

Epidemiological Features and Survival of Retinoblastoma Patients in Perú

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Summary

Purpose: To describe some of the epidemiologic features of children with retinoblastoma diagnosed during a 14-years period at the main oncological center of a developing country, and to estimate their survival rate, identifying risk factors related to an increased mortality. **Methods:** The records of all retinoblastoma patients examined from 1987 through 2000 were retrospectively reviewed. Survival during followup was analysed by the Kaplan-Meier method and Cox regression model. **Results:** Three hundred and thirty four children were followed for a median time of 307 days. The estimated five-years survival rate was 73%. Mortality was significantly related to an advanced TNM stage (III or IV; RR=11,11) and proceeding from Lima (RR=2,56). **Conclusions:** As in most developing countries, retinoblastoma is still associated with a high mortality which is essentially consequence of the advanced stages of disease at diagnosis.

Keywords: Retinoblastoma, Survival Analysis, Human, Peru, Developing Countries

Introduction

Retinoblastoma is the most common malignant intraocular tumor of childhood, with a reported incidence of 1:18000 to 1:30000 newborns.^{1,2} In developed countries the five year survival is about 90%. Many patients in developing countries are diagnosed with extraocular disease, so the survival is significantly lower.³

The Instituto Nacional de Enfermedades Neoplásicas (INEN) in Lima is the greatest peruvian oncology center to which patients all over Peru are referred for evaluation and treatment of presuntive neoplastic diseases.

In this brief report, we describe some of the epidemiological characteristics of the patients with retinoblastoma attended at INEN during a 14-years period as well as the factors identified related to an increased mortality.

Methods

The records of all retinoblastoma patients examined at INEN from 1987 through 2000 were retrospectively reviewed. The suspected factors that could contribute to increased tumor extension and mortality were evaluated.

The age at diagnosis between patients with unilateral and bilateral disease was compared with the student t test, and a possible overall gender predominance was evaluated with the z test, assuming a normal distribution of p.

Tumor extension for each patient was obtained retrospectively according to the TNM classification of the International Union Against Cancer.⁴

A Kaplan-Meier survival curve was obtained for all the patients and for each TNM stage. Differences between mortality curves were determined with the logrank test.

A Cox proportional hazard regression was done to determine risk factors of mortality using as covariates the relevant variables available in the clinical records, which were: gender, origin (Lima vs other regions), extension of

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disease (TNM I or II vs TNM III or IV), unilateral vs bilateral disease, age at diagnosis, and duration of disease.

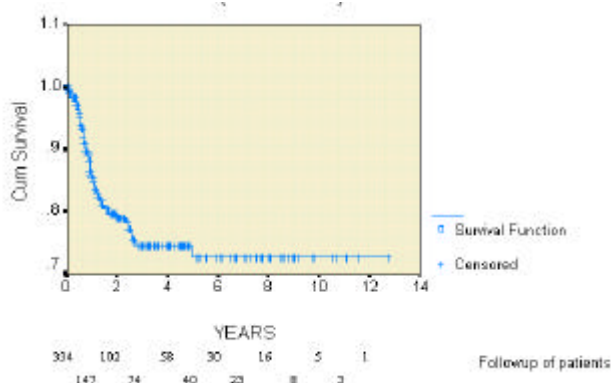
Results

Three hundred and thirty four patients with retinoblastoma were diagnosed at INEN since January 1st 1987 through December 31st 2000. Patients were followed for a median time of 307 days.

The average age at diagnosis for patients with unilateral disease was 3 years and 5 months, while for patients with bilateral tumors it was 1 year and 9 months, a statistically significant difference ($p < 0,001$). There was no predominance of either sex ($p > 0,1$). The median duration of disease at diagnosis was 6 months (IQR, 2 - 12 months).

One hundred and one patients (30,2%) had bilateral disease while only eight patients (2,4%) had family history of retinoblastoma, either from the father (6 patients), the mother (one patient) or brothers and sisters (five patients). All but one of the patients with family history had bilateral disease.

Figure 1. Kaplan-Meier Survival Curve for Retinoblastoma Patients. INEN (1987-2000)



The overall five year survival rate was 73% (95% confidence interval, 65,4% - 80,6%) (Figure 1). More than half of patients (54,79%) had an advanced disease (TNM III or IV) at diagnosis (Figure 2). The Kaplan-Meier survival curves for each TNM stage were significantly different ($p < 0,0001$) (Figure 3). In the Cox regression analysis, the main factors independently related to an increased mortality were an advanced disease (TNM III or IV), and being from Lima (Table 1).

Table 1. Independent Risk Factors for Mortality. INEN (1987-2000)

COVARIATE	RELATIVE RISK	95% CONFIDENCE INTERVAL	P
AGE AT DIAGNOSIS (MONTHS) (*)	-	-	0,98
FEMALE SEX	1,02	0,55 - 1,89	0,95
DURATION OF DISEASE (MONTHS) (*)	-	-	0,86
BILATERAL DISEASE	0,78	0,37 - 1,61	0,50
COMING FROM LIMA	2,55	1,32 - 5,00	< 0,01
ADVANCED TNM (Stage III or IV)	11,11	4,78 - 25,00	< 0,0001

(*) $R^2 = 0,00$ for both variables

Figure 2: TNM Stage of Patients with Retinoblastoma. INEN (1987-2000)

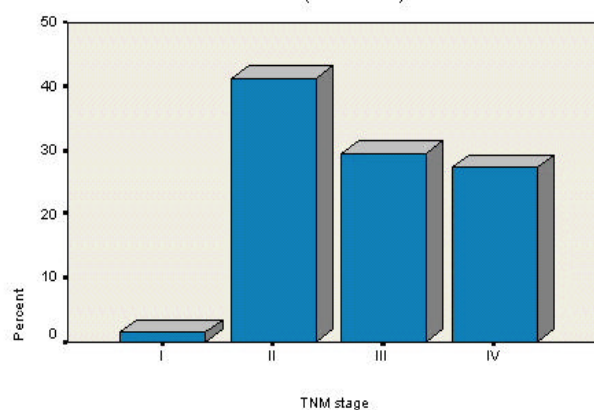
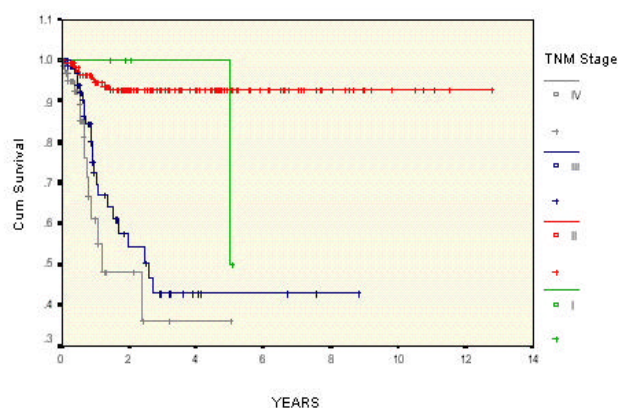


Figure 3: Kaplan-Meier Survival Curves for Each TNM Stage. INEN (1987-2000)



Discussion

INEN is the only oncological medical institute in Perú and one of the few centers in the country where neoplastic diseases can be adequately treated. Hence, it is probably the only place where cancer patients all over Perú are referred. The number of patients included in this study (average, 24

per year) falls within what is expected from the reported incidence of retinoblastoma worldwide and the birth rate in Perú.⁵

As well as in other series, there was not sex predominance and patients with bilateral disease were diagnosed at a younger age than unilateral cases. However, our patients were older than what has been reported for developed countries (12 months and 24 months for bilateral and unilateral cases, respectively).³

Although at least thirty percent of our patients had hereditary disease (at least almost all bilateral cases), only eight patients (2,4%) had family history of retinoblastoma. This is not surprising since in hereditary retinoblastoma, the mutation carried by the patient occurs in a germinal cell of a parent.⁶

Survival in our patients was significantly lower than what has been reported in developed countries (about 90% for five years).³ It appears that this high mortality is due to a high proportion of patients with advanced disease rather than a suboptimal treatment in our institution, given that patients with TNM II have a similar survival than patients in developed countries (Figure 3). Moreover, the treatment techniques available at INEN are similar to what is used in other well known institutions.⁷ The finding of an increased mortality in patients from Lima could be secondary to a greater loss of followup in patients coming from rural regions and consequently a deficient death report.

The followup of patients with retinoblastoma during the first five years after diagnosis was very poor (Figure 1) considering the high mortality expected for this period and the possibility of metachronic disease (later tumor appearance in the contralateral eye) in patients with an hereditary component. Another issue that must be assessed is the advanced disease at diagnosis (TNM III or IV) in 54,79% of our patients which, as noted above, dramatically increased

mortality in our series. In developed countries patients with retinoblastoma are diagnosed earlier, when signs as leucocoria and strabismus have recently appeared, so that extraocular and metastatic disease are much less frequent.⁸

Further research will be done to evaluate treatment variables in the mortality analysis. The data presented so far, suggest that efforts are urgently needed to implement screening campaigns of retinoblastoma in children with subtle but easily detectable symptoms in order to improve survival of these patients in Perú.

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