Reduced Cerebrospinal Fluid Inflow to the Optic Nerve in Glaucoma

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Purpose: To determine whether cerebrospinal fluid (CSF) entry into the optic nerve is altered in glaucoma.

Methods: Fluorescent 10-kDa dextran tracer was injected into the CSF of 2-month-old (n = 9) and 10-month-old DBA/2J glaucoma mice (n = 8) and age-matched controls (C57Bl/6; n = 8 each group) . Intraocular pressure (IOP) was measured in all mice before tracer injection into CSF. Tracer distribution was assessed using confocal microscopy of optic nerve cross-sections of mice killed 1 hour after injection. Paravascular tracer distribution in the optic nerve was studied in relation to isolectin-stained blood vessels. Tracer intensity and cross-sectional area in the laminar optic nerve were quantitatively assessed in all four groups and statistically compared. Aquaporin 4 (AQP4) and retinal ganglion cell axonal phosphorylated neurofilament (pNF) were evaluated using immunofluorescence and confocal microscopy.

Results: IOP was elevated in 10-month-old glaucoma mice compared with age-matched controls. One hour after tracer injection, controls showed abundant CSF tracer in the optic nerve subarachnoid space and within the nerve in paravascular spaces surrounding isolectin-labeled blood vessels. CSF tracer intensity and signal distribution in the optic nerve were significantly decreased in 10-month-old glaucoma mice compared with age-matched controls (P = 0.0008 and P = 0.0033, respectively) . AQP4 immunoreactivity was similar in 10-month-old DBA and age-matched control mice. Half of the 10-month-old DBA mice (n = 4/8) showed a decrease in pNF immunoreactivity compared to controls. Altered pNF staining was seen only in DBA mice lacking CSF tracer at the laminar optic nerve (n = 4/5) .

Conclusions: This study provides the first evidence that CSF entry into the optic nerve is impaired in glaucoma. This finding points to a novel CSF-related mechanism that may help to understand optic nerve damage in glaucoma.

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