Ghost Cell Glaucoma

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The presence of fresh blood and blood products in the anterior chamber is well-known as a cause of increased intraocular pressure (IOP). Hemorrhage in the vitreous cavity can also be the origin of secondary glaucoma. In 1960, Vannas [1] blamed hemosiderin and hemosiderin-filled macrophages for IOP elevation occurring years after the initial bleed. Later, in 1963, Fenton and Zimmerman [2] stressed the role of hemoglobin-filled macrophages in obstructing the trabecular meshwork of a patient with vitreous hemorrhage. It was not until 1976, when Campbell and colleagues [3] published their studies, that ghost cells were described as a cause of secondary open-angle glaucoma related to vitreous hemorrhage.

■ Pathophysiological Features

Ocular trauma—blunt, penetrating, accidental, or iatrogenic—often is accompanied by vitreous hemorrhage. Red blood cells trapped within the vitreous cavity undergo an important transformation as they age. Fresh red blood cells, which are extremely deformable, can easily pass through the trabecular meshwork. However, aging erythrocytes, held back by an intact anterior hyaloid, undergo morphological and colorimetric changes [4]. The normal, red, biconcave, pliable cell (Fig 1) slowly degenerates into a smaller, khaki-colored, spherical, and more rigid hollow structure (Fig 2) [3]. Part of the intracellular hemoglobin is lost into the extracellular vitreous space, where it forms clumps adherent to the vitreous strands. The remaining intracellular hemoglobin denatures, forming clumps known as Heinz bodies. This "ghost cell" transformation takes from 1 to 3 weeks.

Ghost cells have been shown to lower the outflow facility three times more than the same amount of fresh red blood cells, presumably because

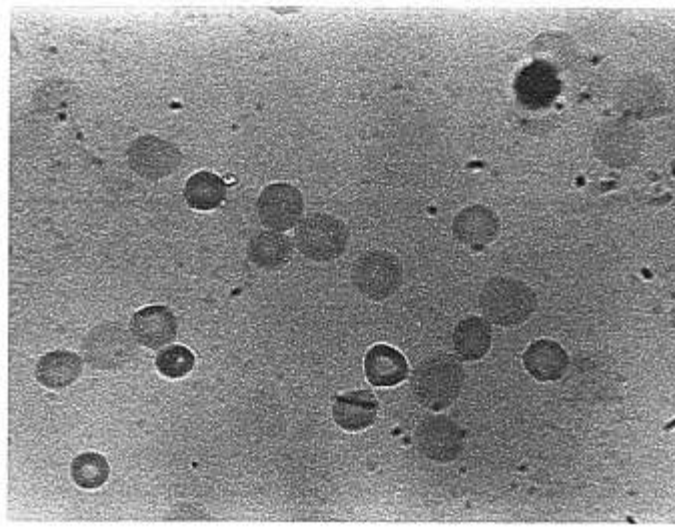

Figure 1 *Normal, biconcave, pliable erythrocytes.*

they are rigid and cannot deform themselves to pass through the trabecular meshwork [3]. Whereas hemoglobin clumps stay trapped in the vitreous network, ghost cells are free gradually to move anteriorly. Any disruption of the anterior hyaloid face allows the ghost cells to pass in large numbers to the anterior segment, where they obstruct the trabecular meshwork and cause increased IOP.

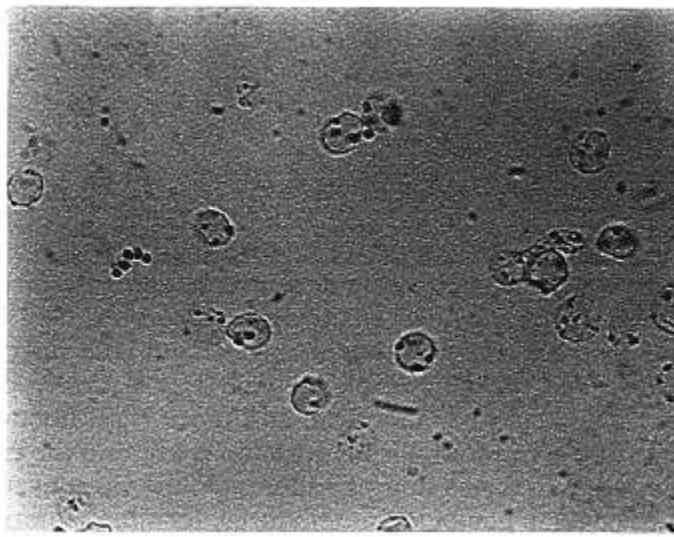

Figure 2 *Trapped red blood cells, as they age, slowly degenerate into smaller, khaki-colored, spherical, and more rigid hollow structures.*

■ Clinical Presentation

The natural history of ghost cell glaucoma frequently includes three features: vitreous hemorrhage, disruption of the anterior hyaloid, and increased IOP. However, ghost cell glaucoma can occur whenever aged red blood cells are trapped within the globe and obstruct the trabecular meshwork. Because red blood cells commonly are trapped within the vitreous cavity for long periods, ghost cell transformation and subsequent ghost cell glaucoma is especially common after vitreous hemorrhage.

Vitreous hemorrhage after blunt or penetrating ocular trauma is not infrequent. Some of these cases will present with raised IOP if a concomitant anterior hyaloid tear is present or after the initial surgical treatment has been attempted. When accompanied by hyphema, gradual clearance of the anterior chamber blood will not normalize the IOP, as a flow of ghost cells passes forward.

Surgical trauma is another potential source of vitreous hemorrhage and late ghost cell glaucoma. Hyphema and vitreous hemorrhage during intracapsular and extracapsular cataract extraction are well-known to be at the origin of late rise in IOP. The presence of ghost cells in anterior chamber aspirates has been proved to be the cause of such glaucoma [4]. Spontaneous vitreous hemorrhage due to primary vitreoretinal disease can be further complicated by ghost cell glaucoma if an incomplete vitrectomy is attempted and the anterior hyaloid is disrupted. The surgical trauma caused to the anterior hyaloid opens the pathway for some of the denatured cells to reach the anterior segment. The glaucoma presents days to weeks after the procedure and lasts for weeks to months unless a new vitrectomy is done [5].

■ Signs and Symptoms

Typically, the patient presents 2 or more weeks after trauma, complaining of poor vision and pain in the presence of an uninflamed or mildly inflamed eye. On examination, visual acuity usually is severely compromised, and the IOP is invariably high. Perilimbal conjunctival injection is evident, and the cornea may show mild to severe stromal edema. No keratic precipitates are seen unless a concomitant uveitis is present. The anterior chamber is deep, and the aqueous is filled with a multitude of small tan-colored cells. When they precipitate inferiorly, these cells form a typical tan, white, or khaki layer, which can be confused with hypopion. If fresh blood cells coexist, a double-layered precipitate of light khaki on top of red is present, which has been called the *candy-stripe sign* and which is pathognomonic for ghost cell glaucoma [6]. On gonioscopic examination, the angle appears wide open, with a discolored trabecular meshwork due

to the presence of a fine khaki-colored layer. Finally, vitreous examination will disclose the khaki hue that is typical of degenerated hemorrhage.

When unclear, the diagnosis can always be confirmed by phase-contrast microscopical examination of an unstained anterior chamber aspiration specimen [3]. Large numbers of 4- to 7-μm spherical hollow cells with Heinz bodies at their periphery are seen. Some specimens contain occasional macrophages, but polymorphonuclear leukocytes and lymphocytes are not present. A modified cytological preparation has been described that permits the identification of ghost cells with routine hematoxylin-eosin stain under light microscopy [7].

Ghost cell glaucoma can be transient or long-lasting, depending on the quantity of ghost cells present. If small numbers of ghost cells are present, IOP will eventually return to its normal level when the ghost cell supply from the vitreous is exhausted. No permanent damage to the trabecular meshwork has been described thus far [8].

■ Differential Diagnosis

High IOP and vitreous hemorrhage may coexist in neovascular, hemolytic, and various other forms of secondary glaucoma. Neovascular glaucoma, frequently associated with vitreous hemorrhage, shows typical rubeosis at the pupillary margin as well as on the angle structures. It usually is complicated by synechial angle closure, and no khaki cells are present in the aqueous.

Hemosiderotic glaucoma is a very rare entity presenting years after the initial hemorrhage [1]. It has been described in cases of recurrent vitreous hemorrhages as well as in cases of retained intraocular iron foreign bodies. Trabecular meshwork denaturation secondary to the hemosiderin is the apparent cause of the obstruction, and no ghost cells are found. Hemolytic glaucoma, similar to ghost cell glaucoma, has the same clinical presentation and treatment. Uveitic glaucoma may be differentiated by the presence of severe conjunctival inflammation, keratic precipitates, and white cells in the anterior chamber [8].

■ Management

On designing a treatment course for ghost cell glaucoma, one should consider the importance of the intraocular hemorrhage. This will lead to the appropriate decision about whether to use a vitrectomy, an anterior chamber washout, or standard medical therapy.

For the emergency situation, where a very high IOP and a painful eye are to be relieved, systemic carbonic anhydrase inhibitors and topical apraclonidine have shown their efficacy. The addition of beta blockers is

useful and effective in long-term medical treatment. Topical steroids are not necessary as this is not an uveitic process, and their use often can cause increased IOP in steroid responders. Frequently, maximal tolerated medical therapy is not enough to lower the pressure, and repeated irrigation of the anterior chamber is necessary to decrease the number of ghost cells. This procedure can be done under local anesthesia. The anterior chamber is entered through a paracentesis and the angle profusely irrigated with 10 to 20 ml of balanced saline solution, in an attempt to clear obstructing matter from the angle [6].

Finally, if the vitreous hemorrhage is large, the best procedure would be a complete vitrectomy. Special attention must be given to the removal of all ghost cells, including those at the vitreous base which, if not removed, will be further released by the vitrectomy procedure, actually producing worsening of the glaucoma [9].

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