Proliferative Vitreoretinopathy and Genetic Profile

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Proliferative vitreoretinopathy (PVR) is the principal cause of failure in retinal detachment (RD) surgery and is characterized by the proliferation of different cell types leading to the formation of cellular membranes on both sides of the retina. These membranes have the capability of contracture resulting in retinal redetachment. Despite marked improvement in vitreoretinal surgical techniques and instruments over the recent years, a significant proportion of affected eyes suffer from surgical failure due to development or recurrence of PVR. Many researchers are exploring the pathogenesis of this condition to discover modalities for its prevention and treatment.

Known risk factors for PVR include vitreous hemorrhage, repeat RD surgery, preoperative PVR, large breaks, choroidal detachment, heavy retinopexy, long duration of retinal detachment, RDs involving more than two quadrants, presence of uveitis at initial examination, and inability to locate and treat retinal breaks. Moreover, a significant role has been proposed for different cytokines in the pathogenesis of PVR. The levels of a wide variety of cytokines including interleukin (IL)-1, IL-2, IL-3, IL-6, vascular endothelial growth factor, interferon-c, matrix metalloproteinases 2 and 9 and intercellular adhesion molecule-1 have been revealed to be higher in the vitreous, membranes or subretinal fluid of patients with PVR.

Recently, the contribution of genetic background to PVR has been described. Sanabria Ruiz-Colmenares et al reported an association between transforming growth factor (TGF)-beta-1 genetic profile and PVR. They identified a higher frequency of TGF-beta-1 codon 10 allele T in PVR patients as compared to patients with simple retinal detachments. Researchers of the Retina 4 Project, a European multicenter study, evaluated DNA from 138 patients with PVR and 312 patients with non-PVR RD and analyzed 224 single nucleotide polymorphisms (SNPs) from 30 genes involved in inflammatory cascades. Replication was carried out in a larger population undergoing RD surgery among 546 new patients. They reported genetic markers for PVR development in tumor necrosis factor (TNF), TNFR2, SMAD7 and PI3KCG genes, and observed replication in the SMAD7 and TNF locus. They described the best genetic models for predicting the risk of PVR and reported 3 algorithms of 42, 10 and 2 SNPs with accuracy of 78.4%, 70.3%, and 69.3%, respectively. The best individual marker was rs2229094 within the TNF locus. Retina 4 Project investigators also studied the distribution of a p53 gene polymorphism among subjects undergoing primary RD surgery in relation to the development of PVR and found that the Pro variant of p53 codon 72 polymorphism is associated with a higher risk of PVR.

Huang et al showed Robo1 expression in proliferative membranes. The Robo family of proteins are related to transmembrane receptors and play a major role in neurogenesis. They employed small interfering (si) RNA technology to knockdown Robo1 expression in a rabbit model and found that silencing Robo1 expression not only reduced human retinal pigment epithelium cell proliferation in vitro but also effectively suppressed the development of PVR.

These findings strongly suggest the contribution of genetic background to PVR. The genetic associations of PVR could provide new therapeutic targets for prophylaxis against PVR.

Conflicts of Interest
None.
Suggested Readings

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