PRESENTING SIGNS OF RETINOBLASTOMA IN CONGOLESE PATIENTS

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ABSTRACT

Objective:
To report the relative frequency of the signs of presentation in Congolese children with retinoblastoma.

Methods:
A retrospective study was undertaken of all (29) patients with retinoblastoma examined between January 1995 and December 2000.

Results:
There were 19 (66%) boys and 10 (34%) girls. For all cases, mean age at diagnosis was 2.94 years±1.6 (range, four months to six years). For bilateral cases, it was 1.12 year±1.4 (range, two months to three years) whereas for unilateral cases it was 3.23 years±1.5 (range, four months to six years)(P = 0.016). More than seven distinct signs were identified. Leukocoria was the most common presenting sign in 49% of diagnosed cases followed by proptosis (28%). Other signs were strabismus, red eye, anterior scleral staphyloma, hyphema and buphthalmia.

Conclusion:
Strabismus seemed to be uncommon whereas proptosis is important in our small series when compared to signs reported in the developed world.

RÉSUMÉ

Objectif:
Décrire les signes de présentation de rétinoblastome chez les patients congolais.

Méthodes:
Etude rétrospective de 29 patients avec diagnostic de rétinoblastome, examinés de janvier 1995 à décembre 2000.

Résultats:
La répartition des patients en fonction du sexe est de 19 garçons (66%) et 10 filles (34%). L'âge moyen de tous les patients au moment du diagnostic est de 2,94 ans±1,6 (limites, 4 mois à 6 ans). Pour les cas bilatéraux, l'âge moyen est de 1,12 ans±1,4 (limites, 2 mois à 3 ans) et pour les cas unilatéraux, il est de 3,23 ans±1,5 (limites, 4 mois à 6 ans) (P = 0,016). Au total, plus de 7 signes de présentation sont identifiés. La leucocorie est le signe le plus fréquent (49%) suivi d'exophtalmie (28%). Les autres signes sont: strabisme, oeil rouge, staphylome scléral antérieur, hyphéma et buphtalmie

Conclusion:
Le strabisme semble être moins fréquent et l'exophtalmie plus importante dans notre petite série par rapport aux autres signes de présentation de rétinoblastome rapportés dans les pays développés.

KEY-WORDS

Retinoblastoma. Presenting signs.
Democratic Republic of Congo

MOTS-CLÉS

Rétinoblastome. Signes de présentation.
République Démocratique du Congo

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received: 23.11.01
accepted: 19.02.02

INTRODUCTION

Retinoblastoma is by far the most frequent and important malignant intraocular tumor of childhood, and one of the most common of all paediatric solid tumors, with an incidence of about 1 in 18,000 live births. In Africa, where melanoma is rare in all age groups, retinoblastoma assumes the position of the commonest and most important life threatening ocular neoplasm (6,8,10,14).

The presenting signs of retinoblastoma are well known in the developed world, with leukocoria invariably as most common and strabismus making up much of the remainder (1,2). However, relatively little information exists about the presenting signs of retinoblastoma in the developing countries such as the Democratic Republic of Congo. In most cases, the diagnosis of retinoblastoma is made later in these countries.

This study is undertaken to report the relative frequency of different presenting signs of retinoblastoma in Congolese children. This information could help in the early management of this disease in the developing world.

PATIENTS AND METHODS

The records of all patients with diagnosis of retinoblastoma seen in the department of Ophthalmology, University of Kinshasa, between January 1995, and December 2000 were reviewed.

The diagnosis of retinoblastoma was based on history, clinical examination and ancillary studies. The history included familial history including age of parents, any history of child's death, loss of vision or enucleation. A detailed perinatal and developmental history was obtained, including inquiries about premarurity and birth weight. Clinical examination included complete ocular examination including dilated ophthalmoscopy under general anaesthesia and physical examination by a paediatrician. Ancillary studies consisted of ocular ultrasonography and computed tomography, which showed the presence of solid intraocular tumor with calcium deposits.

For each patient age at diagnosis, sex, ethnicity, family history, referral person, laterality of retinoblastoma, alarming symptom noted by parents, presenting signs or symptoms at presentation and status of ocular examination of the eye(s) were considered.

RESULTS

Among 30,907 consecutive patients seen during the study period, we identified 29 patients (35 eyes) with retinoblastoma, giving a relative frequency of 0.1%. All patients were black Congolese. There were 19 (66%) boys and 10 (34%) girls. The male/female ratio was 2:1.
There were 23 (79%) unilateral cases and six (21%) bilateral cases. The right eye was affected in 11 (38%) patients, the left eye in 12 (41%), and both eyes in 6 (21%). All cases were sporadic and no familial cases were seen.
For all cases, mean age at diagnosis was 2.94 years±1.6 (range, 4 months to 6 years). For bilateral cases, it was 1.12 years±1.4 (range, 2 months to 3 years) whereas for unilateral it was 3.23 years±1.5 (range, from 4 months to 6 years) ($P = 0.016$). The mean age±SD at the time a parent first noted an ocular symptom was 2.24 years±1.6 (range, 1 month to 5 years) (2.24 years vs. 2.94 years, $P = 0.132$).
The mean time interval (delay) between the first symptom noticed by a parent and the first consultation at our Institution was 6.5 months (range, two weeks to 23 months).
Fourteen patients were referred by ophthalmologists, two by paediatricians and two patients brought by their parents. Information could not be obtained from 3 (10%) patients. The parents of two patients admitted that traditional healers first saw their children before referring to a health care center. For all cases, before referring to us, patients were first seen either by a general practitioner or a health care professional. The majority (80%) of cases came from the underprivileged social classes.

Leukocoria was the most frequent first alarming symptom, noted by the parents in 22 (76%) patients. It was followed by strabismus (four patients), proptosis (two patients) and hyphema (two patients). Of the 22 patients with leukocoria as alarming symptom, leukocoria was

Table 1 *Alarming symptoms of retinoblastoma as noted by parents*

Symptom	Patients	Percentage
Leukocoria		
alone	12	41
with strabismus	4	14
with proptosis	2	7
with photophobia	1	3.5
with ocular pain	1	3.5
with tearing	1	3.5
with nystagmus	1	3.5
with hyphema	1	3.5
Hyphema	1	3.5
Unknown	5	17
Total	29	100

seen alone in 10 patients and in association with other symptoms in 12 patients (Table 1). On examination, more than seven distinct presenting signs were identified. Leukocoria was the presenting sign in 17 (59%) patients (17 eyes, 49%). It was combined with redness (3 patients, 3 eyes), strabismus (2 patients, 2 eyes), anterior uveitis with secondary glaucoma (one patient, one eye) and vitreous hemorrhage (one patient, one eye). Proptosis was the presenting sign in 8 (28%) patients (8 eyes, 23%). It was combined with scleral anterior staphyloma and corneal necrosis in 4 patients (4 eyes), strabismus in one patient (one eye), scleral anterior staphyloma in one patient (one eye) and hypopyon in one patient (one eye). Hyphema as presenting sign was seen in three (10%) patients (three eyes, 9%). This sign was associated with redness in two patients and anterior uveitis, cataract, corneal oedema and strabismus in one patient. Other presenting signs were phthisis bulbi (one patient, one eye), buphthalmos (one patient, one eye) and redness (one patient, one eye). Pseudohypopyon and vitreous seeding occurred in one eye (one patient). The diagnosis of retinoblastoma was made under general anesthesia in the second eye of three patients during a routine examination.
In all but 3 patients (eyes) loss of vision was noted due to extension of the tumor. Visual acuity was assessed by the illiterate E-test and/or the ability to fixate and follow a light.

At the time of diagnosis, 23 (80%) patients had stage IV of the Reese-Ellsworth classification. In 11 patients the white, nodular mass extended into the vitreous (endophytic), in 9 patients the retinoblastoma presented as a mass underlying a retinal detachment (exophytic). In 4 patients, the retinoblastoma extended into the anterior chamber and in 4 patients there was an orbital extension of the tumor with proptosis. The tumor underwent spontaneous regression (phthisis bulbi) in one eye.

An average of 12 months passed between detection of the first sign of retinoblastoma and the beginning of therapy. Treatment modalities included enucleation and chemotherapy. Prior to and after enucleation, chemotherapy was given by the paediatrician, consisting of an association of cyclophosphamide, vincristine sulfate, and methotrexate. Mortality was 90%. Only two patients survived (follow-up ranging from 12 months to 38 months).

DISCUSSION

Over a period of 58 months, we found in this study a relative frequency of retinoblastoma of 0.1% of patients who consulted an ophthalmic service. This frequency can be compared with 0.1 to 0.83% reported in other similar studies in Africa (3,11,12,15).

In developed countries, the average age of retinoblastoma at diagnosis is 18 months. The mean age at diagnosis in this study was extremely high - 2.94 years as compared to 1.5 years in the United States. The mean age of diagnosis reported in other African studies, ranged from 24 months to 44 months (3,5,11,12,16).

A number of studies in Africa have reported a male/female of 1:1 (3,11,12). We don't have any explanation to our male/female ratio of 2:1. Is it the reality, due to environmental factors, or could it be related to bias referral?

Hereditary cases were absent in this study, probably because in the past cases have almost invariably succumbed without an opportunity to transmit the gene.

The presenting signs and symptoms of retinoblastoma are determined by the extent of tumor at diagnosis. In developed countries, the most common presentation of retinoblastoma

is leukokoria (50% to 60%) (1,2,13), referred to by the parents as ''white pupil'' or a ''cat's-eye reflex'' (1). The second most common presentation is strabismus (18% to 22%), secondary to sensorial deprivation. It occurs when the visual acuity is decreased by a tumor in the posterior pole (1). Other signs of retinoblastoma may include orbital cellulitis (17), neovascular glaucoma (18), pseudohypopyon (19) and hyphema (4). Nystagmus can also be a manifestation of bilateral macular disease due to sensorial deprivation (1,7). Older children may complain of decreased visual acuity and floaters; however, these visual symptoms are infrequent because most tumors present in preschool age children. In advanced cases phthisis bulbi may present, or the child may develop proptosis after orbital extension of the tumor. In poorly developed countries, proptosis with orbital invasion is a common presentation (11,12,15). In this study, leukokoria (49%) was the most common presenting sign followed by proptosis (28%) and strabismus (11%).

The mean time (delay) before a parent consulted a physician after noticing something wrong with the child's eye was 6.5 months in this study. This delay in diagnosis found in this study is consistent with other studies in Africa (3,5,11,12,15). It is higher when compared with that of 2 to 3 months reported in the developed world (9,20).
The marked delay in diagnosis of the tumor in this study may explain a higher incidence of extraocular extension, a more advanced stage of the disease and poorer survival rates. The most important risk factor associated with death is extraocular extension of tumor. The prognosis for survival in children with retinoblastoma in developed countries is very good, with overall survival rates over 90%. In this study, most patients presented late and the mortality rate was hight (90%).

Poor parental education, relative paucity of ophthalmic and oncological services in the country as well as psychological attitudes to disease might play a role in delayed diagnosis in this study. Many patients live also far from medical services and may be treated by traditional healers before coming to a hospital. Early diagnosis is essential for a good prognosis. The ability to recognize the presenting signs and symptoms of retinoblastoma can lead to early diagnosis and treatment. Educating parents, and those persons who are the first to examine children with retinoblastoma about the presenting ocular signs, will be helpful in quick ophthalmic examinations and more accurate diagnosis.

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