

Lesions Simulating Retinoblastoma at a Tertiary Care Center

Fariba Ghassemi, MD; Fatemeh Bazvand, MD; Ali Makateb, MD

Eye Research Center, Farabi Eye Hospital, Tehran University of Medical Sciences, Tehran, Iran

Abstract

Purpose: To determine the types and frequency of ocular conditions simulating retinoblastoma (pseudo-retinoblastoma) at Farabi Eye Hospital, Tehran, Iran.

Methods: We reviewed data of patients who were referred with a diagnosis of retinoblastoma to Farabi Eye Hospital oncology clinic, from January 2009 to July 2013. Examination under general anesthesia was performed for all patients. Other investigations, such as ultrasonography, were performed as required.

Results: Of a total of 331 patients (aged 1-60 months), 138 (42%) were found to be suffering from a benign disorder. Among these pseudo-retinoblastoma cases, Coats' disease was the most prevalent condition (n = 36, 26%); persistent hyperplastic primary vitreous (PHPV) and familial exudative vitreo-retinopathy (FEVR) were the next two common pseudo-retinoblastoma cases in our series.

Conclusion: The rate of misdiagnosis upon referral to our center was close to 40%. The most common pseudo-retinoblastomas entities include Coats' disease, PHPV and FEVR. An accurate diagnosis is essential for management of pseudo-retinoblastoma cases.

Keywords: Coats' Disease; Pseudo-retinoblastoma; Retinoblastoma

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INTRODUCTION

Lesions with clinical similarities to retinoblastoma are known as pseudo-retinoblastoma. Differentiation of pseudo-retinoblastoma lesions is essential for proper management and to avoid unnecessary chemotherapy or enucleation. The two conditions commonly confused with retinoblastoma are Coats' disease and PFV.^[1] In 1965, the first report of lesions that simulated retinoblastoma was published by Howard and Ellsworth.^[2] They

noted that 265 (53%), out of 500 children referred for suspected retinoblastoma had pseudo-retinoblastoma. The conditions included persistent hyperplastic primary vitreous (PHPV, or more recently known as persistent fetal vasculature [PFV]), retrolental fibroplasia or retinopathy of prematurity (ROP) and posterior cataracts, which together accounted for 46% of pseudo-retinoblastoma cases. Later, many case series of pseudo-retinoblastoma were reported.^[3-7] In the reported series, different abnormalities simulating retinoblastoma were presented from different centres.^[8,9]

Herein, we report the rate and types of lesions simulating retinoblastoma at Farabi Eye Hospital as a referral center, during 5 years period.

Correspondence to:

Fariba Ghassemi MD. Eye Research Center, Farabi Eye Hospital, Qazvin Square, Tehran 13366, Iran.
E-mail: fariba.ghassemi@gmail.com

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METHODS

This study includes all patients who were referred specifically for suspicion of retinoblastoma to the ocular oncology clinic at Farabi Hospital, Tehran University of Medical Sciences, between January 2009 and July 2013. Institutional review board approval was obtained. Patients data were reviewed for age, gender, and signs and symptoms at presentation. A complete ocular examination was done under general anesthesia for each patient. A diagnosis was established, based on clinical findings and the results of diagnostic test results. Statistical analysis was performed using SPSS statistical software (Version 19, SPSS, Chicago, IL, USA). The data were reported in mean values \pm standard deviation (SD).

RESULTS

A total of 331 patients (395 eyes) with mean age of 17.92 ± 15.16 (range, 1-60) months including 90 male patients (65%) were referred to our center during the specified time. The rate of pseudo-retinoblastoma diagnosis was 41.6% (138 cases). The right eye was involved in 50 cases (36.2%) and the left one was affected in 45 cases (32.6%). Both eyes were involved in 43 cases (31.2%). The common presentations were strabismus ($n = 55, 39.9\%$) and leukocoria ($n = 54, 39.1\%$), while microphthalmia ($n = 8, 5.8\%$), nystagmus ($n = 4, 2.9\%$), red eye ($n = 3, 2.2\%$) and decreased vision ($n = 2, 1.4\%$) were other presentations among our patients. The pseudo-retinoblastoma diagnoses are listed in Table 1.

A total of 22 entities simulating retinoblastoma (pseudo-retinoblastoma) were encountered, the three most common of which included Coats' disease ($n = 36; 26.1\%$), PHPV ($n = 31; 22.5\%$), and familial exudative vitreoretinopathy (FEVR) ($n = 14; 10.1\%$).

Bilateral cases of pseudoretinoblastoma included PHPV (14 subjects), spontaneously regressed ROP (9 cases), FEVR (7 subjects), coloboma (4 cases), astrocytoma (3 subjects), non-attached retina (2 cases), TORCH (toxoplasma, rubella, cytomegalovirus and herpes simplex virus infection) syndrome (2 subjects), Coats' disease (1 patient), and organized vitreous hemorrhage (1 patient).

DISCUSSION

The current series represents an extremely heterogeneous constellation of pseudo-retinoblastoma cases including 3 major conditions, namely Coats' disease, PHPV and FEVR, accounting for the majority (58.7%) of cases, along 19 other entities comprising the other 41.3% of cases.

The management of retinoblastoma has evolved to globe-saving methods, leading to decreased enucleation rates in misdiagnosed cases of pseudo-retinoblastoma

Table 1. The differential diagnosis of pseudo-retinoblastoma

Diagnosis	Frequency (%)
Coats Disease	36 (26.1)
PHPV	31 (22.5)
FEVR	14 (10.1)
Coloboma	10 (7.2)
ROP	10 (7.2)
Nonattached retina	6 (4.3)
Combined hamartoma	5 (3.6)
TORCH	5 (3.6)
Astrocytic hamartoma	5 (3.6)
Congenital cataract	3 (2.2)
Organized vitreous hemorrhage	2 (1.4)
Acute lymphocytic leukemia	1 (0.7)
Congenital retinal fold	1 (0.7)
Medulloepithelioma	1 (0.7)
Vitritis (JRA)	1 (0.7)
Incontinentia pigmenti	1 (0.7)
Myelinated retinal nerve fiber layers	1 (0.7)
Morning glory syndrome	1 (0.7)
Norrie's disease	1 (0.7)
Retinocytoma	1 (0.7)
Toxocariasis	1 (0.7)
Prephthical eye with media opacity	1 (0.7)

PHPV, persistent hyperplastic primary vitreous; FEVR, familial exudative vitreoretinopathy; ROP, retinopathy of prematurity; TORCH, toxoplasma, rubella, cytomegalovirus and herpes simplex virus infection; JRA, juvenile rheumatoid arthritis

from 4% in 1960, to <1% in 2000.^[10] Retinoblastoma may be detected by indirect ophthalmoscopy, as a yellow-white retinal tumor with a dilated retinal artery and vein often with surrounding subretinal fluid, subretinal seeds and vitreous seeds.^[11]

Other pediatric fundus abnormalities can mimic retinoblastoma, leading to difficulty in differentiation.^[6,10,11] A precise ocular examination by an ocular oncologist is the best way to differentiate retinoblastoma from pseudo-retinoblastoma, due to distinguishing clinical features.^[11,12] However, ultrasonography, computed tomography (CT), and magnetic resonance imaging (MRI) may be helpful in diagnosis.^[1,13]

The rate of misdiagnoses varies from 5 to 50% and is influenced by several factors, including patient age, academic center versus non-academic center and laterality (6% in bilateral versus 12% in unilateral cases).^[1,2,6,14,15] In the current series the rate of misdiagnosis was 42%.

The report by Howard and Ellsworth back in 1965 showed that the leading simulators of retinoblastoma cases, included PFV (19%), ROP (14%), posterior cataracts (14%), choroidal coloboma (12%), uveitis (10%), toxocara granuloma (7%), congenital retinal fold (5%) and Coats' disease (4%).^[2] In 1991, Shields et al reported

a slightly different spectrum that included PFV (28%), Coats' disease (16%), toxocariasis (16%), ROP (5%), combined hamartoma of the retina and RPE (4%), coloboma (4%), vitreous hemorrhage (4%), astrocytic hamartoma (3%) and FEVR (2%).^[3] Maki et al found that 42 of 111 patients (38%) referred for retinoblastoma evaluation from 2004 to 2008 were pseudo-retinoblastoma cases.^[16] PFV (31%) and Coats' Disease (29%) were the most common simulating lesions.

In the recent report by Shields et al from a larger series of 604 cases of pseudo-retinoblastoma, Coats' disease (40%), PFV (26%) and vitreous hemorrhage (5%) were the most common entities while ROP (1%) and cataract (1%) have become much less frequent.^[1] Shields et al divided the patients into three age groups and the most frequent misdiagnoses belonged to PFV in patients \leq one year old and Coats' disease in children older than 1 year.^[1] Recent improvements in the clinical diagnosis and screening programs for ROP patients has changed the spectrum of pseudo-retinoblastomas.

Histopathologically, different etiologies have been reported.^[3,4,17-19] In 1962, Kogan and Boniuk studied 257 enucleated eyes for suspected retinoblastoma and found pseudo-retinoblastoma in 24% of cases.^[17] In 1969, Howard reported that the rate of mistaken diagnosis was 6% if the condition was bilateral, and 12% if it was unilateral.^[4] In 1977, Robertson and Campbell evaluated 49 eyes enucleated for retinoblastoma at the Mayo Clinic from 1954 through 1974 and discovered 8 pseudo-retinoblastomas cases (16%).^[5] Similarly, Margo and Zimmerman found that 15 of 56 (27%) eyes removed for retinoblastoma and submitted to the Armed Force Institute of Pathology between 1974 and 1980 were pseudo-retinoblastomas, most often Coats' disease and retinal detachment.^[19] In the study by Balmer et al, Coats' disease was the most common misdiagnosis.^[20] In another report, various congenital malformations and ocular inflammations were found as the most prevalent misdiagnosis causes.^[21]

In an earlier study from our center, endophthalmitis was the most common diagnosis in pseudo-retinoblastoma.^[7] The rate of pseudo-retinoblastoma in some consequent reports from a single center showed decreased rates of misdiagnoses.^[1,3] A reduction in erroneous enucleation for presumed malignancies, over the previous five decades, has been reported by Huang.^[6]

Leukocoria was the most clinical presentation in pseudo-retinoblastoma among our cases. The clinical presentation in our series is in accordance with other studies reporting different signs and symptoms such as, leukocoria, strabismus, red eye, phthisis bulbi, hyphema, proptosis, pseudohypopyon, decreased vision and photophobia.^[1,15,18]

In summary, ocular oncology centers continue to experience inaccuracy in referral diagnoses. A careful

evaluation and accurate diagnosis is essential for proper management of pseudo-retinoblastoma cases and avoiding undue diagnostic or therapeutic procedures.

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Conflicts of Interest

There are no conflicts of interest.

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