DELAYED DIAGNOSIS OF RETINOBLASTOMA

WIRIX M. [1], PARYS-VANGINDERDEUREN R.*, CASTEELS I.*, UYTTEBROUCK A.***

SUMMARY

The aim of our study was to evaluate the age of the patient and the stage of retinoblastoma at diagnosis and to determine the time delay between the first symptoms noticed by proxy and the diagnosis of retinoblastoma. Therefore, thirty-three children between the age of zero and seven with the diagnosis of uni- or bilateral retinoblastoma were studied retrospectively.

Thirty-one patients were diagnosed with advanced disease; two patients had small tumors. The mean time delay between the first clinical symptoms and the diagnosis of retinoblastoma was 3.2 months (range 2 months to 1 year).

In our study most children with retinoblastoma were diagnosed with advanced disease. In some patients there was a significant time delay between the first symptoms and the final diagnosis of retinoblastoma. Better parental and environmental information regarding symptoms of retinoblastoma could help to assure earlier detection of tumors.

RÉSUMÉ

L'objectif de notre étude fût l'évaluation de l'âge du patient en fonction du stade de rétinoblastome au moment du diagnostic. De plus, nous avons voulu déterminer le laps de temps écoulé entre les premiers symptômes aperçus par l'environnement du patient et le diagnostic de rétinoblastome effectué par le médecin. Pour atteindre notre objectif, trente-trois enfants, âgés de zéro à sept ans, ayant été diagnostiqués avec un rétinoblastome uni- ou bilatéral, ont été examinés rétrospectivement.

Trente-et-un patients furent diagnostiqués avec la maladie dans un stade avancé, deux patients avaient des tumeurs peu développées. Le laps de temps moyen entre les premiers symptômes cliniques et le diagnostic de rétinoblastome fût de 3,2 mois (variant de 2 mois à 1 an).

Dans notre étude, la plupart des patients ayant le rétinoblastome furent diagnostiqués avec un stade avancé de la maladie. Pour certains patients, il y eut un laps de temps important entre les premiers symptômes et le diagnostic final.

Une meilleure information concernant la détection des symptômes de rétinoblastome pourrait aider à la détection plus rapide des tumeurs.

KEY WORDS

Delayed diagnosis; Retinoblastoma

MOTS CLÉS

Diagnostic tardif; Rétinoblastome

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* *Department of Ophthalmology, St-Rafael University Hospital, Capucijnenvoer 33, 3000 Leuven, Belgium*

** *Department of Pediatric Oncology, Gasthuisberg University Hospital, Herestraat 49, 3000 Leuven, Belgium.*

received: 17.08.00
accepted: 27.09.00

INTRODUCTION

Retinoblastoma is the most common, primary malignant intraocular tumor of childhood. Even so, it is a rare tumor, occurring in only about 1 in 20,000 live births. The mean age at diagnosis is 18 months and the vast majority become clinically apparent before the age of 3 (12). Children with bilateral tumors present earlier than those with unilateral involvement. The inheritance of bilateral tumour is autosomal dominant but only 6% have a positive family history. These cases have an early onset and are predisposed to develop non-ocular malignancies. Sporadic cases may be bilateral or unilateral. All bilateral cases are considered to have a germinal mutation and are therefore gene carriers. Between 10 and 15% of unilateral cases are also the result of a germinal mutation and carry the gene just as the bilateral cases. Therefore it is very important to notify the parents about the possibility of inheritance (3, 8).

The most frequently occurring symptoms of retinoblastoma at presentation are leukocoria (60%) and strabismus (20%). Secondary glaucoma, pseudouveitis, orbital inflammation and proptosis can also be seen (6).

Indirect ophthalmoscopy with scleral indentation and biomicroscopic examination with visualization of the tumor using a 90 diopter lens should be performed on both eyes.

CT scan, MRI and ultrasonography to detect the presence of calcifications in the tumor are helpful to confirm the diagnosis of retinoblastoma as well as to evaluate the extension of the tumor (1).

Treatment depends on the location and extension of the tumor. Enucleation is the treatment of choice for advanced unilateral cases. In bilateral cases radiotherapy is applied to both eyes to save useful vision in at least one eye. More recently, techniques of chemoreduction and chemo-thermotherapy have achieved popularity in the management of retinoblastomas. (7, 9, 11).

The overall mortality rate is about 15 %.

PATIENTS AND METHODS

We examined retrospectively records of 33 patients (18 girls and 15 boys) with retinoblastoma. The patients were recorded between 1968 and 1998. They all presented at our department between the age of one month and seven years. The mean age at presentation was two years and nine months.

Seven children were found to have a bilateral retinoblastoma, five were diagnosed at presentation, the other two at follow-up. Twenty-six children had a unilateral retinoblastoma.

We studied in detail the time delay between the moment a symptom was noted by the parents or by the environment, and the time of diagnosis.

RESULTS

Primary healthcare professional first consulted by parents

Only one patient was referred to our clinic by a general practitioner, 2 were referred by their pediatrician, while the other thirty patients were referred by their own ophthalmologist.

Alarming symptoms

The first symptoms noted by parents can be divided in five main groups: leukocoria, strabismus, a combination of both, redness of the eye and visual loss (6).

Leukocoria, denoting a large intraocular lesion, was the initial symptom in 13 patients. Parents often described leukocoria as ''being able to see right through the eye'' or ''a difference in color between the two eyes''.

Strabismus, due to reduced central vision secondary to tumor or retinal detachment was the first symptom in 6 patients.

In four children, strabismus progressed to leukocoria as the tumor enlarged.

In 4 patients loss of vision was the first symptom. One of them also had pain. All four of them where over the age of 5 years. Another four patients consulted because of a red eye. In one patient the redness was associated with leukocoria and in another one with pain and leukocoria. We also saw the redness combined with strabismus in one patient and with pain only in another patient.

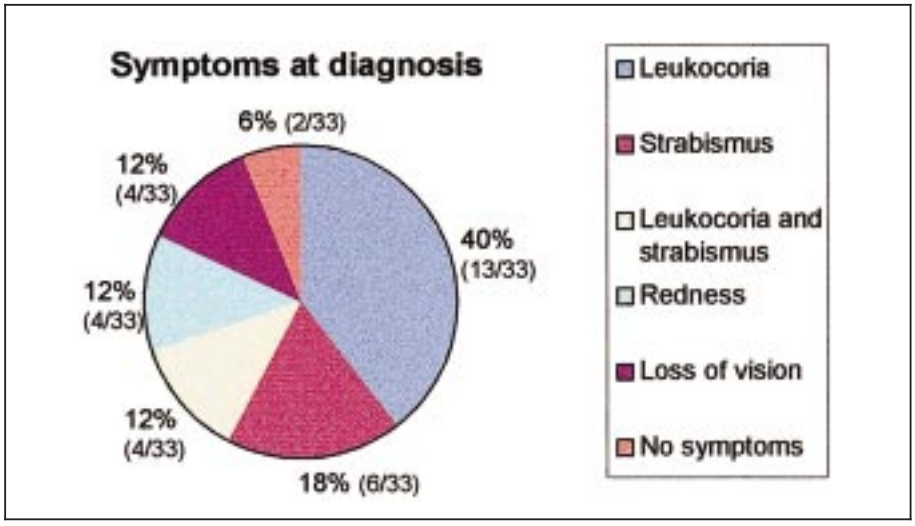

Fig. 1. Symptoms at diagnosis.

Two patients showed no symptoms at all. One of them was seen for the first time at the age of one month because of a positive family history. Her father was known to have bilateral retinoblastoma. In the other child the retinoblastoma was coincidentally detected on fundoscopy to exclude signs of intra-cranial hypertension after a head trauma.

Time interval between first symptom and first consultation

In most of the patients 2 to 4 months passed (mean delay 3,2 months) before the parents went to see a physician after noticing something wrong with the child's eye.

One patient was excluded from the study to calculate the mean time delay between noticing the first symptom and the first consultation. She was followed up for four years for strabismus without having a proper fundus examination.

In two patients it took a year before referral. One patient showed visual loss at a medical school examination, but was not referred to an ophthalmologist. She was only referred the year after she had complete loss of vision. In the other patient leukocoria was noticed by the parents at the age of 18 months. The general practitioner denied the symptom and the parents only consulted an ophthalmologist a year later.

Age of child when first symptom noted

The mean age of the patient at the first ocular symptom was 21 months. Eight patients were over 3 years old when the first symptom was noted.

The mean age of patients with leukocoria as the first symptom was 20.6 months. Those in whom strabismus was the first symptom had an mean age at presentation of 32 months.

Pathological examination

From all twenty-six enucleations pathological examination was performed. Optic nerve invasion was present in seven patients of whom six had prelaminar invasion and one distal end invasion. Nine patients showed choroidal invasion only. Ten patients showed no invasion at all.

Treatment

All 26 children with unilateral retinoblastoma were treated with enucleation because of very advanced disease and no hope for better visual outcome with conservative treatment.

Three patients with the unilateral form had additional chemotherapy because of deep cho-

roidal invasion and optic nerve invasion in one patient.

Two patients with the bilateral form had enucleation of the worst affected eye and external beam radiotherapy of the other eye. In two other patients both eyes were at first treated with external beam radiotherapy but eventually needed enucleation of the worst affected eye.

Two patients, also with the bilateral form, underwent enucleation of the worst affected eye and xenon laser photocoagulation of the other eye.

In the baby with the positive family history the retinoblastomas were found at a screening examination. They were bilaterally successfully treated with xenon laser photocoagulation.

Follow-up

Follow-up ranged in this study from 12 to 60 months. In our youngest patient we have a follow-up of 12 months.

Of the thirty three we lost follow-up of two patients.

Twenty-nine patients survived.

Two patients died, both had a unilateral advanced retinoblastoma and they both received adjuvant chemotherapy. One of them had optic nerve and choroidal invasion and died one year after the diagnosis of the retinoblastoma. The other patient only had deep choroidal invasion without optic nerve invasion and died two years after diagnosis.

DISCUSSION

In our study we found that leukocoria and strabismus were the two most frequent symptoms of retinoblastoma. Six of them showed less frequent symptoms like pain, redness off the eye and loss of vision. The mean delay between noticing the first symptom and the diagnosis was 3.2 months. The mean age at first symptom of patients with bilateral tumors was 10 (range 1 to 24) months. Patients with unilateral tumors were significantly older with an mean age of 37 (range 6 to 94) months.

Presenting symptoms were in accordance with clinical experience of retinoblastoma in other developed countries. (5)

Unilateral cases were treated with enucleation because of very advanced disease at diagnosis with loss of vision without hope for better visual outcome.

The management of retinoblastoma has gradually changed over the past few decades. There is a trend away from enucleation and external beam radiotherapy toward focal conservative treatments, plaque radiotherapy, laser photocoagulation, cryotherapy, thermotherapy and chemo-thermotherapy, intravenous chemoreduction and subconjunctival chemoreduction (7, 9, 11).

In our study most children were diagnosed with advanced disease (Reese-Ellsworth Group IV-V) which explains why most of them had enu-

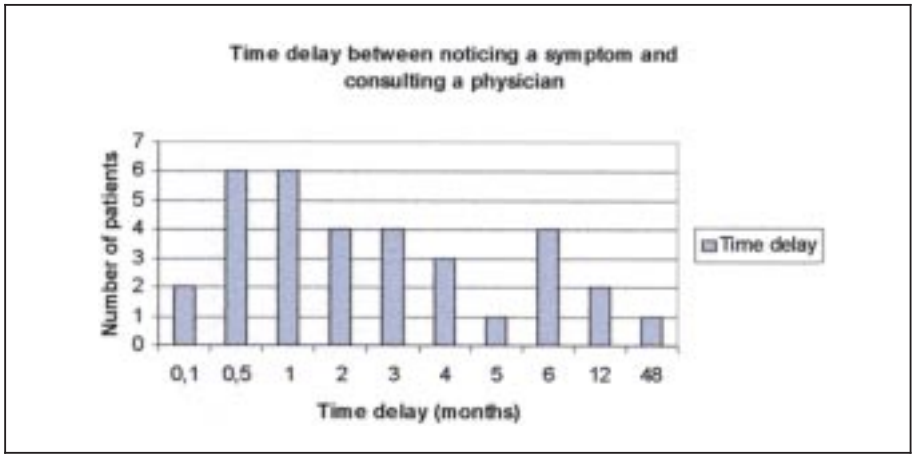

Fig. 2. Time delay between noticing a symptom and consulting a physician

cleation of the worst affected eye because there was no hope for better visual outcome.
The smaller the tumor at presentation the greater the possibility that methods of treatment such as laser and cryotherapy can be utilized, minimizing morbidity and mortality.
Choroidal invasion can be detected in thirty-three percent of enucleated eyes and is a prognostic factor even if the optic nerve is not invaded (1, 2).
Compared to the study done by Goddard et al. our time delay before parents went to see a physician after noticing there was something wrong with the child's eye was longer (3.2 months compared to 2 months).
General practitioners, pediatricians as well as social health care institutions should be aware that the best way to prevent visual loss or enucleation secondary to this disease, is to incorporate visual prevention assessment into everyday general practice in a timely, appropriate and rewarding way. Primary healthcare professionals require education about ocular symptoms, especially squint and leukocoria in pediatric patients. Leukocoria is not a symptom that is noticed constantly but depends on the way the eye is illuminated.

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Address of correspondence: Dr. Wirix M.
Department of Ophthalmology
St-Rafael University Hospital Leuven
Capucijnenvoer 33, B-3000 Leuven
Belgium