secondary Malignancy (Rhabdomyosarcoma)	1(2.3)

Table 4: Comparative view between our report and other studies

Study	Bilateral cases(%)	Age at diagnosis (months)	Leukocoria (as most common primary symptom) (%)	Death (as poorest prognosis) (%)	References
Other studies in Iran	28.8 [13], 6.96 [14]	26.9	56.7	19	13, 14, 19
Turkey	30	26.4	61.9	7.7	20-22
China	32	23.0	73	--------	23
Nigeria	15	30.69	54	65	16, 18, 19
England	34.6	8.8	--------	7	4, 24
Our report	23.0 %	24.49	44.2 %	11.6	

Leukocoria was the most common primary symptom (44.2%) in our patients followed by leukocoria and red eye (20.9%), red eye (11.6%), strabismus (7%), proptosis (7%), decreased vision (2.3%), and leukocoria and strabismus (2.3%). Enucleation was performed in 34 (79.1%) patients. Only 9 (20.9%) patients underwent bilateral enucleation.

Results of histopathological examination are presented in table 2. Choroid was the most common organ affected by retinoblastoma (n=5, 11.6%). Most patients were presented at stage IV (n=34, 79.1%). Treatment protocols consisted of enucleation, exenteration, external beam radiotherapy, and cryotherapy. Chemotherapy as a complementary therapeutic strategy was used after enucleation for the patients (table 3). According to available data 4 (9.3%) patients had distant metastasis and in 3 (7 %) patients, retinoblastoma had invaded the optic nerve. Five (11.6%) patients died due to progressive disease and 37 (86%) patients survived until January 2013.

Discussion

Retinoblastoma is the most common embryonic tumor of the retina in children under 5 years of age. Early diagnosis has an important role in response to treatment and outcome [1,2]. Most patients with retinoblastoma are diagnosed before the age of 36 months. Previous studies [13,14] from Iran report the age at diagnosis to be 26.3 and 6.9 months, respectively. In our study the mean age at diagnosis was 24.49 months that was similar to a similar report[13]. Discrepancy between our results and previous reports from Iran in terms of age at presentation may be related to different genetic mutations and delayed diagnosis in our series. In our series leukocoria was the most common primary symptom which was compatible with other studies from Iran [13,14]. Leukocoria as the primary manifestation of retinoblastoma was also reported in other reports [15,16]. Therefore, any child with leukokoria should be referred to an ophthalmologist within one week.

Progression and invasion of disease contributes to extra-ocular involvement. In our study, five (11.6%) patients were presented by choroid and 3 (7%) by optic nerve involvement. Extra-ocular retinoblastoma was introduced as a risk factor for poor prognosis and involvement of the central nervous system (CNS) which is associated with poorest outcome [15]. CNS involvement was not observed in any of the patients in our study. Most of the infantile cases of retinoblastoma were diagnosed in stage IV based on their clinical presentation and histopathological reports. One study that reviewed the status of retinoblastomas in Brno during 1985 to 1998, introduced stage III and IV as the most common stages in their population [17]. This is similar to our results in which most of the infantile retinoblastoma cases were diagnosed in stage IV based on histopathological examinations. Stage IV is associated with advanced disease and poor prognosis in retinoblastoma which necessitates enucleation in most cases [4]. In

our study, enucleation along with chemotherapy contributed to a favorable outcome in stage IV retinoblastomas that was compatible with previous studies.

In our study 23% of the children had bilateral retinoblastoma which was different from other studies. This discrepancy may be attributable to ethnic variations or have genetic explanations (e.g. RB1 gene mutation). In our study 30% of the bilateral cases had germ line mutation of the RB1 gene. It should also be noted that heritable retinoblastoma is less documented in developing countries [18].

Table 4 shows the comparisons made between our report and other studies.

Conclusion

We found that leukocoria, stage IV, and choroid involvement were the most common symptom, stage and organ involvement, respectively, and also heritable cases were rare in our population. The results of our study can be as a base for further related studies.

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