ORIGINAL ARTICLE

Pathology Section

Retinal Dysplasia-A Mimic Of Malignant Ocular Pathology

NEHA AGARWAL, PRASHANT GUPTA, ASHA AGARWAL, CHAYANIKA PANTOLA

ABSTRACT

Retinal dyplasia is considered as a lesion with specific morphological characteristics, rather than a disease or a syndrome in itself .It may occur in otherwise normal individuals as a unilateral lesion, or it may be observed as a component of several syndromes with intraocular involvement and may present a diagnostic dilemma in the differentiation between benign and malignant ocular pathologies.

Here, we report a case of retinal dyplasia in a one and a half month old child, who initially presented to us with red eye which was clinically suspected and radiolgically supported as a case of retinoblastoma.

Key Words: Retinal dysplasia, Retinoblastoma, Rosette, Mimic

INTRODUCTION

Retinal dysplasia is a rare cause of childhood leucocoria, which can cause considerable diagnostic difficulty in the differentiation of benign and malignant intraocular pathologies. When they are present as the component of a group of congenital disorders, the ocular findings are mostly bilateral. Clinically, retinal dysplasia may present itself in a wide range of severity. Leucocoria and retinal detachment in children require prompt further investigation because retinoblastoma should be included in the differential diagnosis.

The primary histopathological feature is the formation of rosettes which is an attempt towards the formation of embryonic retinal tissues, rods and cones.

CASE REPORT

A one and a half month old female child presented with unilateral red eye which was noticed by the parents 10 days after birth, for which she was prescribed antibiotics. Later on, the attending ophthalomolgist noticed unilateral leucocoria. The child was subsequently investigated. Ultrasonography suggested a differential diagnosis of retrolental opacity, a neoplastic lesion and retinoblastoma. No other congenital abnormality was noted.

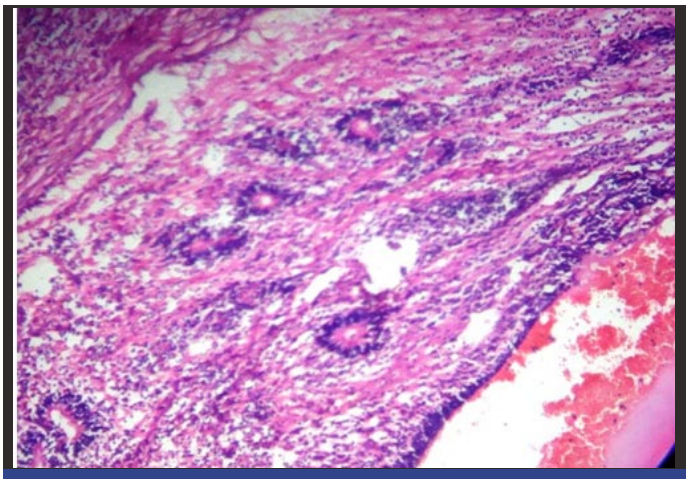
A diagnosis of retinoblastoma was made and an enucleation surgery was performed. The resected eyeball was sent to our laboratory, where multiple hematoxylin and eosin sections were prepared.

GROSS FINDINGS

The specimen comprised of a dissected part of the eyeball, measuring 2 cm in maximum diameter. The cut surface showed a small retrolental grayish white area. The rest of the posterior chamber was filled with gelatinous vitreous. A very tiny area marking the attachment of the optic nerve stump was also seen.

MICROSCOPIC FINDINGS

The sections showed the complete eyeball tissue with intact anterior and posterior chambers. The ciliary body was surrounded on either side by organised inflammatory exudates comprising fibroblastic cells, proliferating capillaries and inflammatory infiltrates, merging with the displaced retinal tissue which was lying behind it. The immediate retrolental area showed the displaced polypoidal folds of the retina. The underlying loose stroma of the disorganised retina also showed glial tissue and many tubular rosettes which were formed by the dipping of the cells of the retinal lining. These well defined tubular pseudo rosettes were seen around the central empty spaces which were surrounded by well defined basement membranes along with peripheral rows of elongated, evenly arranged nuclei [Table/Fig 1]. However there was no proliferation of the atypical round cells and no atypical mitosis was seen. The posterior area showed thin layers of pigmented choroid and no retinal epithelium was seen posteriorly. The optic nerve stump area showed a few nerve fibres and no tumour cells were seen. [Table/Fig 1]



[Table/Fig 1]:]: H & E 400X dysplastic retinal epithelium showing formation of tubular rosettes with well defined basement membrane

These findings were suggestive of retinal dysplasia showing many retinal pseudorosettes, with suggestion of retinal detachment and iridocyclitis.

DISCUSSION

Three major diagnostic considerations that come to the mind of an ophthalmologist when evaluating a white pupillary reflex in a child, are- retinoblastoma, cataract and the so called pseudogliomas or pseudoretinoblastomas. There are numerous classifications of pseudoretinoblastomas, most of which are grouped according to incidence. Amongst them, one of the best classifications to date is that of Howard and Ellsworth [1].

They studied 500 consecutive patients. Of these patients, most

of whom had unilateral or bilateral leucocoria, a diagnosis of non retinoblastoma was made in 265 cases (53%) and that of retinal dysplasia was found in 7 (2.5%) cases.

In 1950, Reese and Blodi[2]described the clinical and histopathological features of retinal dysplasia and defined it as a congenital syndrome, combining the retinal abnormalities with the systemic anomalies which affected the brain, heart, extremities and other organs.

It may be a component of a group of congenital disorders such as Norrie's disease and the trisomy 13 or the Walker-Warburg syndrome.

A primary histopathological feature of retinal dysplasia is the formation ofrosettes [3].

The retina is bordered on its vitreal surface by the retinal ganglion cells, while the scleral surface is bordered by the retinal pigment epithelium. The anglion cell layer and the retinal pigment epithelium are the first layers to differentiate and establish the polarity of other layers. Adjacent to the retinal pigment epithelium, the photoreceptor nuclei comprise the outer nuclear layer, while the interneurons and the muller glia make up the inner nuclear layer which is adjacent to the ganglion cell layer. In some pathological states, this orderly arrangement is disrupted, resulting in retinal dysplasia which is characterised by the formation of tubular structures known as rosettes.

A rosette represents an attempt to form embryonic retinal tissuesrods and cones. The cells lining the rosette are analogous to the nuclei in the outer limiting membrane of the retina. These benign rosettes of retinal dysplasia should be distinguished from the malignant Flexner-Wintersteiner rosettes which are fomed in retinoblastoma. The cells that form the Flexner-Wintersteiner rosettes are characterised by all the cytological features of anaplasia that are typically associated with malignant neoplasms. On the other hand, the rosettes which are seen in retinal dysplasia also show analogous differentiation which simulates the photoreceptor elements but they are of course, not malignant. Dysplastic rosettes represent a developmental or embryopathic aberration rather than a true neoplastic aberration [4].

Also, in contrast to the neoplastic rosettes of the Flexner-Wintersteiner type, the rosettes of the dysplasic retina contain multiple cell types [5].
Furthermore, the rosettes in retinoblastoma are typically positive for cone opsin and are negative for rod opsin. The dysplastic rosettes show the opposite pattern which mainly expresses rod opsin [6].

Also, muller cell differentiation is not observed in the rosettes of retinoblastoma. In addition to the formation of rosettes, retinal dysplasia occasionally shows an attempt by the faulty neuroepithelium to form a simple cuboidal epithelium resembling that of the embryonic retina or the ciliary body.

Clinically, retinal dysplasia may present itself in a wide range of severity from a simple to the massive folding of the retina, the central stalks with the retinal tissue extending from the optic disc to the back of the lens and complete retinal detachment, leading to highly disorganised microphthalamic eyes [7].

If the intraocular proliferation is large enough, it may produce leucocoria. Graaf et al reported a case of a 6 month old boy who presented with unilateral leucocoria, retinal detachment and a retrolental mass in a microphtalamic eye, based on retinal dysplasia with concurrent optic nerve aplasia in 2007 [8].

Leucocoria and retinal detachment in children require a prompt further investigation because retinoblastoma should be included in the differential diagnosis. Usually the underlying disease which causes leucocoria can be detected by ophthalmoscopy alone or in combination with ultrasonography. The dysplastic retinal tissue-a rare congenital defect, may create a clinical and a radiological picture of an intraocular mass which closely resembles tumour tissue. The awareness of this disease and its histopathological features therefore might be helpful in differentiating between retinal dysplasia and malignant ocular pathology, so as to reach an early diagnosis.

REFERENCES:

[1] Howard GM and Ellsworth RM: Differential Diagnosis of retinoblastoma: a stastica survey of 500 children. 11. Factors relating to the diagnosis of retinoblastoma. Am J Ophthalmol.1965; 60:618.
[2] Reese AB, Blodi FC: Retinal dysplasia. Am J Ophthalol.1950; 33:23.
[3] Fundus. In: Apple DJ, Rabb MF, eds. Ocular Pathology (Clinical applications and self –assesment), Toronto: The C.V. Mosby Company;1985:292.
[4] Retinoblastoma, leucocoria and phakomatoses. In: Apple DJ,Rabb MF, eds. Ocular Pathology (Clinical applications and self–assesment),Toronto: The C.V. Mosby Company;1985:365-366.
[5] Chan A,Lakshminrusimha S, Heffner R et al: Histogenesis of retinal dysplasia in trisomy 13. Diagnostic Pathology. 2007; 2:48.
[6] Gonzalez-Fernandez F, Lopes MB, Garcia-Fernandez JM et al:Expression of developmentally defined retinal phenotypes in the histogenesis of retinoblastoma. Am J Pathol.1992; 141:363-375.
[7] Godel V,Nemet P,Lazar M:Retinal dysplasia.Doc Ophthalmol.1981;51:277-88.[Medline]
[8] Graff PD, Van der valk P, Moll AC et al: Reinal dysplasia mimicking intraocular tumor: MR imaging finding with hitopathologic correlation. American J of Neuroradiology. 2007; 28:1731-33.

AUTHORS:
1. Dr. NEHA AGARWAL
2. Dr. PRASHANT GUPTA
3. Dr. ASHA AGARWAL
4. Dr. CHAYANIKA PANTOLA

NAME OF DEPARTMENT(S) / INSTITUTION(S) TO WHICH THE WORK IS ATTRIBUTED:
Dept of Pathology, GSVM Medical College, Kanpur

NAME, ADDRESS, TELEPHONE, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Neha Agarwal, Junior Resident, Dept of Pathology,
GSVM Medical College, Kanpur-208002
Email-id: neha_doc2005@yahoo.co.in

DECLARATION ON COMPETING INTERESTS: No competing Interests

Date of Submission: **Nov 24, 2010**
Peer Review Completion: **Jan 05, 2011**
Date of Acceptance: **Jan 25, 2011**
Date of Final Publication: **Apr 11, 2011**