Proteomic Analysis of Macular Fluid Associated With Advanced Glaucomatous Excavation

The association of maculopathy with advanced glaucomatous cupping is known, but controversy remains over the origin of fluid.1-3 Reports using enhanced depth imaging have demonstrated a track communicating from cavities posterior to the lamina cribrosa to the peripapillary retina, and these cavities presumably consist of cerebrospinal fluid (CSF).2,3

The protein composition of a fluid can identify its origin. To our knowledge, there have been no previous reports on proteomic analysis of fluid from maculopathy associated with optic nerve excavation. We present a case of advanced glaucomatous cupping in which macular schisis fluid was analyzed for protein content.

Report of a Case | A patient with low-tension glaucoma and advanced cupping presented with progressive loss of vision in her right eye (visual acuity decreased from 20/30 to counting fingers). Fundus examination revealed macular schisis (Figure 1). Enhanced depth imaging optical coherence tomography did not demonstrate an obvious track or visible defect in the lamina cribrosa, and fluorescein angiography did not demonstrate retinal or choroidal leakage (Figure 2).

Undiluted vitreous was collected at the beginning of vitrectomy surgery before the infusion cannula was opened. A complete vitrectomy was performed, followed by air-fluid exchange. The surface of the macula was then repeatedly dried under air until pooling ceased. A retinotomy superotemporal to the fovea was made with diathermy, a clean 25-gauge soft tip was inserted into the cavity, and viscous fluid was aspirated with visible flattening of the cavity. Endolaser was applied in a limited pattern around the optic nerve, and the air was exchanged with 20% sulfur hexafluoride gas. Approximately 30 μL of undiluted schisis fluid was extracted and immediately stored at −80°C for later analysis. Samples were digested with trypsin prior to proteomic analysis.

Results | Two-dimensional liquid chromatography tandem mass spectrometry4 identified approximately 240 unique proteins in the collected vitreous sample. Peptides derived from opti- cin, beta-crystallin B2, and alpha-crystallin B were detected and are unique to vitreous (not seen in CSF).5 Because of the small volume of schisis fluid, a more targeted analysis was performed and identified approximately 80 proteins. Opticin, beta-crystallin B2, and a large number of other vit-
reous proteins were detected in the schisis fluid. No CSF-unique proteins were found.

Discussion | Several theories regarding the mechanism behind maculopathy due to optic nerve abnormalities have been proposed. Accumulation of macular fluid due to transudate from poorly developed peripapillary choroidal vasculature, liquefied vitreous, and CSF have all been reported as putative sources of macular fluid. Several reports using enhanced depth imaging have demonstrated a track extending from the peripapillary retina to cystic cavities posterior to the lamina cribrosa, providing indirect support for CSF, but no such connection has been confirmed histologically or after subarachnoid injection of India ink in a dog model.

Proteomic analysis of macular fluid collected in this case confirms the presence of vitreous, which to our knowledge is the first direct clinical evidence that liquefied vitreous can enter the intraretinal or subretinal space (presumably through an optic nerve defect). While vitreous could have contaminated our aspirate, meticulous drying of the retina and direct aspiration of the cavity under air were done to reduce this possibility. While there is no consensus on the treatment of chronic maculopathy, reported methods or combinations thereof include the following: vitrectomy, peripapillary laser, application of fibrin sealant, macular scleral buckling, removal of the internal limiting membrane, internal drainage, and long-acting tamponade. Verification of the source of fluid might influence therapeutic approaches but should be weighed against additional risks.

In conclusion, this detailed proteomic analysis of macular schisis fluid associated with advanced glaucomatous cupping suggests that vitreous was the source of fluid. These findings may have important implications for the management of similar future cases.

Shriji Patel, MD
Jeanie Ling, MD
Stephen J. Kim, MD
Kevin L. Schey, PhD
Kristie Rose, PhD
Rachel W. Kuchtey, MD, PhD

Author Affiliations: Vanderbilt Eye Institute, Vanderbilt University Medical Center, Nashville, Tennessee (Patel, Ling, Kim, Schey, Rose, Kuchtey);
Periorbital Necrotizing Fasciitis Following Dexamethasone Intravitreal Implant Injection

Periorbital necrotizing fasciitis (PNF) is a life-threatening bacterial infection involving superficial and deep fascia with secondary necrosis of overlying skin. There are multiple reports of different inciting events such as local blunt trauma or penetrating injuries. 1 Iatrogenic PNF has been reported after blepharoplasties, dacryocystorhinostomies, and retrobulbar injections. 2,3 We report a case of PNF after a dexamethasone intravitreal implant injection for diabetic macular edema.

Report of a Case | A man in his 50s presented to the emergency department with substantial ocular pain, periorbital edema, headache, and vomiting 72 hours after undergoing a dexamethasone intravitreal implant injection in his right eye (Figure 1). Significant medical history included bilateral diabetic macular edema, type I diabetes mellitus, and purpuric nephritis for which the patient was receiving mycophenolate mofetil. He had also had pharyngitis for 10 days. Best-corrected visual acuity was 20/200 OD and 20/50 OS. The right globe was tense and chemosis and purulent discharge were observed, but there was no anterior chamber reaction or vitritis. B-scan ultrasonography localized the dexamethasone intravitreal implant in the posterior vitreous and magnetic resonance imaging confirmed orbital cellulitis. Blood cultures and a pharyngeal swab grew Streptococcus pyogenes. The patient’s temperature was 39°C and his right superior eyelid had signs of skin necrosis and anesthesia. A preliminary diagnosis of PNF was made. The patient was treated with intravenous amoxicillin (2 g twice daily) and clindamycin phosphate (600 mg 4 times daily) and admitted to the critical care department owing to renal and cardiac failure and rapid fascitis extension. Surgical debridement of the periorbital region was performed, allowing confirmation of the initial PNF diagnosis after observation of subcutaneous necrosis and turbid fluid spread to the fascial planes (Figure 2). Intraoperative specimens sent for culture confirmed the presence of S pyogenes. Systemic signs and symptoms gradually improved. Three months postoperatively, the skin wound had completely healed; however, vision in the right eye was lost.

Discussion | Dexamethasone intravitreal implant injections are an effective treatment for the management of macular edema secondary to retinal vein occlusion, noninfectious uveitis, and diabetic retinopathy. Infectious complications are rare, but 2 cases of endophthalmitis have been reported. 4,5 To our knowledge, this is the first case of PNF after a dexamethasone intravitreal implant injection. As reviewed by Amrith et al, 6 the most

Figure 1. Patient at Presentation

Painful eyelid and periorbital inflammatory edema was observed.

Department of Biochemistry, Vanderbilt University, Nashville, Tennessee (Schey, Rose); Department of Molecular Physiology and Biophysics, Vanderbilt University, Nashville, Tennessee (Kuchtey).

Corresponding Author: Stephen J. Kim, MD, Vanderbilt Eye Institute, Vanderbilt University Medical Center, 2311 Pierce Ave, Nashville, TN 37232 (skim30@gmail.com).


Author Contributions: Drs Patel and Kim had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Patel, Kim, Schey, Rose, Kuchtey.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Patel, Ling, Kim, Schey, Kuchtey.

Critical revision of the manuscript for important intellectual content: Patel, Kim, Schey, Rose, Kuchtey.

Obtained funding: Kim.

Administrative, technical, or material support: Kim, Schey, Rose.

Study supervision: Kim, Kuchtey.

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

Funding/Support: This work was supported by an unrestricted grant from Research to Prevent Blindness to the Department of Ophthalmology and Visual Sciences, Vanderbilt University School of Medicine. Dr Kuchtey was supported by grant 5R01EY020894 from the National Eye Institute.

Role of the Funder/Sponsor: The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Previous Presentation: This paper was presented in part at the 38th Annual Meeting of the Macula Society; February 25, 2015; Scottsdale, Arizona.


OBSERVATION

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