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ADVANCES IN OPHTHALMOLOGY AND OPTOMETRY

Vitreous Disease in Retinoblastoma

Clinical Findings and Treatment

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Keywords

• Retinoblastoma • Vitreous seeds • Vitreal seeds • Intravitreous chemotherapy • Melphalan • Electroretinogram

Key points

- Vitreous seeds can be classified into 3 categories based on morphologic characteristics.
- Vitreous seed classes are associated with response to intravitreous melphalan, including amount of drug received and time to regression.
- Intravitreous melphalan is relatively safe with the adoption of safety techniques but can be toxic to the retina as demonstrated in preclinical and clinical studies.
- The toxicity of intravitreous melphalan may be influenced by the extent of ocular pigmentation, and when given within 1 week of concomitant ophthalmic artery chemosurgery (OAC).

INTRODUCTION

Retinoblastoma is the most common primary cancer to occur in the eyes of children. It has a frequency of 1 per 15,000 births, and this rate is relatively equal and stable worldwide. Retinoblastoma can either be unilateral or bilateral, and in the latter case is typically hereditary and associated with a germline mutation in the

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RB1 gene, although most children who have bilateral disease are the first in the family to be affected. Hereditary cases typically present at the age of 1 year, and nonhereditary cases present at 2 years of age. Diagnosis occurs most commonly after a caretaker notices a white glint in the pupil of the eye. An ophthalmologist confirms the presence of white tumor(s) on dilated fundus examination.

The tumors derive from the cone precursor cells and, as such, tumors grow out from the retina toward the vitreous cavity. On occasions, these retinal tumors can generate little pieces of tumor that break off and float in the vitreous cavity, so-called vitreous seeds. Five years ago, active vitreous disease was an ominous sign. Due to a lack of adequate treatment, vitreous disease likely committed the eye to a destiny of enucleation. In recent years, however, due to developments in treatment, eyes with vitreous seeds can be saved. From these advancements, understanding of vitreous disease and its treatment has also deepened immensely. This article outlines these latest advances.

VITREOUS DISEASE

In his comprehensive ophthalmic oncology textbook published in 1963 entitled, *Tumors of the Eye*, Algernon Reese [1] sums up his entire description of vitreous seeds in 4 sentences. His fundus examination was restricted to a direct ophthalmoscope, making the larger context of the vitreous cavity difficult to fully appreciate. He called them, ''globules of disseminated tumor seeds of a rather dull, light gray color'' emanating ''from the site where tumor first breaks through its confines.'' Amemiya and colleagues [2] wrote a descriptive account of vitreous seeds in 1979, titling their account.'' They explained that approximately a third of retinoblastoma eyes contain vitreous seeds, and they are rare in eyes where the tumor encompasses less than one-quarter of the retina [2]. Histopathologically, they label seeds as either necrotic tumor cells or ''almost intact'' tumor cells [2].

Describing vitreous disease, however, with the blanket term, *seeds*, does not explain the variability that is observed clinically. Therefore, the authors' group differentiates vitreous seeds into 3 classes based on morphologic characteristics: dust (class 1), spheres (class 2), and clouds (class 3) [3,4]. This classification system is useful as a clinical descriptor and allows for comparisons between eyes in the literature (Table 1). Furthermore, as recently discovered, the classification system can be associated with distinct patient and tumor characteristics along with response to treatment [3,5].

Dust

Dust appears like powder sprinkled over the tumor surface. These small granules of vitreous opacities can often be appreciated as haze (Fig. 1). One belief is that they originate from tumor cell displacement into the vitreous [4].

Dust typically occur in children of the youngest age (median 11 months) compared with spheres and clouds [5]. They can originate in all locations of the fundus and do not have preponderance between unilateral and bilateral