Alteration of Vitreal Retinoschisin Level in Human Primary Retinal Detachment

Retinoschisin (RS1), the product of RS1 located on the X chromosome, is expressed mainly in retina. The 24-kDa RS1 encodes a highly conserved sequence motif termed the discoidin domain, which is a critical determinant of the structural and functional integrity of the retina. Mutations in RS1 that lead to either complete loss of RS1 expression or its accumulation as a nonfunctional misfolded form are the underlying causes of X-linked retinoschisis (XLRS). This disorder, seen exclusively in young males, is characterized by splitting, or schisis, affecting all retinal layers. The precise molecular mechanism by which RS1 functions is still undefined. During development, there is a wave of RS1 expression beginning at the retinal surface and spreading progressively in more distal retinal layers as they differentiate. In adult mice, RS1 is expressed in all retinal neurons except horizontal cells, with a predominance in photoreceptor inner segments and bipolar cells.

In patients with XLRS, the retina is more prone to retinal detachment (RD) compared with the general population (10% vs 0.01%, respectively). These detachments are difficult to surgically reattach, making the postoperative outcome unfavorable. To assess the potential role of RS1 in retinal response to detachment, we analyzed RS1 levels in vitreous samples derived from patients’ eyes with or without RD.

Methods | The research procedures were in accordance with institutional guidelines and the Declaration of Helsinki. Approval for the study was obtained from the Committee of Ethics, University Hospital, Lund, Sweden.

Surgery | Fourteen patients (mean age, 59 years) with primary RD of less than 7 days’ duration and with no previous retinal surgery or intravitreal treatment were included in this study. After explanation of the planned operation and answering the questions, written informed consent was obtained directly from each participant. As healthy control participants, 12 patients (mean age, 68 years) with epiretinal membrane and no previous retinal surgery were included. All patients underwent a standard 3-port pars plana vitrectomy including a biopsy of 1.0 to 1.5 mL of undiluted central vitreous obtained under air infusion via suction through the vitrectomy probe (Innovit and Constellation; Alcon Laboratories). The sample was thereafter kept at −80°C for later examination.

Immunoblot Analysis | The protein concentrations of the vitreous samples were determined by bicinchoninic acid assay (Thermo Scientific). Equal amounts of vitreous protein from different samples (10 μg each) were resolved on a gradient 4% to 12% nonreducing sodium dodecyl sulfate-polyacrylamide gel electrophoresis and electrotransferred to a polyvinylidene difluoride membrane (Bio-Rad Laboratories, Inc). After blocking the membrane in 5% nonfat milk in phosphate-buffered saline/Tween (PBST) solution (3.2mM disodium hydrogen phosphate, 0.5mM monopotassium phosphate, 1.3mM potassium chloride, 135mM sodium chloride, 0.1% Tween 20, pH 7.4) for 1 hour at room temperature, the blot was incubated overnight at 4°C with anti-RS1 antibody produced in rabbit (titer, 1:1000). The membrane was then subjected to three 5-minute rinses in a PBST solution. The membrane was then incubated with a horseradish peroxidase–conjugated goat antirabbit antibody (titer, 1:10 000; GE Healthcare Life Sciences) for 1 hour at room temperature. After three 5-minute rinses in a PBST solution, the blot was developed with Super Signal West Dura Chemiluminescent Substrate (Thermo Scientific). The chemiluminescent images were acquired by imaging the membrane on a Kodak image station (Image Station 2000R; Eastman Kodak Co), and the intensity of each approximately 200-kDa octameric RS1 band was analyzed using the spot density analysis software provided. The relative protein levels were calculated from the band intensity of each protein normalized to the intensity of recombinant histidine-tagged RS1 (purified from baculovirus/insect cell expression system). Western blotting and quantification analysis were performed in at least 3 biological replications.

Results | Vitreous concentrations, measured as intensity units, of RS1 were significantly lower in patients with newly detached retinas compared with control vitreous samples from nondetached retinas (epiretinal membrane). The mean (SE) RS1 vitreous concentration was 49 609 (7192) intensity units in detached retinas and 80 540 (12 379) intensity units in nondetached retinas (Mann-Whitney U test, P = .04) (Figure).

Discussion | Like most previous studies, we have used data from samples of vitreous collected from patients undergoing pars plana vitrectomy for epiretinal membranes as a reference for considering the changes in vitreous. To our knowledge, this is the first study showing decreased levels of RS1 in vitreous of patients with primary RD in comparison with control samples collected from patients undergoing peeling of epiretinal membranes. The decreased levels of RS1 in patients with RD could possibly be explained by depletion of RS1 in the detachment phase.

The potential role of RS1 in patients with RD is still unknown. In a mouse model of RD, Farjo et al reported upregulation of RS1 messenger RNA within 2 hours of RD, which is consistent with the potential role of RS1 in retinal cell adhesions and extracellular remodeling. Furthermore, gene therapy in a mouse model of XLRS has also demonstrated a decrease in schisis cavities and improved retinal signaling evaluated by...
The nondetached retina uses the epiretinal membrane for analysis. RS1 indicates retinoschisin; center horizontal lines, mean; and error bars, standard error.

electroretinography. If RS1 has a key role in retinal remodeling after RD, the lack of RS1 could be one reason why treatment of RD in patients with XLRS would be particularly challenging. Further studies are needed to clarify the role of RS1 in the remodeling process following RD.

Successful Management of Secondary Iris Cysts With Viscoelastic-Assisted Endophotocoagulation

The new clinical finding of an iris cyst can cause diagnostic and management uncertainty. Iris cysts are uncommon and can be primary or secondary as well as benign or malignant. Management options for benign secondary iris cysts include observation, drainage, surgical excision, cryoaablation, photocoagulation, or even intracystic irrigation of a cytotoxic agent such as ethanol. We report a case series of 4 secondary iris cysts in 4 patients, all successfully managed with endophotocoagulation assisted with viscoelastic.

Report of Cases | The patients included 2 males and 2 females, with a mean age of 36.8 years (range, 4-83 years). Three cases had a definitive history of preceding trauma, and the other was uncertain. The cyst was located superiorly in 3 cases and inferonasally in the fourth. The largest cyst diameter ranged between 4 and 5 mm in all cases. The main indication for surgery was visual symptoms (Figure and Table).

All patients underwent initial surgical aspiration of the cyst for cytological analysis. Cyst drainage was accomplished with a 26-gauge needle on a syringe via a small paracentesis through clear cornea overlying the cyst midperiphery. The anterior chamber was maintained with balanced salt solution. The aspirated fluid was sent for cytological analysis, and no evidence of a malignant neoplasm was identified in any case.

One month later, the cyst was redrained via the original paracentesis. A second peripheral corneal paracentesis, diagonally opposite the cyst, was fashioned to allow viscodissec-