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Case Report

Management of Retinoblastoma Associated with Persistent Fetal Vasculature: Case Report

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Abstract

Purpose: To report the challenging diagnosis, treatment, and follow-up of a patient with persistent fetal vasculature (PFV) and retinoblastoma (RB).

Case Report: A 22-month-old male was referred to our clinic for a white retinal lesion in the right eye (OD) to rule out retinoblastoma versus persistent fetal vasculature. In the examination under anesthesia (EUA), the anterior segment showed lenticular cataract both eyes (OU), more prominent OD. Fundus examination of OD revealed an optic nerve calcification mass with vitreous seeding overlying a transvitreal stalk. Vascular ectasia was present with a retina fold and a tractional retinal detachment. Fundus examination of the left eye (OS) showed an attached retina without mass lesion. The patient was diagnosed with unilateral RB stage Vb and PFV OD. The patient started treatment with systemic chemotherapy with 2 drugs and transpupillary laser ablation OD.

On subsequent fundoscopic examination OD revealed a completely RB regression type 1 of the primary tumor mass overlying the optic nerve head.

A magnetic resonance imaging (MRI) of orbits, neuroimaging and a high-resolution ultrasound was repeated every 6 months without evidence of progressive disease.

Two years after the las systemic chemotherapy treatment, MRI showed increased signal intensity with progressive optic nerve enhancement and cannot exclude intraneural malignancy, due to this diagnosis the enucleation of OD was decided. Histopathologic review showed no residual active malignancy in the enucleated globe.

Conclusion: It is crucial to do a thorough clinical examination and use B-scan ultrasound as an important ancillary test to rule out RB before any surgery, to avoid the dissemination of malignant RB cells and this case also highlights the importance of regular follow-ups after tumor regression with full ophthalmological examination, B-scan, FA and periodical MRI.

Keywords: Retinoblastoma; Persistent Fetal Vasculature; Retinoblastoma Mimickers; Pseudoretinoblastoma; Systemic Chemotherapy; Laser Ablation Therapy

Introduction

Leukocoria or white pupillary reflex is an alarming sign in children. It is usually found at birth during screening for red reflex or noticed later in children by family members or pediatricians. Although there are many differential diagnoses for leukocoria, the main concern remains retinoblastoma (RB).

RB is the most common ocular malignant tumor in pediatric population, with 1 in 15,000 to 34,000 births, and could be devastating if left undiagnosed and untreated [1,2].

Other eye conditions are also responsible for leukocoria, including persistent fetal vasculature (PFV).

PFV, (also referred to as persistent hyperplastic primary vitreous PHPV) is a rare developmental malformation most frequently unilateral, characterized by a failure of primary vitreous regression, causing a retrolental fibrovascular tissue. 90 to 95% of the cases are non-heritable [3].

RB and PFV are two distinctive conditions, with completely different management and prognoses. They only share leukocoria as a common possible sign, and they both may compromise vision. In addition, retinal dysplasia, an important characteristic of PFV, has been shown to be found in 2% of the eyes with RB [1].

Therefore, the coexistence of RB and PFV, two presumable unrelated diseases, is extremely infrequent and only a few cases have been reported [2].

The authors report a rare case of Retinoblastoma and Persistent Fetal Vasculature in a 2-year-old male. This case is unique considering the challenging diagnosis, the treatment approach aiming at saving the life and the eye, and the importance of strict and structured follow-up.

Case Report

A 22-month-old male, with leukocoria and exotropia OD, was referred to our clinic to rule out retinoblastoma versus persistent fetal vasculature. He was born at term by vaginal delivery. The pregnancy was uneventful. His parents and siblings had normal visual development with no family history of ocular diseases.

On presentation, best-corrected visual acuity (BCVA) was fix and follow in both eyes (OU). Examination under anesthesia (EUA) showed: Intraocular pressures of 13 OD and 14 OS. The anterior segment showed lenticular cataract OU more prominent OD. Fundus examination of OD revealed an optic nerve calcification mass with vitreous seeding overlying a transvitreal stalk with vascular ectasia and retina fold with mild tractional retinal detachment. Fundus examination OS showed an attached retina without evidence of retinal tumor.

Quantitative A-scan measured axial lengths of 17.4 mm OD and 18.4 mm OS. B-scan ultrasound of the right eye revealed mild vitreous opacities, a dome shape mass lesion with thickness of 4 mm, temporal retina with irregularly thickened surface, and several hyperechoic areas. The optic nerve was difficult to evaluate on A and B scans with hyperechoic echo source anterior to the retrobulbar optic nerve. B-scan OS revealed an attached retina without any mass lesion.

Fluorescein angiography (FA) showed hyperfluorescence of the optic nerve mass with a pinpoint of leakage and anastomosis with avascularity on the periphery of the retina OD and some avascularity in the peripheral retina more prominent in the temporal side with some staining in the posterior pole OS. The patient was diagnosed with unilateral RB stage Vb (Reese Ellsworth classification) and PFV OU asymmetric more prominent OD. The patient was treated with systemic chemotherapy using vincristine and carboplatin with a total of 6 cycles, in addition to 6 sessions of local transpupillary laser ablation OD. There was complete tumor resolution with type 1 regression pattern with a stable vascular ectasia and tractional retinal detachment associated to PFV.

Patient continued to be monitored regularly with EUA, fundus photography, FA and B-scan, monthly initially then extending progressively. In addition, magnetic resonance imaging (MRI) of orbits, with contrast was performed every 6 months with no evidence of progressive disease.

Two years after last systemic chemotherapy treatment, MRI showed increased signal intensity with progressive optic nerve enhancement OD, which cannot exclude intraneural malignancy. Due to this finding, enucleation was decided. Histopathologic review showed no evidence of residual malignancy in the enucleated globe with fibrovascular tissue and rare psammoma bodies. The findings in the optic nerve head and choroid revealed no evidence of neoplasia or meningothelial proliferation.

Five months after OD enucleation, patient remains stable, with BCVA of 20/40 OS.

Figure 1: Color fundus photographs. A: Fundus photographs of the right eye before treatment showed a lenticular cataract artifact with an optic nerve calcification mass overlying transvitreal stalk with vascular ectasia and retina fold. B: Late-phase fluorescein angiography revealed optic nerve mass staining with mild leakage in the superior area with anastomosis and avascularity on the periphery of the retina in the right eye. C: Fundus photographs of the right eye after finished the treatment revealed optic nerve mass with type 1 regression with the atrophy and pigmentary changes secondary to the treatment, without vitreous seeding overlying the persistent fetal vasculature stalk in the optic nerve and some retina folds with mild traction causing a mild tractional retinal detachment treated with laser in the peripheral retina. D: Late- phase fluorescein angiography after treatment of the right eye showed hypofluoresce in the optic nerve mass with staining around the optic nerve mass and hypofluorescence in the peripheral retina secondary to laser.

Figure 2: Color fundus photographs. A Fundus photographs of the left eye revealed a lenticular cataract artifact with an attached retina without evidence of retinal tumor. B Late-phase fluorescein angiography of the left eye showed avascularity in the peripheral retina more prominent in the temporal side with some staining in the posterior pole.

Discussion and Conclusion

This unusual case of unilateral leukocoria originating from both RB and PFV was diagnostically complex. The patient was referred with suspicion of either RB or PFV, with the diagnosis being uncertain.

With any leukocoria, the most feared disease is retinoblastoma. RB affects children of less than 4 years old.2 RB can cause local spread along the optic nerve head into the orbit, and it can also metastasize hematogenously to brain, bone, liver and other organs [4].

Early diagnosis of RB can improve the patient's visual prognosis as well as survival rate. RB must always be in the differential diagnosis for pediatric patients presented with strabismus, uveitis or leukocoria. Another important differential diagnosis is PFV, as this is one of the most common retinoblastoma mimickers in 20% of the cases [5].

In PFV, leukocoria is a common sign; it is usually diagnosed during the first year of life. The classical presentation of PFV is leukocoria, cataract, elongated ciliary processes, shallow anterior chamber, retrolental fibrovascular membrane and microphthalmia [6].

In normal development, fetal vasculature regresses; however, in 3% of full-term infants and 95% of premature, the fetal vasculature can persistent and cause different disorders [7].

PFV is most of the time diagnosed by ophthalmoscopic examination, however, differentiate PFV from retinoblastoma is sometimes challenging and ultrasound and other imaging tools can be employed such as: magnetic resonance imaging, doppler associated ultrasonography and fluorescence angiography [6,8].

MRI is currently the preferred imaging modality for estimating metastatic risk and assessing disease extent; however, differentiation between PFV, Coats disease and RB can be extremely difficult due to similar funduscopic and MRI characteristics [2]. Differentiation is vital for initiating adequate treatment. A missed retinoblastoma diagnosis and treatment delay can be life-threatening.

In this report there were signs that raised the suspicion of the association of both conditions in the same eye. First, during the ophthalmological exam, there was an optic nerve mass with calcification and vitreous seeding. This alone confirmed the presence of RB and prompted the initiation of treatment. The presence of the white fibrous structure in the vitreous with tractional retinal detachment could be secondary to RB-associated traction [9] or to PFV. But the configuration of the stalk emerging from the op-

tic nerve to the anterior vitreous with the presence of lenticular cataract was highly suspicious of the RB associated to PFV. This was also confirmed with ancillary tests especially B-scan.

In this case, two reasonable options to treat were considered: systemic chemotherapy with enucleation, or a globe salvaging approach with systemic chemotherapy combined with transpupillary thermal laser therapy. The latter was preferred after discussion with the patient's parents.

Patients with RB need frequent follow-up examinations. Tumor regression must be followed closely, paying attention to the appearance, location, number, and size of tumor during each examination.

Follow-up regimen decisions are even more challenging in a patient with the combined presentation of retinoblastoma and PFV, as it is important to recognize if the patient needs more ablation sessions and if the RB is stable or progressing [10]. In our case, we relied on full ophthalmological examination under anesthesia, using the help of fundus photography, B-scan, and FA. In every follow up, we would analyze each test carefully with constant comparison to former results and treat accordingly with laser therapy. The patient was treated successfully with full RB remission.

An important point to address is whether to perform surgery for PFV repair and release tractional retinal detachment. There are two key points that must be considered: first it is known that vitrectomy cannot be performed in eyes with retinoblastoma until 18 months of full remission to avoid tumor dissemination [11].

Our patient was in remission for more than 18 months. The other point is to weigh risk versus benefits, assessing the visual gain and discussing with the family prior to surgery. In our case the risk was higher than the benefit and we opted for observation.

This case also highlights that close follow-up is of utmost paramount, even after complete tumor regression. Periodic MRI and B-scan ultrasound is exceptionally important, during the treatment and after tumor control. As in this case, the MRI showed increased signal intensity with progressive optic nerve enhancement that could not exclude intraneural malignancy, which prompted enucleation of the OD 2 years after remission. The pathology report showed no tumor invasion of the optic nerve; however, to ensure patient safety, enucleation was the adequate measure.

It is extremely rare that RB and PFV present simultaneously. To the best of the authors' knowledge, there has been only one other documented report of combined PFV and RB [4].

As this case demonstrates, it is crucial to do a thorough clinical examination and use B-scan ultrasound as an important ancillary test to rule out RB before any surgery, to avoid the dissemination of malignant RB cells from an unsuspected tumor [12].

In addition, this case also highlights the importance of regular follow-ups after tumor regression with full ophthalmological examination, B-scan, FA and periodical MRI [12].

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