·Clinical Research·

Characteristics and clinical presentations of pediatric retinoblastoma in North-western Iran

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Abstract

• AIM: To report the characteristics and clinical presentations of retinoblastoma in a series of pediatric patients from Iran.

• METHODS: In this retrospective study, profiles of pediatric patients with retinoblastoma archived in a referral eye hospital in north-west of Iran during 7 years (n=40 patients with 57 eyes) were reviewed. Demographics, as well as the laterality, clinical manifestations and the types of treatment were the major endpoints. The Student's t test, Mann-Whitney U-test, Chi-square or Fishers' Exact test was used for analysis where appropriate.

• RESULTS: There were 23 cases (57.7%) with unilateral and 17 cases (42.5%) with bilateral involvement. The male to female ratio was 1 to 1.4 with a mean admitting age of 24.0± 11.3 (range: 5-62) months. The mean diagnosis delay was (7.4± 9.6) months (range: 10 days to 13 months). The most common presenting sign was leukocoria (97.5%) followed by proptosis (7.5%), strabismus (7.5%), hyphema (5%), orbital cellulitis (5%) and glaucoma (2.5%). Enucleation was performed in 95.7% of the cases with unilateral involvement and at least one eye of the patients with bilateral disease. A second enucleation was performed in other 3 patients (17.6%) of the latter group.

• CONCLUSION: This is the first study evaluating a series of Iranian children with retinoblastoma.

• KEYWORDS: retinoblastoma; epidemiology; clinical presentation
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INTRODUCTION

Retinoblastoma is the most frequent intraocular malignancy during childhood [1]. It could be unilateral (2/3) or bilateral (1/3) [2]. As an uncommon tumor, physicians may not be familiar with clinical presentations of retinoblastoma, resulting in notable delay in diagnosis and treatment. Furthermore, its clinical manifestations vary greatly depending on location, size and duration. Leukocoria, squint, red eye and orbital cellulites have been reported as the frequent presentations of the disease [3]. Proptosis is more common in developing countries [4,5]. This study aimed at evaluating the manifestations of retinoblastoma in a series of patients in a developing country.

SUBJECTS AND METHODS

Subjects In this prospective setting, profiles of children with diagnosis of retinoblastoma archived between the years 1995 and 2011 in a referral eye hospital in Tabriz, Iran were reviewed. Forty four profiles were found with fully accessible data in 40 cases. This study was approved by the Ethics Committee of Tabriz University of Medical Sciences.

Methods

Procedures and diagnosis Indirect ophthalmoscopy (12500, Welch Allyn, New York, USA) was performed in all cases. This was carried out under anesthesia only in uncooperative patients.

Diagnosis of retinoblastoma was suspected when there was a mass lesion in initial fundoscopy. These cases, in the second phase, underwent computer tomography (CT) scanning of eye before and after intravenous injection with 0.6mm-2.5mm slice thickness (Hitachi, Japan; or Siemens, Germany). Presence of calcification in CT images indicated histological confirmation following enucleation or excentration.

Variables Demographics, laterality, age of admission, diagnosis delay, familial history, clinical manifestations, and the type of treatments were recorded.

Statistical Analysis Statistical evaluation was made using SPSS for Windows Version 18.0 (SPSS Inc., Il, USA). The independent samples T-test, Mann-Whitney U-test, Chi-square test or Fisher's exact test were employed for comparison where appropriate. P<0.05 was regarded as significant.

Table 1 Characteristics and general data of the studied population with retinoblastoma

Variable		Unilateral(n=23)	Bilateral(n=17)	Total(n=40)	^1P
Gender	Male	11 (47.8)	6 (35.3)	17 (42.5)	0.43
	Female	12 (52.2)	11 (64.7)	23 (57.5)	
Age of admission (month)		29.5±13.2	18.5±10.2	24.0±11.3	0.03
Diagnosis delay (month)		9.5±11.0	5.4±4.5	7.4±9.6	0.01
Presenting sign	Leukocoria	16 (69.5)	13 (76.4)	39 (97.5)	0.73
	Proptosis	2 (8.6)	1 (5.8)	3 (7.5)	0.62
	Strabismus	2 (8.6)	1 (5.8)	3 (7.5)	0.62
	Glaucoma	1 (3.4)	0 (0)	1 (2.5)	0.58
	Hyphema	1 (3.4)	1 (5.8)	2 (5)	0.68
	Orbital cellulitis	1 (3.4)	1 (5.8)	2 (5)	0.68

Data are presented as mean±standard deviation or frequency (%); ^{1}Unilateral *vs* bilateral.

RESULTS

Profiles of 40 patients (57 eyes) were reviewed. In 23 cases (57.7%) the disease was unilateral and in 17 cases (42.5%) it was bilateral. In the unilateral group, the right eye was involved in 8 cases (34.8%) and the left in 15 cases (65.2%). Demographics and general data of the studied population are outlined in Table 1. Familial history of retinoblastoma was negative in both groups. The age of admission ranged between 5 to 62 months in the unilateral group and 2 to 36 months in the bilateral group. The age of admission was significantly lower in the bilaterally involved patients (29.5± 13.2 *vs* 18.5±10.2; P=0.03). Diagnosis delay, i.e. the time between initial emergence of signs/symptoms and final diagnosis ranged between 10 days to 13 months in the unilateral group *vs* 15 days to 13 months in the bilateral group. The mean diagnosis delay was significantly higher in the unilateral group (9.5±11.0 *vs* 5.4±4.5, P=0.01). Among the presenting signs, the leukocoria was the most common manifestation in both groups (16 cases in the unilateral group and 13 cases in the bilateral group) followed by the proptosis and strabismus each one in 2 cases, and the hyphema, glaucoma and orbital cellulitis each one in 1 case in the unilateral group. There was no case of glaucoma in the bilateral group with the other sings each one in one patient with bilateral involvement (Table 1). There was no significant difference in terms of theses ocular findings between the two groups. In the unilateral group, 22 eyes (95.7%) underwent enucleation. Only in one case (4.3%) who presented with strabismus at the age of 9 months the globe was salvaged with employment of plaque therapy. In the bilateral group, at least one eye was enucleated in all patients. A second enucleation was performed in other 3 patients (17.6%). All of the patients were referred to oncologist following the operations. Outcome of the preserved eyes in the bilateral group was not clarified due to lack of follow up.

DISCUSSION

In the present stud, the unilateral and bilateral retinoblastoma consisted 57.5% and 42.5% of the studied population, respectively. In an Irish study on 785 cases with retinoblastoma, the unilateral and bilateral involvements were reported in 75.6% and 24.4% of the cases, respectively[5]. In another study in Nigeria, 75% of the cases with retinoblastoma were unilateral and 25% were bilateral[6]. The two groups were almost equal in number in an Indian series consisting of 354 patients with retinoblastoma [7]. It is previously reported that the common age of presentation in retinoblastoma is between 15 to 24 months [2]. The mean age of admission was 29.5 months for unilateral cases and 18.5 months for the bilateral involvement in our series. These ages were on average 24 and 12 months, respectively in a study in the UK [8]; 3.2 and 1.1 months, respectively in a report from Congo [9]; and 29 and 16 months, respectively in a Turkish series [10]. Although there is a wide variation in this regard, all the studies, as well ours show a significantly lower age for the patients with bilateral involvement than for the unilateral cases. More severe disease in the bilateral involvement justifies this earlier admission. We did not find any positive familial history of retinoblastoma in our patients. This is in contrast with the result of a previous study by Dondey *et al* [11] which indicated that the earlier detection of disease in bilateral cases is due to more frequent positive familial history in this group. Except for a study by Khandeker *et al* [12] in which the female gender was predominant in a group of patients with retinoblastoma. We, in line with other studies, show a borderline male predominance in the disease [8-11]. In our patients the leukocoria was the leading sign at the time of admission. Although the leukocoria is reported to be the most common clinical manifestation in many reports (ranging from 49% to 82%) [5,9,10], in Nigeria the proptosis and chemosis were the most frequent presentations (each one in 84.6% of the cases)[6]. In Nepal the proptosis was also the main presenting sign in a

group of patients with retinoblastoma (42.2% of the cases)[13]. This difference may be due to lower standards of health care systems and national screening programs in some developing countries with consequent progression of the disease at the time of diagnosis. In the present study 22 cases (96.6%) with unilateral involvement underwent enucleation, in all of which the disease was first noted by parents or in few cases by pediatrician. Only in one case the globe was preserved due to early detection of the disease. In bilateral group, the disease was first noted by parents or pediatrician and at least one eye was enucleated in all the cases. The rate of enucleation is estimated less than 50% for the cases in whom the diagnosis is made by an ophthalmologist through routine examination, whereas this rate rises up to 90% when the disease is detected by a family member for the first time[14]. In the present study, the mean diagnosis delay was 9.4 months in the unilateral group and 5.3 months in the bilateral group. Similar studies in the UK, Argentina and Switzerland reported this time averagely 8 weeks, less than 6 months and 3.8 months, respectively [15]. This important difference between the studies indicates lower efficacy of the screening methods or low rate of familiarity with the disease among the health care staff in developing countries. So, the results of current study may be useful for enhancing patients' outcome by increasing the awareness of physicians in dealing with these cases.

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