correlative diabetic retinopathy, central retinal vein occlusion, and retinal detachment. Although data in the literature regarding the presence of VEGF in uveal melanoma are conflicting, our report shows the presence of VEGF in an iris melanoma.

Kvanta and colleagues demonstrated the presence of VEGF protein in retinoblastoma but not in posterior uveal melanomas. Similarly, in a study of VEGF expression in central retinal vein occlusion, Pe’er and coworkers used eyes with uveal melanoma as control specimens after finding that VEGF messenger RNA was undetectable or barely detectable in all 5 cases.

In contrast, Ijland and colleagues showed that human uveal melanoma cell lines expressed both VEGF and angiopoietin-2, a factor that appears to inhibit early maturation of newly formed vessels, suggesting that these tumors undergo a high degree of vascular remodeling. Two additional studies found 27% (10 of 37 eyes) and 22% (11 of 49 eyes) of uveal melanomas to be positive for VEGF protein on immunohistochemical staining. In a study by Sheidow and coworkers, 94% of 47 choroidal melanomas had VEGF-protein immunoreactivity. In a number of eyes with choroidal melanoma, evidence of breakdown of the blood-ocular barrier, including sites remote from the tumor such as the iris or ciliary body, suggests the presence of a soluble mediator of vascular permeability.

In the studies described earlier, investigators found high levels of VEGF protein centrally within the uveal melanoma and in the immediate perivascular distribution as well as in the adjacent retina and choroid. Likewise, VEGF receptor levels are elevated in the endothelial cells of the tumor vasculature and in uninvolved retina, choroid, and iris vasculature. The combination of up-regulation of VEGF receptors and elevated VEGF levels locally could explain the neovascularization responses seen in some eyes with intraocular melanomas.

Our patient had a vascularized iris mass with an associated hyphema. Histopathologic examination confirmed the diagnosis of iris melanoma and demonstrated that VEGF was indeed present. These findings are consistent with some recent studies that have found an association between uveal melanomas and VEGF expression. Future intraocular tumor therapy research targeting VEGF and its activity might also warrant an investigation of the applicability of this approach in the treatment of iris melanomas.

Figure 3. High magnification view of positive vascular endothelial growth factor immunostain (original magnification ×100).

Localized, Central Optic Snowflake Degeneration of a Polymethyl Methacrylate Intraocular Lens: Clinical Report With Pathological Correlation

Snowflake degeneration is a slowly progressive opacification of polymethyl methacrylate (PMMA) intraocular lenses (IOLs), occurring sometimes 10 years or more after implantation. It has been hypothesized that this degeneration is a result of long-term UV exposure. The dry snowflake lesions, which represent a breakdown in the PMMA material, should be differentiated from...
glistenings, which are fluid-filled intraoptical vacuoles.\(^3,4\) We report a case where the snowflake lesions were limited to the central 2 mm of the optic on examination of the explanted PMMA lens in the dry state. However, clinically and on hydration of the explanted lens, the area of central optic opacification extended to a 4-mm diameter. An unusual collection of water may have occurred because of the numerous cracks and fissures present within this area.

**Report of a Case.** A 90-year-old man with a history of diabetes mellitus since 2001, as well as hypertension and Parkinson disease, underwent an uneventful bilateral extracapsular cataract extraction with a 3-piece posterior chamber PMMA IOL (Precision-Cosmet Kratz Johnson Co, Minnetonka, Minn) implantation in the left eye on February 17, 1987, and then in the right eye (IOLAB Corp, San Dimas, Calif) on July 16, 1991. On March 29, 1992, best-corrected visual acuity was 20/30 OD and 20/50 OS. Initial changes due to macular degeneration were observed bilaterally, especially in the left eye.

The patient was referred to 1 of us (L.F.) in December 2003 for a second opinion on the status of the IOL in the right eye. Best-corrected vi-

**Figure 1.** Photograph obtained from the video of the patient’s surgical explantation procedure. Note the central opacification of the lens (approximately 4 mm in diameter).

**Figure 2.** Explanted lens in the dry state. A. Note the small central area of opacification (approximately 2 mm). B-D. Dark-brown and multicolored particles are observed within the substance of the intraocular lens at different levels (original magnification ×40, ×100, and ×200, respectively).
visual acuity was 20/40 OD and counting fingers OS because of an optic nerve atrophy, possibly from an old anterior ischemic optic neuropathy. Examination of the lens in the right eye through the somewhat small pupil (although no actual measurement was performed) showed structures similar to glistenings in the central part of the optic. After instillation of 1% tropicamide, the pupils dilated to an estimated 5 mm. Slit-lamp examination revealed lesions with a crystal-like appearance within the central portion of the IOL optic in the right eye (approximately 4 mm), with a clear optic periphery (Figure 1). The IOL optic in the left eye was clear.

In May 2005, the patient returned with complaints of a progressive decrease in vision in the right eye. Best-corrected visual acuity was 20/70 OD. The “crystallization” of the central optic of the lens in the right eye was denser but within the same area. This lens was explanted and exchanged on May 31, 2005. On June 30, 2005, visual acuity was 20/30 –2 OD.

Gross examination in the dry state revealed the presence of a slight whitish discoloration at the level of the central portion of the optic (approximately 2 mm) (Figure 2A). Microscopically, the specimen showed the presence of multiple structures consistent with snowflake lesions. They had the appearance of “particles” or “crystals” within the central area of the lens optic, causing the whitish discoloration. Some of these structures appeared mostly dark brown under small magnification, and some were multicolored under higher magnification (Figure 2B-D). They did not exhibit birefringence under polarizing light.

Because the central area of whitish discoloration in the dry state appeared smaller than the area observed by the surgeon (Figure 1), the explant was immersed in balanced salt solution (Alcon Laboratories, Fort Worth, Tex). This was then placed under a temperature of 37°C for 24 hours. Gross examination showed an increase in the central area of opacification, to approximately 4 mm. The whitish discoloration also appeared denser in the hydrated state (Figure 3A). Under light microscopy, the lesions with a particular appearance seen in the dry state could not be observed; larger, irregular structures with a vacuole-like aspect were present, as well as linear cracks within the optic, seen as brown lines (Figure 3B-D).

Comment. The structures observed within the central part of the lens optic in the dry state appear similar to those observed in snowflake degeneration. Three-piece PMMA lenses implanted between the early 1980s and the mid 1990s (such as those explanted because of this condition and analyzed in our laboratory) were generally manufactured by injection molding. The explants had lesions clustered in the central zone and mid-peripheral portion of the optic. This led to the hypothesis that the central area of whitish discoloration in the dry state was due to the injection molding process, which could result in microcracks or other defects within the lens.

Figure 3. Explanted lens in the hydrated state. A, The central area of opacification is denser and extends to approximately 4 mm in diameter. B-D, Multiple linear fissures (arrows) and large vacuole-like structures can be observed in the substance of the lens (original magnification ×40, ×100, and ×200, respectively).
optic was exposed to UV light over an extended period, whereas the peripheral optic may be protected by the iris. In the present case, the lesions characteristic of snowflake degeneration were restricted to the central 2 mm of the lens optic in the dry state. This is the smallest area we have ever observed and may be related to the fact that the patient's pupils were relatively constricted as noted on the examination before and after dilation. This fact presumably supports the hypothesis that snowflake changes are facilitated by UV light.

For the first time, to our knowledge, a lens explanted because of snowflake degeneration was analyzed in the dry and hydrated states. The snowflake lesions per se are dry lesions and should be differentiated from glistenings. Glistenings are fluid-filled vacuoles and were largely described in association with hydrophobic acrylic lenses but can also be associated with other materials, including PMMA.3,4 On hydration of the explanted lens described herein, we did not observe the formation of small vacuoles throughout the lens optic, as seen with glistenings. An unusual amount of water was collected within the central 4 mm of the lens optic, where multiple linear cracks were present. These cracks were not evident under light microscopy in the dry state. They may represent the initial injury before the typical snowflake lesions are seen or they may be secondary to the initial presence of the more central snowflake lesions. In any case, the clinical significance of snowflake degeneration may depend on the amount of water collected within the area of cracks.

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Octreotide as a Treatment for Uveitic Cystoid Macular Edema

Cystoid macular edema (CME) is the most frequent cause of irreversible blindness and visual impairment in patients with uveitis.1 There is no consensus on the most effective treatment for uveitis-associated CME; many agents are used with variable responses. Because there is a constant release of inflammatory mediators that can disturb retinal pigment epithelial pump function in active uveitis, the first and most important step is to control the uveitis. In addition, CME can be treated with conventional options, including corticosteroid agents administered topically, by pericocular or intraocular injection, or orally; nonsteroidal anti-inflammatory drugs administered orally or topically in aphakic eyes; and carbonic anhydrase inhibitors. Additional treatment methods such as hyperbaric oxygen, pars plana vitrectomy, and laser grid photocoagulation are more controversial treatments. Despite aggressive treatment, CME frequently progresses.

Octreotide is a somatostatin analogue. It is an even more potent inhibitor of the release of growth hormone and other hormones than somatostatin is, and it is used for the treatment of acromegaly, carcinoid tumors, and vasoactive intestinal polypeptide-secreting tumors. Studies have shown that somatostatin is also synthesized in the retina, and, furthermore, its receptors sst1, sst2, and sst5 are present in retinal pigment epithelial cells and other parts of the human retina.2,3 Based on published evidence demonstrating the efficacy of octreotide in treating macular edema from other causes, we explored its use in 5 patients with uveitic CME refractory to conventional treatment.

Methods. This investigation was approved by the Human Research Committee of Massachusetts Eye and Ear Infirmary, Boston. After discussing the risks and benefits, informed consent was obtained from the patients.

Five patients (9 eyes) received treatment. All patients had long-standing (≥6 mo) CME secondary to uveitis, which persisted after clinically evident control of the inflammation with immunomodulatory therapy. Furthermore, the macular edema did not respond to additional treatment with corticosteroid agents (systemic, peribulbar, or intraocular), oral nonsteroidal anti-inflammatory agents, and acetazolamide.

All patients were given octreotide acetate (Sandostatin; Novartis Pharmaceuticals Corp, East Hanover, NJ), 100 µg injected subcutaneously 3 times daily. In 3 patients, treatment was switched to a long-acting depot formulation of octreotide acetate (Sandostatin LAR Depot; Novartis Pharmaceuticals Corp), administered as a monthly 20-mg intragluteal injection.

The course of macular edema was monitored with clinical examination, fluorescein angiography, and optical coherence tomography (OCT-1 or OCT-3; Carl Zeiss Meditec Inc, Dublin, Calif). Additional data on age, sex, previous treatments, Snellen visual acuity, duration of octreotide treatment, and adverse effects were recorded.

Results. All 5 patients were women aged 24 to 61 years. One had unilateral CME; 4 had bilateral CME. The uveitis was idiopathic in 2 patients, and was associated with sarcoidosis in another 2 patients and with the HLA-B27 gene in 1 patient. In all patients, immunomodulatory therapy had resulted in clinical remission of the inflammation. The agents used were methotrexate, azathioprine, cyclophosphamide, or mycophenolate mofetil as monotherapy or combined with intravenous immunoglobulin. Conventional treatment for CME failed either because the edema was resistant or recurrent or because of adverse effects (patients 1 and 3 had acetazolamide intolerance). Cor-