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RESEARCH ARTICLE

Pathological Risk Factors in Retinoblastoma Patients Underwent Enucleation

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Abstract

Objective: Retinoblastoma is a malignancy that originates from primitive retinal cells and is usually found in children under 4-5 years of age. Retinoblastoma is the second largest cause of death among other malignancies in developing countries. The purpose of this study was to determine the characteristics and pathological risk factors of enucleated retinoblastoma Patients and Methods: This is a descriptive study with a cross-sectional study design conducted retrospectively by evaluating data from the patient's medical record. A total of 18 subjects were enrolled in this study. Characteristics observed were sex, age, and laterality. Data was compiled and calculated by Microsoft Excel 2017 software. All calculations and presentations were conducted in descriptive manner. Results: Unilateral retinoblastoma cases (77.2%) were found more often in this study. Leucochoria was the most often presenting symptoms (61.1%), followed by propotosis, strabismus, and cellulitis. Out of 18 subjects, 72.2% subjects had intraocular retinoblastoma. The most common PRF finding in this study was optic nerve invasion (44.4%), followed by choroid invasion, and scleral invasion. While 11.1 % of the subjects had no PRF findings. Conclusion: Invasion to the optic nerve was the most common pathological risk factors found in enucleated retinoblastoma. Other PRFs include choroid invasion and sclera invasion. PRFs may become a sign that determines the progressivity of retinoblastoma, and it can also determine further decisions regarding the prevention of recurrence and possible adjuvant therapy in retinoblastoma patients.

Keywords: *Pathological risk factor, Retinoblastoma, Enucleation.*

Introduction

Retinoblastoma is a malignant intraocular neuroblastic tumor that originates from primitive retinal cells and is found in children under 4-5 years of age. This tumor is a primary intraocular malignant tumor with an incidence of 1:14,000 to 1:20,000 every live birth in the United States. An estimated 250-300 new cases found in the United States each year and 90% of cases diagnosed in patients under the age of 3 years [1-3]. This malignancy is the second most common cause of death among children in developing countries, where there is generally a delay in diagnosis and therapy [4].

Parents of patients are just looking for help when the tumor has progressed to an advanced stage. The clinical symptoms of retinoblastoma that are often found are leukocoria or white reflex in the pupil (60% of cases) and strabismus (20% of cases). Other clinical symptoms that can be found include heterochromia, spontaneous hyphae, amaurotic cat's eye (if the eye is exposed to light will reflect light like a cat's eye) and cellulitis [1, 5].Histologically, retinoblastoma consists of round, oval or coil cells estimated twice lymphocytes, hyperchromatic, with a small number of cytoplasm. Nuclei are said to be as large, rosette or pseudorosette forms with the proliferation of surrounding cells. When a tumor grows into the vitreous or sub retinal space, the tumor often grows out following the bloodstream, producing a characteristic pattern of necrosis and calcification that is often found in the area of necrosis [6].

To the best our knowledge, there has been no research on pathological risk factors (PRF) in patients with retinoblastoma enucleated at the Sanglah Central General Hospital which is the central referral hospital in eastern Indonesia.

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This study is expected to be used for the purpose of education and early detection of retinoblastoma, so that better given and the number of deaths from retinoblastoma can be suppressed.

Patients and Methods

This is a descriptive, cross-sectional study conducted retrospectively by evaluating data from medical records. The subjects of this study were patients with retinoblastoma underwent enucleation at Sanglah Hospital from 2014 to 2017.

Enucleation is an operative procedure that removes the eyeball and a resection of the optic nerve; usually for 10-15 mm. Subjects with incomplete medical records were excluded from this study. The study protocol was approved by the Commiittee of Ethical Research of Udayana University/Sanglah General Hospital. Data were obtained from the results of histopathological examination of the eyes that had been enucleated and then categorized to review the presence of PRF.

Pathological risk factors are grouped into: (1) an invasion of the optical nerve consisting of pre-laminar, laminar, and post-laminar; (2) an invasion of choroid consisting of focal and massive invasion; (3) an invasion of the front chamber; (4) scleral invasion; and (5) vitreous seedlings. Data was compiled and calculated by Microsoft Excel 2017 software. All calculations and presentations were conducted in descriptive manner.

Results

A total of 18 subjects were enrolled in this study. Characteristics observed were sex, age, and laterality (Table 1). Male subjects were found more than female (55.6% vs. 44.4%). Based on laterality, more patients were found with unilateral retinoblastoma (77.2%). Leucochoria was the most often presenting symptoms (61.1%), followed by propotosis, strabismus, and cellulitis. Out of 18 subjects, 72.2% subjects had intraocular retinoblastoma. The most common PRF finding in this study was optic nerve invasion (44.4%), followed by choroid invasion, and scleral invasion. While 11.1% of the subjects had no PRF findings.

Table 1: Characteristics of the subjects

Variables	N	%
Sex		
Male, n (%)	10	55.6
Female, n (%)	8	44.4
Age (months)		
0-12	2	11.1
13-36	11	61.1
37-60	3	16.7
>60	2	11.1
Laterality		
Unilateral	14	77.2
Bilateral	4	22.8
Main presenting symptoms		
Leucocoria	11	61.1
Proptosis	4	22.2
Cellulitis	1	5.6
Strabismus	2	11.1
Type of retinoblastoma		
Intraocular		
IIRC type A	2	11.1
IIRC type B	4	22.2
IIRC type C	2	11.1
IIRC type D	3	16.7
IIRC type E	2	11.1
Extraocular		
Stadium I	1	5.6
Stadium II	2	11.1
Stadium III A	2	11.1

Table 2: Cross tabulation between retinoblastoma types and PRF

Types of retinoblastoma	Pathological Risk Factors			
	Without PRF	Invasion to optic nerve	Invasion to choroid	Invasion to sclera
	n (%)	n (%)	n (%)	n (%)
Intraocular	1 (5.6)	8 (44.4)	3 (16.7)	1 (5.6)
Extraocular	1 (5.6)	2 (11.1)	2 (11.1)	0 (0)

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Discussion

The most clinical symptoms that were commonly found in this study were leukocoria (61.1 %). Suryawanshi *et al* [7]. Reported that 61 % of retinoblastoma patients presented with leukocoria, followed by proptosis (39 %) and strabismus (20.8 %).Another study also reported that leukocoria was found in 50-62% patients with retinoblastoma.[8] Leukocoria is likely the first sign that was recognized by the patients or their relatives. In the early stages, a white plaque lesion is found on the retina. While at a later stage, the tumor cells may grow inward and outward. Other signs include strabismus, orbital cellulitis, proptosis, heterochromia, rubeosis iridis, hypopyon, hifema, and buftalmos [9].

In intraocular retinoblastoma, the first classification system was introduced by Reese and Ellsworth (R-E) in 1960 to predict the possibility of saving the eye after administration of external radiotherapy. When intravenous chemotherapy for intraocular retinoblastoma was introduced in the 1990s, the R-E classification system was no longer suitable and a new classification scheme was formed, the International Intraocular Retinoblastoma Classification (IIRC). This IIRC scheme classifies tumors from A to E, depending on its size, location, and additional features, including the presence of 'seed' retinoblastoma (small colonies of cancer cells in the vitreous), and/or a detachment of the retina [10].

In this study, 72.2% of the 18 samples were intraocular retinoblastoma; with 22.2% belong to group B, which is classified as a low-risk based on IIRC. Rares[8] reported that the prognosis of the patients with localized intraocular retinoblastoma receiving modern therapy had a good prognosis for survival with a percentage exceeding 95%. Extraocular retinoblastoma was classified in 2006 according to the International Retinoblastoma Staging System (IRSS).

This classifies retinoblastoma to stage 0-IV. Stage 0 is an intraocular disease, usually possess good outcome with treatment, and stage IV is a retinoblastoma with metastasis with a poor prognosis [10].In our study, we found 5 patients with extraocular retinoblastoma, ranging from stadium I to III A. In stage I, the eye is enucleated and no residual tumor was found in histology examination. In stage II, the eyes are enucleated but microscopically there is still a residual mass of tumor. Stage IIIA describes regional invasion in the periorbital region. If the invasion of tumor cells reaches the preauricular or cervical lymph node extension, it is called included in stage IIIB [11].This study also found the PRF from patients with retinoblastoma who had enucleation and histopathological examination of the enucleated eye.

PRF, which will later be used to see tumor expansion as a marker of retinoblastoma leading to progressive direction, can also determine whether further procedures to prevent recurrence and to provide adjuvant therapy are needed. Based on the results of data collection in this study PRF was found in 88.9% of the subjects.

55.6% of the subjects had invasion to the optic nerve, prelaminar, laminar, and postlaminar. These results are similar to another study in 2009[12] that found there was a PRF in 54.2% of 142 eyes that were enucleated because of retinoblastoma. Another study reported that 50.5% of the subjects experienced invasion of the optic nerve [7]. The results from Table 2 showed that in the intraocular type there were 44.4% of the subjects showed an invasion to the optic nerve compared to 11.1% in extraocular setting. Berry *et al* [13]. Found that 67% optic nerve invasion in enucleated intraocular retinoblastoma, 56% pre laminar and 11% post laminar. While Chantada *et al* [14].

Reported that 39 subjects were found with choroid invasion compared to 2 subjects with optic nerve in enucleated extra ocular retinoblastoma. Limitations of this study may well be design-related and its small sample size. Descriptive study is the least powerful design to see relations. The small sample size was related to the incomplete medical record prior to 2014. Continuous data recording for retinoblastoma patients is needed in order to gain much more subjects and provide a reliable national data for this pathology.

Conclusion

Invasion to the optic nerve was the most common pathological risk factors found in enucleated retinoblastoma. Other PRFs include choroid invasion and sclera invasion.

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PRFs may become a sign that determines the progressivity of retinoblastoma, and it can also determine further decisions regarding the prevention of recurrence and possible adjuvant therapy in retinoblastoma patients.

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