ORIGINAL ARTICLE

Evaluation of Retinoblastoma According to Histological Grading, TNM Staging and Age at Presentation

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ABSTRACT

Objective: To evaluate retinoblastoma, according to histological grades, TNM staging and age at presentation.

Materials and Methods: This cross sectional study was conducted in Department of Pathology BMSI- JPMC Karachi from 1st January 2009 to 31st December 2013 during which a total of 80 cases of retinoblastoma were received. Out of which 68 were reviewed and morphological diagnosis was done on H&E staining. Histological grades and TNM staging were categorized. The data was analyzed by using SPSS version 22.

Results: In 80 cases of retinoblastoma the mean age of patients was 3.64 years with 3-4 years (53.75%) of age being the commonest. Amongst 68 cases, well differentiated retinoblastoma were seen in 7.35%, moderately differentiated 11.76%, poorly differentiated 26.47% and undifferentiated 51.41% cases. Varied pattern of TNM staging were observed. Majority (60.29%) in stage IV followed by 19.11% in stage I and 10.29% each in TNM stage II and III. Regional lymph node metastasis was seen in 4/68 cases (5.88%) while 3/68 (4.41%) showed distant (CNS) metastasis. All these cases (7/7) were in TNM stage IV with majority showing grade 4 (75%) and grade 3 (25%) histology.

Conclusion: Evaluation of retinoblastoma showed that commonest age group was 3-4 years. Majority of retinoblastoma cases were undifferentiated (G4) followed by poorly differentiated (G3). While in TNM staging system varied pattern was observed, majority were in stage IV followed by Stage I. Majority of lymph node and distant metastasis were seen in grade 4 histology and all of them were in TNM stage IV.

Keywords: Retinoblastoma, Histological grading, TNM staging, Age, Optic nerve, Rb1 gene

INTRODUCTION:

The commonest primary intraocular cancer in younger age is retinoblastoma[1,2,3] generally affects children, early diagnosis is curable while untreated cases lead to complications and even death[4]. Retinoblastoma arises as mutation in both alleles of Rb1 gene which occurs pre-zygotically or post-zygotically in germ cells[5]. Rb1 gene is situated in long arm of chromosome 13q14 [4,6,7,8] Hereditary form consists of 30-40% and non hereditary form 60-70%. Former had bilateral retinoblastoma, diagnosed in < 1 year of age and have more risk of secondary neoplasm that is bone and soft tissue sarcoma, melanoma and brain cancer. Latter have unilateral retinoblastoma, diagnosed at 2-5 years of age and is not prone to secondary neoplasm. [9,10,11,12]

Globally one case of retinoblastoma is recorded in up to 20,000 live births. Incidence is generally equal in North America, Europe, Australia and Asia whereas higher in Africa and other developing countries.[13,14,15,16,17] When retinoblastoma spread to the optic nerve, choroid and extra ocular tissue the mortality is high and prognosis is poor[18,19,20,21] Grossly retinoblastoma are presented as endophytic, exophytic, mixed endophytic and exophytic, diffuse infiltrating and complete spontaneous regression.[3,7,8,22]

On the basis of Flexner-Winter Steiner rosette (Lined by tall cuboidal cells that circumscribed an apical lumen and basal ends of the cells contain nuclei), Homer-Wright rossettes (cells are not arranged about a lumen but sends out cytoplasmic processes and form a tangle within the center) and pseudo rosette, retinoblastoma are divided into well differentiated, moderately differentiated, poorly differentiated and undifferentiated variant.[7,9,22,,23,24] On involvement of optic nerve, choroid, extraocular tissue and secondary metastasis to lymph node and distant tissue, TNM staging system of retinoblastoma developed, T is primary tumor, N is lymph node and M is distant metastasis.[7,22,23,24,25] This study was designed to evaluate retinoblastoma cases according to different histological grades, TNM staging and age at presentation in our local population.

MATERIALS AND METHODS:

The study was performed after approval from BASR, Karachi University at department of Pathology Basic Medical Sciences Institute, Jinnah Postgraduate Medical Center (BMSI-JPMC) Karachi from 1st January 2009 to 31st December 2013. A total of 80 cases of retinoblas-

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toma were received and 12 cases were excluded due to inadequate material. In remaining 68 cases histological grading and TNM staging was done. These patients were operated at ophthalmology department of JPMC, Karachi. All enucleated eye specimens were included, while poorly fixed and inadequate tissue, ocular tumor other than retinoblastoma and metastatic tumors were excluded. Formalin fixed, paraffin embedded blocks, surgical pathology, clinical records and hematoxyline and eosin slides were used. Sections were taken and stained with H&E. all slides were studied under light microscope using scanner (4X), low power (10X) followed by high power (40X). The data was analyzed by using statistical package for social sciences (SPSS) version 22.

RESULTS:

Distribution of retinoblastoma according to age amongst 80 cases was, majority that is 53.75% cases were between ages 3-4 years followed by 20% cases in 5-6 years. The mean ± SD were 3.64 years (43.68 months) ±1.74, median age was 48 months. The minimum age was 02 months while maximum age noted was 09 years (Table 1)

Table: 1
Distribution of retinoblastoma according to age
(n=80)

Age (years)	No of cases	Percentage %	Cumulative index
<1 year	04	05	05
1-2 years	11	13.75	18.75
3-4 years	43	53.75	72.5
5-6 years	16	20	92.5
7-8 years	02	02.50	95
9-10 years	01	01.25	96.25
Unknown	03	03.75	100
Total	80	100	

Out of 68 cases, 7.35% were well differentiated (G1), 11.76% were moderately differentiated (G2), 26.47% were poorly differentiated (G3) and 54.41% were undifferentiated (G4) respectively. Out of 68 cases 5.88% cases showed regional lymph node and 4.41% showed distant metastasis, majority i.e. 75% of them were in G4 histology and 25% showed G3 histology (Table 2).

Table: 2
Distribution of retinoblastoma according to histological grades
(n=68)

Grades	No of cases	Percentage %	95% CI
G1	05	07.35	2.74-15.54
G2	08	11.76	5.61-21.11
G3	18	26.47	17.0-37.9
G4	37	54.41	42.51-65.94
Total	68	100	

CI: Conbidence interval

Distribution of retinoblastoma according to TNM staging system showed that out of 68 cases majority that is 60.29% were in TNM stage IV followed by 19.11% were stage I and 10.29% each were in TNM stage II and stage III. All the cases that showed regional lymph node and CNS metastasis, were in TNM stage IV (Table 3)

Table: 3
Cases of retinoblastoma according to TNM staging
(n=68)

Stage	No of cases	% of total cases	95% CI
Stage I	13	19.11	11.06-29.75
Stage II	07	10.29	4.61-19.3
Stage III	07	10.29	4.61-19.3
Stage IV	41	60.29	48.34-71.4
Total:	68	100	

CI: Confidence interval

Comparison and correlation of retinoblastoma according to TNM staging and histological grading showed that out of 68 cases majority that is 60.29% were in TNM stage IV. Out of these 2.43% were in histological grade I, 7.13% in G2, 29.26% in G3 and 60.29% in G4. TNM stage III showed 10.29% out of these 0% were in grade I, 14.28% in G2, 28.57% in G3 and 57.14% in G4. TNM stage II showed 10.29% out of these 28.57% each were in grade I, grade 2 and grade 4 histology While 14.28% in G3. TNM stage I showed 19.11% out of these 15.38% each were in histological grade 1 and grade 2, 23.07% in G3 and 46.15% in G4 (Table 4).

Table: 4
Retinoblastoma according to histopathological grading and TNM staging
(n= 68)

TNM Stage	Histopathological Grades				Total
	G1	G2	G3	G4	
Stage I	02 15.38%	02 15.38%	03 23.07%	06 46.15	13 19.11%
Stage II	02 28.57%	02 28.57%	01 14.28%	02 28.57%	07 10.29%
Stage III	00 00	01 14.28%	02 28.57%	04 57.14%	07 10.29%
Stage IV	01 2.43%	03 7.13%	12 29.26%	25 60.29%	41 60.29%
Total	05 7.35%	08 11.76%	18 26.47%	37 54.41%	68 100%

P value = 0.22; Chi Square = 11.77

DISCUSSION

In present study the most common age group was 3-4 years that is 53.75% cases followed by 20% cases in 5-6 years age group. These findings are comparable to the studies in Mumbai, India, Tata Memorial Hospital by Yeole[13] and Akhiwu[6] have reported 76.5% and 78% cases in under 4 years of age and 3-3.5 years of age groups respectively. Studies by Chintagumpala[1] and Rodrigues [20] have reported 80% cases under 3 years and

53% cases under 2 years of age respectively. In this study the mean age was 43.68 months. This finding was comparable with the work by Akhiwu [6] who has reported mean age 24 to 48 months, but dissimilar to Antoneli [21] and Arif [2] who have documented 28.7 and 32 months respectively. Dissimilarity with present study may be due to lack of awareness, lack of education and poverty leading to late presentation for medical consultation. In the present study varied histopathological grades were seen. Majority that is 54.41% were in grade 4 histology followed by 26.47% in G3, 11.76% in G2 and 7.35% in grade 1 histology. A Nigerian study conducted by Owoeys[9] have reported 82% and 17.4% cases in G3 and G1 and none of case in grade 1 and grade 4 histology. While Chinese study performed by Jia[19] has reported 24%, 14% and 62% cases in histopathological grade 1, G2 and G3 respectively. No case was reported in histological grade 4 while present study found majority of cases in grade 4 histology. This variation could be due to late presentation or genetic and environmental factors.

Similarly an interesting observation in this series was that TNM staging had variable pattern of presentation and majority were in stage IV followed by stage I and equal number of cases were in TNM stage II and stage III. The reason for patient being in high TNM stage at the time of clinical presentation as mentioned earlier may be due to lack of awareness and inaccessibility of proper medical services. Moreover, people prefer alternative medical therapy such as Hakeems before consulting doctors.

CONCLUSION:

Maximum number of retinoblastoma cases was seen in the age group of 3-4 years and majority of them had grade-4 histology. Most of these cases were seen in Stage IV. All cases of lymph node and distant metastasis were also seen in TNM stage IV.

In view of a high stage and grade at the time of presentation wide scale awareness through education to parents, community and counseling programs is needed. This will help to ensure early presentation of such cases that is in the initial stages and grades of the disease. This in turn could improve the clinical outcomes, morbidity and mortality in such cases.

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