Diffuse Infiltrating Retinoblastoma - Atypical Presentation of Retinoblastoma in late childhood

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Summary
Diffuse infiltrating retinoblastoma is a rare variant of retinoblastoma that presents with atypical features and is usually seen in the older age group. A high degree of clinical suspicion supported by the use of appropriate imaging modalities is necessary for diagnosis.

Keywords: leucocoria, uveitis retinoblastoma

Retinoblastoma (RB) is the most common intraocular malignancy in children that is usually diagnosed before the age of 5 years. An atypical presentation of RB in late childhood and absence of calcification on imaging studies poses a diagnostic challenge for the ophthalmologist. Herein we report the clinical features and management of a similar case with atypical presentation.

A 10 year old boy presented with a history of leucocoria in the right eye for two months. There was no other relevant ocular, medical and family history. On ophthalmic examination, visual acuity was presence of light perception with inaccurate projection of rays in all the four quadrants in the right eye and 6/6 in left eye. The left eye was unremarkable on examination. On slit lamp biomicroscopy, the right eye showed exudates in the anterior chamber that were touching the corneal endothelium and invading the iris (Figure 1). Examination of the posterior segment on B scan ultrasonography demonstrated retinal detachment with haemorrhages, without any evidence of a distinct retinal mass or calcification, in the right eye. However, in view of a clinical suspicion of retinoblastoma, CT scan of the orbits was performed which revealed a few specks of calcification in the superotemporal quadrant close to the ora serrata, with findings of retinal detachment and sub-retinal exudation in the right eye (Figure 2). Further imaging with Contrast MRI of the orbits and the brain revealed the presence of a sub-retinal exudates, that showed post contrast enhancement on T1 weighted images. In addition, a small mass noted on T2 weighted images (Figure 3). The general physical examination and systemic examination were within normal limits. On the basis of clinical examination and imaging studies, a working diagnosis of Diffuse Infiltrating Retinoblastoma (DIRB) was made. Enucleation was carried out and a primary implant was inserted. The postoperative period was uneventful. Histopathological examination of the enucleated eye confirmed the presence of a poorly differentiated retinoblastoma and showed diffuse involvement of the ocular coats (Figures 4 & 5). In view of high risk histopathological features, child was advised to receive post-operative adjuvant systemic chemotherapy. An artificial eye was prescribed at six weeks follow-up. At one year follow-up, the patient was doing well, with no local recurrence or systemic metastasis.

Discussion
In 1958, Ashton suggested the term “Diffuse Infiltrating Retinoblastoma” to describe a flat neoplasm that did not produce a tumour mass within the retina. Diffuse infiltrating retinoblastoma, a rare variant of retinoblastoma, shows a unique growth pattern that occurs in 1–2% of cases, in which the tumor grows horizontally with minimal vertical growth. These tumors tend to be unilateral, sporadic, and are more commonly seen in children around the ages of 6–8 years.

In our case, the differential diagnosis were Coats disease, Uveitis, Endophthalmitis, Diffuse infiltrating retinoblastoma and Leukemic infiltration. Unilateral presentation of leucocoria in a 10 year old boy with presence of subretinal exudation and absence of calcium and a mass on B-scan USG can lead to a suspicion of Coats disease. However, in
Figure 3: T1-weighted MRI axial scan showing subretinal exudates (arrow) with gadolinium enhancement in the right eye. A small mass (arrow) is visualized on T2- weighted sagittal section.

Figure 4: Hematoxylin and eosin stain showing poorly differentiated retinoblastoma and calcification with sub-retinal infiltration shown in arrow.

Figure 5: Histopathological section of right eyeball showing involvement of the optic nerve head, anterior chamber, angle structures, and massive choroid infiltration by tumor cells.

Coats disease, the anterior chamber is usually clear and if not, yellow refractile material known as cholesterosis may be seen, unlike the exudates seen in our case. The absence of pain, ocular congestion, posterior synechia, iris bombe, PAS and cataract or any systemic signs were against an ocular inflammatory condition such as uveitis or endophthalmitis. Leukemia with ocular involvement usually presents with orbital infiltration, neuro-ophthalmic signs and systemic association⁴, which was not present in our case. On the basis of imaging findings, a working diagnosis of Diffuse Infiltrating RB (DIRB) was made, which was confirmed on histopathological examination. In the largest series on Diffuse Infiltrating RB (DIRB) by Shields et al, the clinical features and management in 34 eyes has been mentioned. The posterior segment revealed extensive ill-defined retinoblastoma infiltrating the retina that presented with a flat growth pattern and undulating retinal thickening. The study concluded that the tumour could masquerade as uveitis or unexplained hyphema or keratic precipitates.⁵ Our case study also concurred with these observations. Imaging is particularly useful in cases that present with atypical clinical features. In our case, the presence of punctate calcification was noted on CT scan. It has been observed that calcification is usually absent in DIRB and if present, is in the form of punctate calcification.⁶,⁷ In histologic sections also, it has been observed that calcification, a characteristic feature of RB, is present in only 14% of the cases, as compared with 95% cases in the typical forms.⁸ MRI helped us in establishing the diagnosis and also in ruling out extra-ocular spread.
Regarding treatment, in view of the unilateral nature of the tumor, the extent of retinal infiltration, and the frequency of vitreous dissemination, enucleation is the treatment of choice for Diffuse infiltrating retinoblastoma. The survival rate inclusive of all variants of Diffuse infiltrating retinoblastoma has been reported to be greater than 95% in children who underwent enucleation of the affected eye.

To summarize, this case highlights that retinoblastoma can masquerade a variety of ocular conditions. Diffuse infiltrating retinoblastoma should be considered in all cases of refractory uveitis, especially in older children. A high index of clinical suspicion, combined with a systematic approach and judicious use of imaging modalities, aids in the diagnosis. Enucleation is the standard of care and serves as a life saving intervention.

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