A multicentre report from the Mexican Retinoblastoma Group


Background: Retinoblastoma (RB) is a relatively uncommon tumour in childhood. The incidence of retinoblastoma in Mexico is probably higher than the incidence reported worldwide, however there is not enough information about the characteristics of this illness in Mexico. This report aims to present the results of a multicentre clinical survey of RB in Mexico.

Methods: A retrospective study was carried out on all RB cases treated in 16 institutions during the last six years. The variables analysed were age at diagnosis, sex, affected eyes, treatment modalities, and pathological staging. Overall survival was obtained.

Results: The authors analysed 500 cases; age range was 0–182 months. There were 364 unilateral cases (72.8%). Enucleation was performed in 84.9% of the patients. The St Jude's staging was: 7.4% stage I, 52.8% stage II, 18.0% stage III, 11.4% stage IV, 7.2% not evaluated, and 3.2% missing data. Chemotherapy was used in 74.4% of the patients. Disease free survival was 89% at 73 months follow up.

Conclusions: The paper presents a great number of cases and pioneers multicentre studies in pediatric ophthalmology and oncology in this country. Given the great number of patients in advanced stages and the variability on treatment schemes, it is evident that it is mandatory to work in a cooperative group and develop a national early detection programme as well as a treatment protocol which include all specialists involved in the care of patients with RB.

Materials and Methods

A multicentred, retrospective, and descriptive study was carried out. Sixteen Mexican centres provided information on patients with RB diagnosed between 1 January 1997 and 31 December 2002. The contributing centres are as follows (number of patients shown in brackets): Centro Estatal de Cancerología de Jalapa (4); Centro Médico de Occidente, IMSS Jalisco (13); Centro Médico La Raza (41); Centro Médico Nacional SXXI (43); Hospital Civil de Durango (2); Hospital Civil de Guadalajara (24); Hospital del Niño Morelense (10); Hospital del Niño Oaxaqueño (13); Hospital General de México (21); Hospital Pediátrico de Sinaloa (12); Hospital Infantil de México Federico Gómez (54); Hospital Central Universitario de San Luis Potosí (12); Hospital del Niño de Villahermosa (9); Instituto Nacional de Pediatría (229); Instituto Materno Infantil de Estado de México (7), and Hospital O'Horal de Mérida (6).

Recorded data included age at diagnosis, date of diagnosis, ocular affection (unilateral or bilateral) at diagnosis, stage at diagnosis according to St Jude’s staging system,10 treatment modalities used (radiotherapy, surgery, and chemotherapy), and date of last visit. The survey did not consider information regarding secondary malignancies and treatment related deaths. The status of the patient evaluated by clinical examination and/or radiological studies at last visit was considered to be: alive with no evidence of disease; alive with active disease (patients with neoadjuvancy were considered in this group); dead with no evidence of disease, and dead with active disease.

Statistical analyses were performed using the SPSS system (SPSS for Windows 10.0; SPSS Inc, Chicago, IL, USA). Descriptive statistics for each variable were obtained. The Kaplan-Meier method with log rank test was used to determine overall survival. Differences between groups were considered significant when two sided p value was <0.5.

Results

Between January 1997 and December 2002, a total of 500 patients were diagnosed with RB in the participating centres (mean 83.3 new cases per year). Figure 1 presents the number of patients per year; 262 were male and 238 female.

Abbreviations: RB, retinoblastoma.
The calculated overall survival was 85% at 73 months of follow up, the mean survival time was 23.1 months (median 19.4). Figure 2 presents the overall survival by stage.

DISCUSSION

In Mexico, retinoblastoma is the second most frequent solid malignancy in paediatric patients, the most frequent being central nervous system tumours.1 Several centres that treat RB in Mexico did not participate in this survey so the number of cases of RB in Mexico could be higher than reported here. Hurwitz has suggested that the number of new cases per year could be higher in developing countries than in developed.12 However, with the data collected thus far we could not support this hypothesis.

As mentioned above, 45.8% of the patients were treated in a single institution (Instituto Nacional de Pediatría). This situation could be related to many factors: firstly, it is a national reference centre; secondly, for many years it was one of the few centres in the country for the treatment of retinoblastoma, and even now that other centres are working, ophthalmologists and general practitioners do not refer patients to other centres; finally, because many non-profit organisations support treatment in this centre but not in others. One of the aims of the retinoblastoma group is to create a national reference programme to better distribute the medical attention for RB patients, and reduce the risk of lost follow up by minimising the costs of transportation to the treatment centres. The mean age at diagnosis was similar to what we reported in our previous study,7 and higher than that reported in other series from developed countries.13 Diagnosis at older ages seems to be a common finding in developing countries.14

In patients in advanced stages (orbital and metastatic disease), and 188 patients with ocular disease (in many centres their chemotherapy protocol still considers it use necessary). More than 15 different regimens were used by the participating centres (table 4). Twenty one per cent (106) of the patients received chemotherapy based on cyclophosphamide and doxorubicin, 50.6% (253) received chemotherapy based on cisplatin or carboplatin plus other drugs, and 2.6% (13) received treatment based on research/new drugs protocols or miscellaneous schemas. Twenty three per cent of the patients did not receive chemotherapy agents.

Table 2 Surgery modalities used

<table>
<thead>
<tr>
<th>Unilateral</th>
<th>Bilateral</th>
</tr>
</thead>
<tbody>
<tr>
<td>No surgery</td>
<td>85 1.4 9 6.6</td>
</tr>
<tr>
<td>Rejects surgery</td>
<td>5 1.4 9 6.6</td>
</tr>
<tr>
<td>Eye preservation</td>
<td>9 2.5 14 10.3</td>
</tr>
<tr>
<td>Unilateral enucleation</td>
<td>330 90.6 97 71.3</td>
</tr>
<tr>
<td>Bilateral enucleation</td>
<td>0 0.0 11 8.1</td>
</tr>
<tr>
<td>Unilateral exenteration</td>
<td>17 4.7 5 3.7</td>
</tr>
<tr>
<td>Missing data</td>
<td>3 0.8 0 0.0</td>
</tr>
<tr>
<td>Total</td>
<td>364 100.0 136 100.0</td>
</tr>
</tbody>
</table>

Table 1 Stage at diagnosis

<table>
<thead>
<tr>
<th>St Jude’s stage</th>
<th>Frequency</th>
<th>Frequency</th>
<th>Total</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>I Limited to retina</td>
<td>22 6.0 15 11.0 37 7.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>II Limited to the eye</td>
<td>194 53.3 70 51.5 264 52.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>III Limited to the orbit</td>
<td>75 20.6 15 11.0 90 18.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV Metastatic disease</td>
<td>44 12.1 13 9.6 57 11.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not classifiable</td>
<td>19 5.2 17 12.5 36 7.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Missing data</td>
<td>10 2.8 6 4.4 16 3.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>364 100.0 136 100.0 500 100.0</td>
<td></td>
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</tr>
</tbody>
</table>

Table 3 Radiated patients: stage at diagnosis

<table>
<thead>
<tr>
<th>St Jude’s stage</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>I Limited to retina</td>
<td>4 3.05</td>
</tr>
<tr>
<td>II Limited to the eye</td>
<td>31 23.67</td>
</tr>
<tr>
<td>III Limited to the orbit</td>
<td>47 35.88</td>
</tr>
<tr>
<td>IV Metastatic disease</td>
<td>25 19.08</td>
</tr>
<tr>
<td>Not classifiable</td>
<td>17 12.98</td>
</tr>
<tr>
<td>Missing data</td>
<td>7 5.34</td>
</tr>
<tr>
<td>Total</td>
<td>131 100.0</td>
</tr>
</tbody>
</table>

(M:F ratio 1.1:1.0). The age at diagnosis ranged from 1 day to 182 months, with a mean of 27.68 months (median 24). Initial ocular presentation was unilateral disease in 364 (72.8%) and bilateral disease in 136 (27.20%) patients. Mean age at diagnosis for unilateral cases was 30.96 months (median 28), whereas mean age for bilateral cases was of 18.87 (median 14).

Most of the centres did not provide information concerning the ocular stage at diagnosis (Reese-Elsworth staging system); therefore this data is not included in the report. Stage at diagnosis (St Jude’s staging system) is presented in table 1, showing that almost 30% of the patients were diagnosed at advanced stages. Approximately 13% of the cases could not be staged due to multiple causes such as neoadjuvancy, incorrect management of the enucleated eye, or insufficient material of the optic nerve.

Treatment

The treatment modalities were mainly surgery, chemotherapy, and radiotherapy. Enucleation was performed in 87.62% of the patients (table 2). External radiotherapy was used in 131 patients (26.2%); the indications for this treatment modality were adjuvant therapy in orbital or metastatic disease and eye rescue for bilateral disease when vitreous seedlings were present. The stage at diagnosis for radiated patients is presented in table 3. Among radiated patients 57 (26.8%) and bilateral disease in 136 (27.20%) patients. Mean age at diagnosis ranged from 1 day to 19.4). Figure 2 presents the overall survival by stage.

Figure 1 Frequency of new patients per year.

![Figure 1](http://bjo.bmj.com/)

Figure 2 Overall survival by stage.
reports of a higher prevalence of the disease in rural areas where the patients come from, but this issue does not have reliable data concerning the kind of community.

The distribution by affected eye is similar to our previous report, this series is the first attempt to work in a cooperative multicentre group in paediatric oncology in Mexico.

Chemotherapy regimens used reflect the evolution of treatment of RB. Some centres are still using the regimens proposed by the Paediatric Oncology Group in 1972; other centres have modified their treatments to include drugs such as carboplatin plus VP 16, and in a few centres new drugs such as taxol, irinotecan, and other new agents are being tested in metastatic disease. Even the indications for chemotherapy vary among centres; in some of them chemotherapy is still used for patients in stage II. One of the aims of the Mexican Retinoblastoma Group is the development of a national treatment protocol, which would enhance the medical care of these patients and would open the possibility to perform controlled clinical trials.

The survival of this series of patients is similar to other large series reported before, nevertheless the follow up is still short. In comparison with our previous report, this series presents higher survival rates for stages II and III. Schwartzman et al from Buenos Aires, reported similar overall survival rates (84%). Antoniell et al from Sao Paolo, and Chantada et al from Buenos Aires, report similar survival rates for orbital and metastatic disease. The common finding in all these series is the low survival rates for metastatic disease. As described above, the survival of our patients is similar to other series from Latin America; however the comparison between them is difficult as our follow up period is still short and the reports mentioned are from single institutions with more standardised treatments, whereas our report is a multicentre national study with a great diversity of chemotherapeutic regimens.

Given the number of new cases per year registered in this survey, RB is a frequent neoplasia in Mexico. It is necessary to create a national registry to understand the actual impact of RB in our country. The late diagnosis is a common problem in developing countries, and should be controlled to enhance prognosis and quality of life for these patients. In the same way, treatments need to be standardised so that every centre can offer the best available treatments at the lowest cost for patients. There is a lot of work to be done; nevertheless survival for RB patients in Mexico is similar to what has been reported in other series.

This survey is relevant not just because of the data obtained, but because is the first attempt to work in a cooperative multicentre group in paediatric oncology in Mexico.

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REFERENCES


