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Case Report:

Retinal Dysplasia Mimicking Retinoblastoma.

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Abstract: Retinal dysplasia represents a congenital disorder characterized by abnormal proliferation of retinal tissue causing leukocoria. We present a case of an infant with bilateral leukocoria, clinically diagnosed as retinoblastoma, followed by enucleation of the left eye. Microscopy however, demonstrated retinal dysplasia consisting of a disorderly proliferation of retinal tissue with formation of rosettes, mimicking retinoblastoma. Microscopic features that aid in differentiating this lesion from retinoblastoma are discussed.
Keywords: Retinal Dysplasia; Retinoblastoma; Leukocoria

Introduction

Leukocoria, an abnormal white reflection from the retina, is a condition caused by several lesions. The causes of leukocoria include Retinoblastoma and also non-tumorous conditions like Persistent Hyperplastic Primary Vitreous, Coat's disease, congenital cataract and retinal dysplasia. It is of vital importance that Retinoblastoma be differentiated from the rest of the non-tumorous conditions as treatment options and prognosis are different in cases of retinoblastoma. Retinal dysplasia represents a rare cause of leukocoria. It is the congenital anomaly in which the retinal layer forms a disordered proliferative lesion and leads to congenital blindness in children.

Case Report

We received an enucleated specimen of the left eye from a case of a one year old child with leukocoria in both eyes since birth, the eye being enucleated following a clinical diagnosis of retinoblastoma.

The gross specimen consisted of an eyeball measuring 2 x 1.8 x 1.5 cm. The cornea measured 1.2 x 0.9 cm. At the posterior end, soft tissue bit 2.0 cm long was present. Cut section showed reddish brown material with central tiny grey-white area of 0.8 cm diameter in the retrolental region.

On microscopy, portions of normal eyeball tissue were identified in the anterior segment. In addition, the section from the retrolental tissue showed swirls and whorls of uniform cells in multiple layers reminiscent of normal retinal epithelium. These cells had uniform round nuclei with speckled chromatin, scant cytoplasm and indistinct cell membranes. (Fig. 1) At several places these cells were arranged in rosette-like formations with central lumina typical of Flexner-Wintersteiner rosettes. (Fig. 2) No nuclear atypia was evident. No necrosis or calcification was noted. The skeletal muscle fibers and neural fibers from the posterior end of the specimen were within normal limits. Histological features were that of 'Retinal Dysplasia'.

A request for chromosomal study was made, but was declined by the patient's parents. The other eye was left in situ.

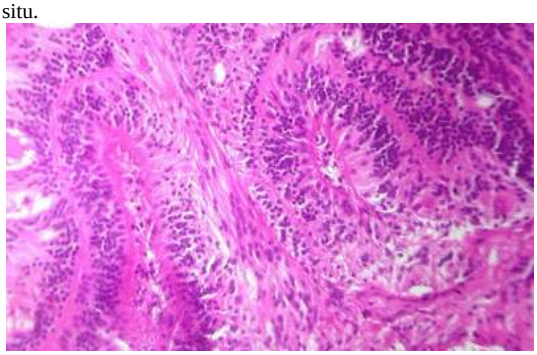

Figure 1: Cells arranged in multilayered swirls and whorls (H&E, X100)

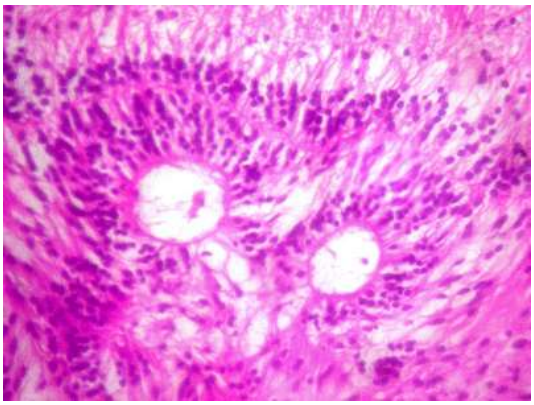

Figure 2: Rosette-like arrangement of cells resembling Flexner-Wintersteiner rosettes (H&E, X400)

Discussion

The normal histology of the retina is characterized by the ordered orientation of cells forming a multilayered tissue. When this orderly arrangement of the retinal layers is disrupted, retinal dysplasia results. The term "retinal dysplasia" was first described by Reese and Blodi in 1950. [1] Retinal dysplasia may be unilateral or bilateral; the latter is often associated with congenital conditions like Trisomy 13, Norrie's syndrome and Warburg syndrome. [2, 3, 4] An X-linked dominant inheritance has been described. [4] Retinal dysplasia is an extremely rare condition; the exact incidence cannot be ascertained as the term "retinal dysplasia" has been used in various contexts to indicate any congenital anomaly of the retina. To the best of our knowledge, only one such case is reported from India. [5]

The major histopathologic differential diagnosis to be considered while making a diagnosis of retinal dysplasia is retinoblastoma, both having in common the presence of rosettes. The rosettes of retinoblastoma are composed of anaplastic cells with poor differentiation while cells of rosettes in retinal dysplasia are more uniform and bland. Moreover, the rosettes in retinal dysplasia show a fundamental alteration in arrangement as observed on immunohistochemical study – the outer nuclear layer is present centrally and the lumen is lined by outer limiting membrane, while the inner nuclear layer is present more peripherally. [2] In addition, the cells lining the rosettes in retinal dysplasia have been shown by immunohistochemistry to be populated by a more diverse population than the rosettes in retinoblastoma. The cells in retinoblastoma are positive for cone opsin while those of retinal dysplasia stain for rod opsin and focally for Muller cells. [2, 6] Other helpful features that distinguish retinoblastoma are the presence of mitoses, necrosis and calcification. (Table 1)

Table 1: Features helpful in differentiating retinoblastoma from retinal dysplasia on microscopy

Character	Retinoblastoma	Retinal dysplasia
Cells	Undifferentiated	Uniform
Mitoses	Frequent	Rare
Necrosis, calcification	Present	Absent
Rosettes (IHC)	Positive for cone opsin	Positive for rod opsin and Muller cells
Layers in rosettes (IHC)	No pattern	Reversal of normal pattern

Other common causes of leukocoria can be excluded on histology: Coat's disease shows cholesterol clefts and foamy macrophages, Persistent Hyperplastic Primary Vitreous contains fibrovascular tissue and Retinocytoma is composed of numerous rosettes. [7]

Retinal dysplasia presenting as leukocoria may be mistaken for retinoblastoma clinically. The routine microscopic findings may also simulate a retinoblastoma. Nevertheless, there are microscopic features that are distinctive enough to warrant a confident diagnosis of retinal dysplasia. The need to not misdiagnose this as a retinoblastoma is of extreme importance given the drastic contrast in prognosis between the two conditions.

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