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Original Research Article

Retinoblastoma – pattern, presentation and management: a quintessential experience of 5 years

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ABSTRACT

Background: Retinoblastoma (RB) is the most common intraocular malignancy of childhood. It accounts for 10-15% of cancers that occur in infants. Objective of the study was to determine the pattern, presentation and management of Retinoblastoma (RB) patients at a tertiary cancer care center in South India, during a period of 5 years (1st November 2009 to 1st December 2014).
Methods: This study was a retrospective analysis of the medical records of patients diagnosed as having retinoblastoma obtained from hospital information system and our cancer registry. Data sought was demographic characteristics, clinical presentation, investigations done, the methods of management and the treatment outcome of retinoblastoma patients.
Results: Total number of cases studied was 31 and total number of eyes studied was 47. Out of 31 cases, 58% were female. 52% had bilateral involvement. The median age at presentation was 24 months. The commonest mode of presentation was leukocoria (55%) followed by proptosis (22%). Out of 47 eyes studied, 87% were advanced tumours belonging to Group D or Group E. Metastasis to the central nervous system was noted in 22.6% patients belonging to either Group D or Group E. Out of the 31 patients, 64.6% patients underwent enucleation. 6 out of 31 cases succumbed to death.
Conclusions: Retinoblastoma continues to be a challenge in developing countries. Lack of awareness and inaccessibility to proper healthcare facilities are major stumbling blocks in achieving high cure rates. Educating the public and healthcare professionals, importance of early diagnosis and prompt referral are vital in reducing morbidity and mortality associated with the disease.

Keywords: Chemotherapy, Developing countries, Enucleation, Survival, Retinoblastoma

INTRODUCTION

Retinoblastoma (RB) is the most common intraocular malignancy of childhood.[1-3] It accounts for 10-15% of cancers that occur in infants.[4] Studies from India show a two-three fold higher incidence of tumors within the eye.[5-7]Age-adjusted cancer incidence rates ranged from 1.9 per million to 12.3 per million for boys and 1.3 to 6.7 for girls in India.[8] There is obvious variance between patient's survival in developed and developing countries. A European study of 954 retinoblastoma patients showed disease free survival of 93% and 91% at 5 years and 10 years.[9] Broaddus et al. reported an increasing 5 year survival rate in the US from 92.3% to 96.5% from 1975 to 2004.[10] In contrast, estimated survival in low income countries was 40%, in lower middle income countries was 77% and in upper middle income countries was 79%.[11] High mortality is reported in developing

countries, which is a matter of concern.[12,13] Factors contributing to the poor outcome include lack of awareness, late presentation, poor compliance and absence of adequate healthcare facilities.[13,14] In North India, Bhavna et al, reported a survival probability of 83%, 73% and 65% at 1 year, 2 years and 5 years, respectively.[15]A comprehensive multimodality treatment is pertinent in RB to improve outcomes. The term chemo-reduction is used to describe the technique of using chemotherapy to reduce the retinal tumor size for better control.[16] India is a densely populated developing country with a large number of children. Our center is a tertiary cancer care center in South India that caters to referrals from primary care and secondary care. This study was undertaken to determine the clinical profile and survival outcomes of Indian children affected by retinoblastoma.

METHODS

This study is a retrospective analysis of cases of retinoblastoma registered and treated in our hospital between November 2009 and December 2014. Data obtained included demographic information, history, clinical features at presentation, treatment details, survival outcomes and duration of follow-up. Detailed history regarding symptoms of white reflex, watering, pain, redness, proptosis and defective vision was obtained. The laterality, duration and progression were noted. Family history regarding affection of sibling was documented. Ocular examination which included vision, pupillary reaction and detailed examination under anesthesia was done. Investigations included complete blood examination, renal and liver function tests, viral markers, CT/MRI of orbit and brain, bone scan, bone marrow examination, CSF analysis, ultrasound abdomen and echocardiogram.

Inclusion criteria included all recorded presumptive clinical diagnosis of retinoblastoma with or without confirmed histological diagnosis of retinoblastoma during the study period.

Exclusion criteria were patients, whose records could not be traced, were excluded from the study. For staging the eye, the International Classification for Intraocular Retinoblastoma was used.[17] Multidisciplinary treatment was tailor made depending upon the stage of the tumor, unilateral or bilateral presentation and visual potential of the affected eye. Treatment methods for retinoblastoma include intravenous chemoreduction, thermotherapy, cryotherapy, laser photocoagulation, plaque radiotherapy, external beam radiotherapy, enucleation, and systemic chemotherapy for metastatic disease.[18] Chemotherapy with intravenous vincristine, etoposide and carboplatin was given at 4-weekly interval.[19] At completion of treatment, all children were meticulously followed up to look for any local recurrence, adverse effects of treatment or systemic metastasis. Data was analyzed and the descriptive analysis is presented in tables.

RESULTS

Total number of cases studied was 31 and total number of eyes studied was 47. Out of which, 18 cases (58%) were female and 13 (42%) were male as mentioned in Table 1. Of the 31 cases, 16 (52%) had bilateral involvement and 15 (48%) had unilateral involvement as mentioned in Figure 1. Age of onset of 13 (42%) cases was less than or equal to 12 months. Age of onset of 11 cases (35%) was between more than 12 months to less than or equal to 36 months. Age of onset of 7 cases (22%) was more than 36 months. The median age at presentation was 24 months.

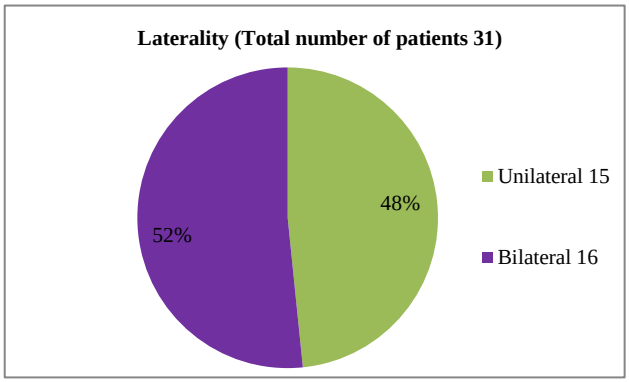

Figure 1: Unilateral or bilateral.

Table 1: Demographic and clinical features of 31 children with RB.

Characteristics	Number of patients	Percentage
Presenting symptoms		
White reflex	14	45.2
Proptosis	7	22.6
Decreased vision	2	22.5
Bilateral lower limb weakness	1	3.2
Headache	1	3.2
Redness of eye	1	3.2
Age (in months)		
1-10	5	16.1
11-20	10	32.3
21-30	2	6.5
>30	14	45.2
Sex		
Female	18	58.1
Male	13	41.9
Laterality		
Unilateral	15	48.4
Bilateral	16	51.6

The commonest mode of presentation was a white reflex in the eye (17 out of 31 cases, 55%). Other presentations included proptosis and defective vision. Out of 31 patients studied, 1 patient (3.2%) was in Group A, 1 patient (3.2%) was in Group B, 2 (6.5%) were in Group

C, 13 (41.9%) were in Group D and 14 (45.2%) were in Group E as mentioned in Figure 2. Out of 47 eyes studied, 1 (2%) was in Group A, 1 (2%) was in Group B, 4 (9%) were in Group C, 14 (30%) were in Group D and 27 (57%) were in Group E.

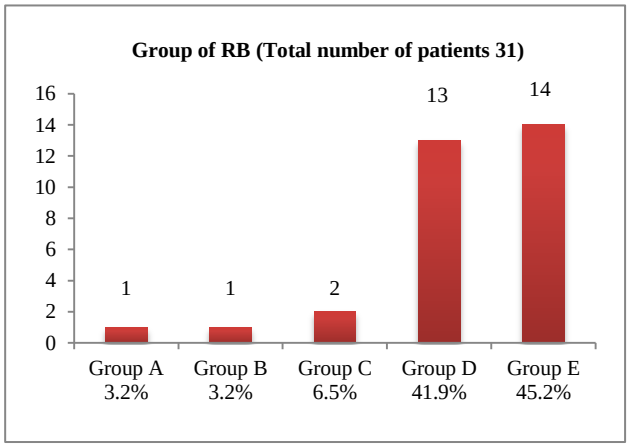

Figure 2: Group of RB in 31 patients.

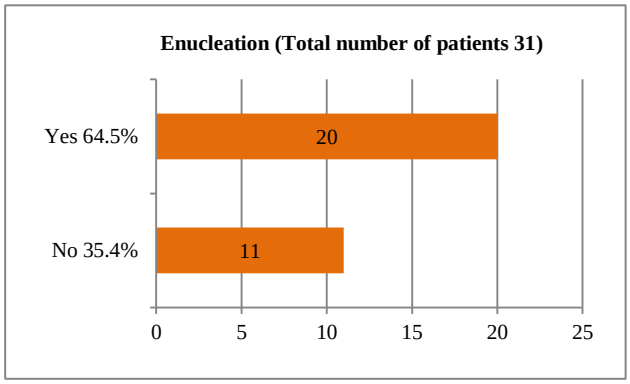

Figure 3: Enucleation.

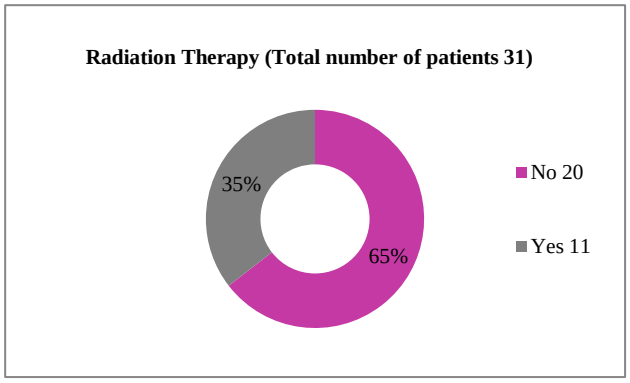

Figure 4: Radiation therapy.

Out of the 31 patients, 20 (64.6%) eyes were enucleated as mentioned in Figure 3. Out of 31 patients, 11 patients (35.5%) eyes were irradiated as mentioned in Figure 4, out of which, 2 patients received only palliative RT for metastatic disease and 1 patient received brachytherapy. 7 (23%) out of 31 cases were metastatic at presentation as mentioned in Figure 5. Out of the 10 metastatic eyes, 5 eyes were Group D and 5 eyes were Group E. 6 (19%) out of 31 cases succumbed to death as mentioned in Figure 6.

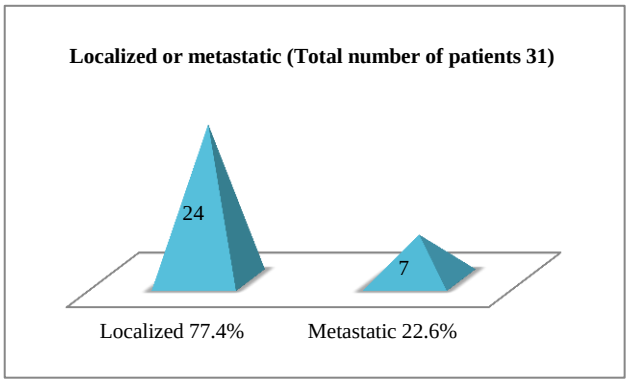

Figure 5: Localized/Metastatic.

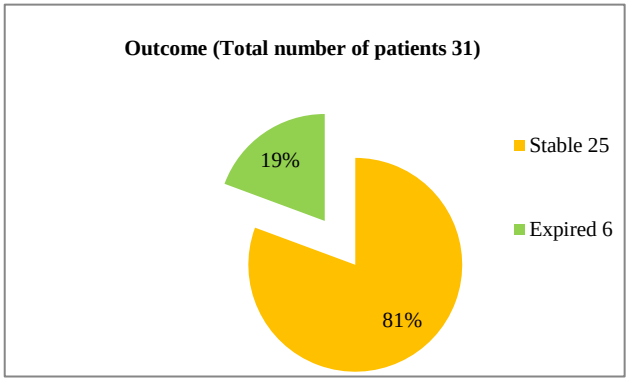

Figure 6: Survival.

DISCUSSION

Clinical presentation and survival outcomes vary in different parts of the world. In our study, median age of presentation was 24 months which is comparable with previous other studies from North India (29 months), Iran (28.5 months), Taiwan (26.3 months) and Malaysia (24.2 months).[15,20,21] A relatively higher median age at diagnosis has been reported from African countries like Ghana (36 months) and Kenya (37.5 months).[14,22] Tumours were relatively diagnosed at an earlier age in Australia and USA.[23,24] This could be due to better awareness and access to medical heath care in developed nations. Previous studies showed no sex predilection.[25,26] In contrast, present study observed a slightly higher incidence in females.

Leukocoria was the commonest mode of presentation in our study which is consistent with the data from developed nations, followed by proptosis and defective vision.[27,28] A study from Taiwan has reported proptosis in 17% cases, whereas another study in Nigerian children found proptosis in 85% cases.[13,29] Delayed presentation was observed in majority of the cases. Out of 47 eyes

studied, 87% were advanced tumours belonging to Group D or Group E. The majority of children with early tumors were picked up due to advanced disease in the fellow eye. Our observation of identifying less advanced disease more often in bilateral RB is consistent with that of reported by Zhao et al, in Chinese children.[30]

The principles of management of RB include protection of life, preservation of globe and when possible, salvage of vision. Primary enucleation is considered as an ideal treatment for Group E eyes to save life and prevent metastasis. In our study, due to advanced stage at presentation, the most common treatment was enucleation which was similar to that of a Chinese study.[30]

In our series, mortality was 19%. In developed nations such as Europe, Canada and USA, mortality due to RB varies between 3% and 5%.[31,32] However, in the developing countries, this rate increases to 40%-70% owing to late presentation.[12] Stage of the disease had a significant impact on the survival outcomes, which is consistent with previous studies that reported an association between severity of disease and the survival outcome.[21,33,34]

The most feared complication of chemotherapy is the risk of developing other tumors in the medium and long term, particularly leukemia by use of Etoposide.[35] Radiation appears to have a higher incidence of non-ocular tumours.[36] The late complications were not observed in our patients due to the short follow-up period.

CONCLUSION

To summarize, our series from South India describes the outcomes and survival of RB in children. Lack of awareness and inaccessibility to proper healthcare facilities are a major hindrance in achieving high cure rates. This impediment needs to be overcome by educating the public and healthcare professionals, making an early diagnosis and facilitating prompt referral. Strengthening medical facilities for diagnosing RB at the primary and secondary levels of healthcare are the keystones in reducing morbidity and mortality associated with the disease and improving outcomes that are comparable with the developed nations.

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