Bol Med Hosp Infant Mex. 2015;72(5):299–306

Boletín Médico del
Hospital Infantil de México

www.elsevier.es/bmhim

REVIEW ARTICLE

Retinoblastoma in Mexico: part I. A review of general knowledge of the disease, diagnosis, and management

Van C. Lansingh[a,b,c], Kristen A. Eckert[d], Barrett G. Haik[c], Blanca X. Phillipps[c], Vanessa Bosch-Canto[e], Carlos Leal-Leal[e], Marco A. Ramírez-Ortiz[f,*]

[a] *Instituto Mexicano de Oftalmología, Querétaro , Querétaro, Mexico*
[b] *Help Me See, New York, NY, USA*
[c] *Department of Ophthalmology, Hamilton Eye Institute, The University of Tennessee Health Science Center, Memphis, TN, USA*
[d] *Independent Public Health Consultant, Tapachula, Chiapas, Mexico*
[e] *Instituto Nacional de Pediatría, Mexico City, Mexico*
[f] *Department of Ophthalmology, Hospital Infantil de México Federico Gómez, Mexico City, Mexico*

Received 27 May 2015; accepted 4 September 2015
Available online 26 October 2015

KEYWORDS
Retinoblastoma;
Epidemiology;
Early cancer detection;
Disease management

Abstract This is the first of a two-part review that aims to report the current knowledge of retinoblastoma (Rb) and its implications in Mexico (including the authors' experience at the leading Rb centers), identify the gaps in practice, and propose solutions to improve diagnosis, treatment, and patient uptake. In this first part, general knowledge of Rb diagnosis and management is summarized with a focus on the latest advances in chemotherapy. A general review of peer-reviewed literature of Rb was conducted on PubMed. Key findings were summarized.

Provided there is early detection and referral of patients followed by appropriate conservative management, Rb is curable. In developed countries, the primary treatment outcome is ocular salvage with sight preservation. Advanced chemotherapeutic options such as intra-arterial and intravitreal chemotherapy can now save even the most advanced tumors.

Advances in Rb therapy are generally limited to developed countries. The implications in Mexico, of the findings from this review will be discussed in Part 2, which will be a comprehensive situational analysis of the state of Rb programming in Mexico, including a review of current demographic data available from hospitals that have Rb programs or treat Rb.

* Corresponding author.
E-mail address: marco@unam.mx (M.A. Ramírez-Ortiz).

http://dx.doi.org/10.1016/j.bmhimx.2015.09.001

PALABRAS CLAVE
Retinoblastoma;
Epidemiología;
Diagnóstico temprano del cáncer;
Manejo de enfermedad

Retinoblastoma en México: parte I. Revisión del conocimiento general de la enfermedad, diagnóstico y tratamiento

Resumen Esta es la primera parte de un trabajo de revisión donde se reportan los conocimientos actuales del retinoblastoma (Rb) y sus implicaciones en México (incluyendo la experiencia de los autores en los principales centros de referencia), así como las brechas en la práctica y las posibles soluciones para mejorar el diagnóstico, tratamiento y referencia de pacientes. En esta parte se resumen los conocimientos generales del Rb, su diagnóstico y tratamiento. Se realizó una revisión de los avances más recientes en esta enfermedad publicados en PubMed y se resumieron los hallazgos más importantes.

La sospecha oportuna y la referencia adecuada de pacientes permiten que el tratamiento conservador del Rb sea curativo. En países en vías de desarrollo, el tratamiento primario es el salvamento ocular y la preservación de la visión. Las opciones de quimioterapia intraarterial o intravítrea permiten ofrecer opciones terapéuticas en estos pacientes.

Los avances en el tratamiento del Rb están generalmente limitados a países industrializados. Las implicaciones de los hallazgos de esta revisión serán discutidas en la segunda parte, la cual será un análisis de la situación de los programas hospitalarios del Rb en México, incluyendo la revisión de los datos demográficos disponibles de los centros de referencia más importantes.

1. Introduction

Retinoblastoma (Rb) is the most common primary malignancy in children, most frequently occurring in children <5 years of age, with an annual incidence ranging worldwide from 36/1,000,000 live births to 67/1,000,000 live births.[1–5] Accurate incident rates can be difficult to estimate, especially in developing countries that lack a national Rb registry. In fact, a recent study from the Asia-Pacific region would suggest that cases of Rb are being underreported by >50%.[6]

A curable cancer, Rb survival rates in the developed world range from 90-95%, mainly due to early diagnosis of the disease and to the advances made over the past few decades in conservative treatment.[5,7,8] However, survival rates are significantly lower in developing countries; in Africa, they are estimated as low as 20%, and >3,000 annual childhood deaths are attributed worldwide to Rb.[8–10] The poorer outcomes in developing countries have been associated with late diagnosis and treatment, lower educational levels of the mother, lack of access to health services, and treatment abandonment by families of the patient.[11–13]

This article is the first part of a two-part review with the objective to report the current situation of Rb in Mexico, including the authors' own experience at the country's leading Rb centers and a review of currently available demographic data of patients with Rb at hospitals with Rb programs or that treat for Rb. We will also identify gaps in practice and propose solutions to improve diagnosis, provide adequate treatment, and improve patient uptake. The situational analysis of Rb in Mexico will be performed within the context of the general universal knowledge of Rb diagnosis and management. In this first part, we will summarize the general knowledge of Rb diagnosis and management including the latest advances in chemotherapy options.

2. Methods

A general, unstructured literature search was performed using PubMed to search for peer-reviewed journal articles on the current knowledge of Rb diagnosis and management. No specific search parameters were applied. Key findings from the literature are summarized.

3. Results

3.1. Pathology, diagnosis, and clinical characteristics

There are two forms of Rb, hereditary or non-hereditary, both of which develop from the mutation of the Rb (RB1) gene.[14–16] In the non-hereditary form, inactivation of the RB1 gene alleles causes a defect of the pRB protein, resulting in unilateral tumors.[14,15] The presence of tumors in both eyes can occur with heritable Rb.[15] A parent carrier of a single mutant allele of the RB1 gene is a hereditary risk factor that predisposes the child to the loss of the second copy by 1,000 times the rate of spontaneous mutation.[14] There is a 50% chance that the parent passes the mutation to their child, who then has a 90% chance of developing Rb.[17] The hereditary form increases the risk of patient susceptibility to other cancers and requires long-term follow-up, genetic counseling, and monitoring for second cancers.[15] The genetic nature of Rb, therefore, is very important in predicting the risk of cancer and guiding treatment.

It has been recently discovered that amplification of the *MYCN* gene (found only in tumor cells) results in another genetic form of the disease.[15,16] Patients with this form are not at risk for second cancers. However, their tumors tend to