Targeted X-ray treatment of mice prevents glaucoma

March 19 2012

Jackson Laboratory researchers have demonstrated that a single, targeted x-ray treatment of an individual eye in young, glaucoma-prone mice provided that eye with apparently life-long and typically complete protection from glaucoma.

In research published March 19 in the Journal of Clinical Investigation, Gareth Howell, Ph.D., Simon John, Ph.D., (professor and Howard Hughes Medical Investigator) and colleagues also used sophisticated genomics methods to uncover some of the very first pathways to change during glaucoma in these mice. The first pathway they detected to change suggests a critical mechanism that could be responsible for the earliest damage that glaucoma inflicts on the optic nerve.

Glaucoma, a leading cause of blindness, affects more than 4 million Americans, at least half of who don't even know they have the disease. Current treatments target intraocular pressure elevation, the best-known risk factor for glaucoma. However, blindness-inducing damage to retinal ganglion cells and the optic nerve can occur in patients with normal intraocular eye pressure. Earlier detection and better treatments could therefore have a powerful impact on preventing blindness due to glaucoma.

About 10 years ago, the John lab made the surprising discovery that just a single dose of whole body irradiation along with bone marrow transfer conferred an unprecedented protection against glaucoma. 96% of treated eyes had no glaucoma a year later compared to only 20% of control eyes.

Although this result was unexpected, there is some evidence that radiation may protect from human glaucoma. Epidemiologists who followed Japanese survivors of the atomic bombings in World War II had noticed that exposure to radiation increased the incidence of thyroid and other cancers but seemed to provide protection against glaucoma.

The John labs' new demonstration that irradiation of just a single eye is protective, and at lower doses than they previously published, raises the possibility of using highly controlled localized radiation of just the eye to prevent human glaucoma.

Further research in other animal models to assess protection as well as safety and efficacy is necessary before attempting human treatments. But, as the authors conclude in their paper, "given both the robust and long-term efficacy of a single dose of X-ray radiation in preventing cellular entry into the optic nerve and retina, it will be important to further evaluate the use of X-rays for preventing glaucoma."

The study showed that in response to early tissue stresses, a class of immune cells known as monocytes, enter the optic nerve and retina in glaucoma. These monocytes express damaging molecules that appear critical for nerve damage in glaucoma. The entry of these cells is controlled in part by endothelial cells that line blood vessels. Radiation treatment appears to change how these endothelial cells respond to the early tissue stresses and affect the entry of the monocytes into the optic nerve and retina.

"While more work is needed to fully understand how the radiation confers long-term protection," Howell says, "radiation appears to hinder the adhesion and migration of monocytes into the areas of the eye prone to nerve damage." This finding strongly implicates the entry of cells into the eye as a key component of the nerve damage that leads to blindness. It also suggests vision may be maintained in eyes with high intraocular

pressure by treatments that block the entry of monocytes into eye.

More information: Radiation treatment inhibits monocyte entry into the optic nerve head and prevents neuronal damage in a mouse model of glaucoma: www.jci.org/articles/view/6113 … 82201f32dfe421d1d337

Provided by Jackson Laboratory