

Study suggests new treatment avenue to prevent serous retinal detachment

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Wet age-related macular degeneration (AMD) is the leading cause of severe vision loss in older individuals. AMD and other serious chronic eye problems that affect younger individuals result when fluid accumulates abnormally under or within the retina. A new study published in *The American Journal of Pathology* shows for the first time that the release of substances from mast cells may be a causal factor in this type of eye pathology, and inhibitors of this release may offer new ways to treat serous retinal detachment.

Mast cells are [white blood cells](#) that circulate in the blood in an immature form and can be found in most body tissues, especially those in close contact with the external environment. Mast cells play key roles in allergic diseases, inflammatory conditions, and autoimmunity, and are also recognized as "sentinels of the immune system" by serving as first responders to invading pathogens. When [mast cells](#) release their contents, the process is known as degranulation.

The current study suggests that repeated exposure to stimuli, such as allergens or infectious agents, may lead to recurring mast cell degranulation and long-term pathological eye changes. "The fact that mast cells progressively reconstitute their granules suggests that if the stimulus persists, successive degranulation could lead to the breakdown of blood-ocular barriers and accumulation of sub-retinal fluid," explained lead investigators Yvonne de Kozak, MD, PhD, and Francine Behar-Cohen, MD, PhD, members of INSERM UMRS1138, Physiopathology of Ocular Diseases: From Physiopathology to Clinical

Developments; University of Paris Descartes†, Sorbonne Paris Cité, Sorbonne Universities, Cordeliers Research Center, Paris, France, and the Department of Ophthalmology of Lausanne University, Jules Gonin Ophthalmic Hospital, Lausanne, Switzerland.

To investigate the role of mast cells in ocular pathology, the researchers injected 120 µg of compound 48/80, which is known to activate and induce the degranulation of mast cells, into the conjunctiva—tissue lining the inside of the eyelids and covering the white part of the eye (sclera)—of the right eye of rats. The treated eye was compared to both the non-injected left eye of the same animal as well as to those of control rats that received injections of saline into the right eye conjunctiva.

Mast cell degranulation in the choroid (the vascular layer of the eye lying between the retina and the sclera) became apparent within 15 minutes of injection and significantly increased over the next three hours. Histological analysis showed reduced density of granules within the [mast cells](#) and an extensive and massive degranulation in the choroid. Mast cell degranulation was accompanied by accumulation of polymorphonuclear lymphocytes and macrophages in ocular tissues.

Many signs of ocular inflammation were evident, including redness, punctate hemorrhages in the iris, synechiae (adherence of the iris to the lens), pus, and other changes, lasting for almost a day. Sixty-eight percent of 25 rats developed a cataract lasting several hours. A localized thickening of the choroid was noted within the first one to three hours, probably corresponding to the compound 48/80 injection site, with the area of thickness expanding completely over the choroidal surface between six and 24 hours. No clinical abnormalities were seen in the untreated left eye.

In the posterior portion of the right eye, investigators found retinal detachments accompanied by subretinal fluid accumulation and dilation

of choroid blood vessels. At 24 hours, retinal detachments and large areas of retinal destruction were observed. The researchers used optical coherence tomography to show large and multiple retinal serous detachments with pockets of subretinal fluid within three to 24 hours of 48/80 injection. Serous retinal detachments are characteristic of some forms of acute posterior uveitis, (eg, Vogt-Koyanagi-Harada disease). However, serous retinal detachments are also present in other ocular disorders, such as central serous chorioretinopathy and wet AMD.

Unilateral administration of disodium cromoglycate, a substance that inhibits release of mast cell mediators, prior to compound 48/80 administration resulted in fewer instances of limited serous retinal detachment. The rate of serous retinal detachment was 80% (8/10) in rats that received saline plus 48/80 injection versus 16.7% (1/6) in those that received disodium cromoglycate plus 48/80.

The investigators also measured levels of cytokines in ocular fluid. Over the first 24 hours, the first cytokine to be elevated in 48/80-treated eyes was tumor necrosis factor- α , followed by CXCL-1, interleukin (IL)-6, IL-5, IL-1 β , IL-18, and CCL-2 whereas vascular endothelial growth factor decreased at 24 hours.

"By inhibiting the release of inflammatory mediators, pharmacological inhibition of mast cell degranulation could have important therapeutic potential for retinal diseases associated with choroidal enlargement and/or serous retinal detachments," noted Dr. de Kozak.

More information: "Choroidal mast cells in retinal pathology: a potential target for intervention," by Elodie Bousquet, Min Zhao, Brigitte Thillaye-Goldenberg, Viera Lorena, Beatriz Castaneda, Marie-Christine Naud, Ciara Bergin, Bernadette Besson-Lescure, Francine Behar-Cohen, Yvonne de Kozak. *American Journal of Pathology*, Volume 185, Issue 8 (August 2015). [DOI: 10.1016/j.ajpath.2015.04.002](https://doi.org/10.1016/j.ajpath.2015.04.002)

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