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Advances in Imaging Techniques for Retinoblastoma with Subretinal Seeding

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Abstract **Case Report**

Retinoblastoma is a rare and highly malignant intraocular tumor primarily affecting young children. Subretinal seeding, specifically Type D, indicates an advanced stage of retinoblastoma with a high risk of metastasis and a poor prognosis. We present a case of a 4-year-old girl who presented with leukocoria, vision loss, and painless redness in her left eye. Examination of the posterior segment revealed a total retinal detachment and abnormal, tortuous retinal vessels in the left eye. No visible mass, vitreous seeding, or hemorrhage was observed. B-mode ultrasound confirmed a detached retina. Due to the poor visual prognosis and strong clinical suspicion of malignancy, enucleation was performed. Further histopathological analysis confirmed the diagnosis of diffuse infiltrative retinoblastoma.

Keywords: Exophytic retinoblastoma, Ultrasonography, Magnetic Resonance Imaging.

INTRODUCTION

Retinoblastoma is the most common primary intraocular malignancy in children, originating from developing cells in the retina [1]. It typically presents with leukocoria, strabismus, or diminished vision in affected children. In some cases, retinoblastoma can progress to subretinal seeding, which significantly complicates the disease course and management [2].

CASE REPORT

A 4-year-old Hispanic girl was referred with leukocoria, vision loss, and painless redness of the left eye lasting for one month. There were no other relevant symptoms or medical history. Uncorrected visual acuity was 20/20 in the right eye and no light perception in the left eye. Intraocular pressure was 16 mm Hg in the right eye and 18 mm Hg in the left eye. The right eye examination under anesthesia was unremarkable. Anterior segment findings in the left eye included leukocoria, mild conjunctival hyperemia, and rubeosis iridis. Fundus examination of the left eye revealed a total serous retinal detachment with a white-yellow hue and abnormal tortuous retinal vessels. No visible mass, vitreous seeding, or hemorrhage were observed. B-mode ocular ultrasound showed normal findings in the right eye but revealed a completely detached retina in the left eye, extending to the ciliary body with some areas of pinpoint echodensity. These findings were suspicious for focal calcification but without acoustic shadowing. Despite a thorough examination, no solid tumor or subretinal or vitreous seeds were found. A presumptive diagnosis of diffuse infiltrative retinoblastoma (DIR), Group D, was made based on the International Classification of Retinoblastoma (ICRB). MRI was performed and showed a retinal mass with hypersignal T1 and T2, enhanced after gadolinium injection, corresponding to Group D with no high-risk features such as extraocular extension, retrolaminar optic nerve infiltration, or massive choroidal infiltration. Although rubeosis iridis was present, there was no tumoral involvement of the anterior chamber. Due to the poor visual prognosis and high clinical suspicion of malignancy, enucleation was performed. Histopathological analysis confirmed the presence of neoplastic cells with rosette formation within the thickened retina and ciliary body, consistent with diffuse infiltrative retinoblastoma. No calcium deposits were found in the specimens, and therefore, no adjuvant chemotherapy was required. Germinal testing on blood was not performed due to institutional limitations. One year after surgery, the patient remained disease-free without recurrence or metastasis.

DISCUSSION

Retinoblastoma (Rb) is the most common eye cancer in children, with an incidence of 1 in 14,000 to 1 in 35,000 births. Although it is a rare disease, early

detection offers excellent chances of cure and preservation of vision [1].

Rb can occur in bilateral, hereditary, sporadic, or familial forms, usually appearing in very young children within the first few months of life [3]. The unilateral form of Rb is hereditary in only 15% of cases and is most often diagnosed around the age of 2 [3].

Advanced retinoblastoma manifests as leukocoria in 60% of cases and can cause strabismus in 20% of cases. In 20% of cases, atypical symptoms such as pain, redness, eyelid swelling, chemosis, conjunctivitis, glaucoma, or even orbital cellulitis may be present [2].

Retinoblastoma with subretinal seeding, Type D, is characterized by the presence of tumor cells within the subretinal space. This form of seeding is associated with advanced disease and often indicates vitreous or choroidal involvement. Clinical signs include yellow-white subretinal deposits, retinal detachment, and vitreous seeding [3].

The examination of the fundus of the eye under anesthesia using indirect ophthalmoscopy allows the diagnosis of retinoblastoma [1]. Rb can present as a single tumor or as multiple foci in the eye. It can grow inward (endophytic Rb) or outward, causing retinal detachment (exophytic Rb).

The International Classification of Retinoblastoma (ICRB) [4], staging system is commonly used to categorize retinoblastoma, including cases with subretinal seeding. Stage D specifically indicates the presence of subretinal and/or vitreous seeding, which suggests a higher risk of extraocular spread [4].

In a small percentage of cases, the signs and clinical appearance may not be sufficiently characteristic for an immediate definitive diagnosis [5]. This raises the issue of differential diagnosis with numerous retinal diseases that can mimic retinoblastoma, such as Coats' disease, hamartomas associated with Bourneville's disease, and inflammatory or infectious diseases (e.g., toxocara canis) [6].

Ultrasonography plays a crucial role in evaluating retinoblastoma, especially in cases with subretinal seeding (7). B-scan ultrasonography provides valuable information about tumor size, location, and extent of seeding. It can visualize subretinal deposits, vitreous opacities, and retinal detachment, aiding in staging and treatment planning. High-frequency ultrasound probes enable detailed imaging of ocular structures and help differentiate retinoblastoma from other ocular lesions [7].

MRI is a non-invasive imaging modality that offers excellent soft tissue contrast and detailed anatomical information [8]. It is particularly useful in assessing the extent of retinoblastoma and identifying subretinal seeding. With the use of gadolinium-based contrast agents, MRI can enhance the visualization of tumors and their spread into the vitreous or subretinal space. MRI also helps detect optic nerve involvement, invasion of the choroid, and central nervous system involvement [8].

Optical Coherence Tomography (OCT) is a non-invasive imaging technique that utilizes light waves to generate high-resolution cross-sectional images of the retina. It is valuable in assessing retinal architecture and detecting subretinal seeding in retinoblastoma. OCT scans provide detailed information about the extent of tumor involvement, retinal detachment, and the presence of subretinal fluid or deposits. This information assists in treatment planning and monitoring the response to therapy [9].

The combined use of ultrasonography, MRI, and OCT provides a comprehensive evaluation of retinoblastoma with subretinal seeding. These imaging techniques aid in accurate staging, guide treatment decisions, and monitor the response to therapy (10). The choice of imaging modality depends on factors such as equipment availability, patient age, and the need for sedation or anesthesia during the procedure [9].

Retinoblastoma can disseminate and metastasize either through continuity along the optic nerve or hematogenously. If tumors invade vascular structures such as the ciliary body, a broader staging assessment is required, including bone marrow puncture/biopsy, bone scintigraphy, and thoracoabdominal CT scan [11].

All children, regardless of the location of their tumor, undergo brain magnetic resonance imaging (MRI) at the time of diagnosis due to the risk of approximately 4-6% of developing a malignant tumor in the pineal gland. This risk is especially present in hereditary forms of the disease and is referred to as trilateral retinoblastoma [9].

The management of retinoblastoma with subretinal seeding involves a multidisciplinary approach, including ophthalmologists, radiologists, oncologists, and radiation specialists. Treatment options include chemotherapy, focal therapies such as laser photocoagulation and cryotherapy, radiotherapy, and enucleation. Each case is unique, considering factors such as the number, size, and location of tumors, laterality and heredity of the disease, possible associated anomalies, the child's age, and their social environment [11].

Recent advancements in the management of retinoblastoma with subretinal seeding have focused on targeted therapies, including intravitreal chemotherapy

and local delivery of chemotherapeutic agents. These approaches aim to enhance tumor control and reduce systemic side effects associated with conventional treatment modalities [8].

The overall prognosis for retinoblastoma is excellent, with 90-95% of children recovering from the disease. Metastatic disease typically develops within the first year after diagnosis. The five-year survival rate is the same for unilateral and bilateral retinoblastoma [9]. Absence of recurrence at five years is considered a cure. However, retinoblastoma with subretinal seeding, particularly Type D, is associated with a guarded prognosis due to the increased risk of metastasis. The presence of seeding indicates more aggressive disease behavior, necessitating prompt and aggressive treatment to prevent extraocular spread [10].

Close and specialized ophthalmological follow-up is necessary because the reappearance of new tumor foci is part of the normal course of retinoblastoma, especially in the hereditary form [5].

Pediatric oncological follow-up is necessary for hereditary cases of retinoblastoma, incuding annual clinical examinations and MRI scans until the age of five, which is the age limit for the development of a pineal tumor [8].

For rare cases of patients treated for metastatic disease, follow-up visits are much more frequent and also include monitoring of all metastatic sites [11].

CONCLUSION

Ultrasonography, MRI, and OCT are valuable imaging techniques in the diagnosis and management of retinoblastoma with subretinal seeding, specifically Type D. These modalities provide crucial information about tumor characteristics, the extent of seeding, and the involvement of adjacent ocular and central nervous system structures. Integrating these imaging techniques with clinical examination and histopathological analysis enhances the accuracy of diagnosis, staging, and treatment planning, ultimately improving patient outcomes.

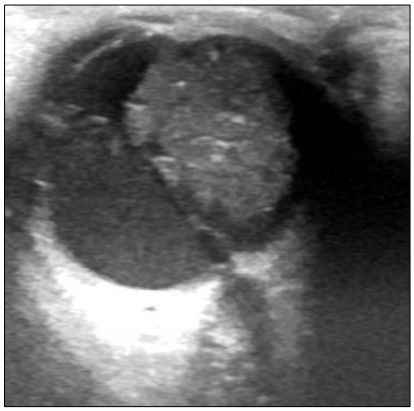

Figure 1: Ultrasound shows a retinoblastoma as hyperechoic with subretinal seeding on retinal detachment.

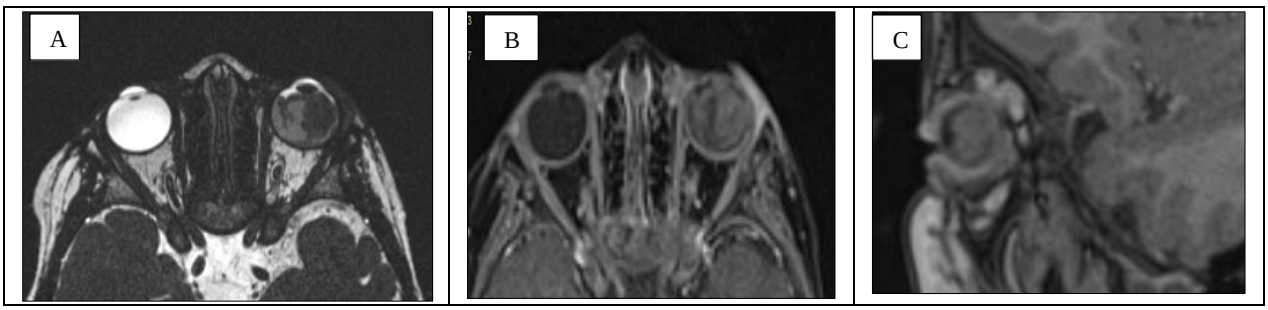

Figure 2: In axial CISS sequences (a) T1-weighted after gadolinium injection (b) and sagittal T1 without enhancment, a retinoblastoma is identified as discreet T1 hypersignal, isosignal T2, and with faint enhancement, along with subretinal seeding on retinal detachment.

Conflict of Interest: The authors declare that there is no conflict of interest.

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