

Juvenile-Onset Normal Tension Glaucoma from Chronic, Recurrent Low Cerebrospinal Fluid Pressure

Imran H. Yusuf¹, Gokularaj Ratnarajan¹, Richard S. Kerr², John F. Salmon¹

Imran H. Yusuf, MRes, MRCP (UK), FRCOphth; imranyusuf@doctors.org.uk

Gokularaj Ratnarajan, BSc, FRCOphth; g.ratnarajan@gmail.com

Richard S. Kerr, BSc, MB BS, MS, FRCS; richard.kerr@ouh.nhs.uk

John F. Salmon MD, FRCS, FRCOphth; john.salmon@ouh.nhs.uk

Corresponding author: John F Salmon MD, FRCS, FRCOphth; john.salmon@ouh.nhs.uk

Telephone: +441865 234736

(1) The Oxford Eye Hospital, West Wing, John Radcliffe Hospital, Headley Way, Headington, Oxford, OX3 9DU, United Kingdom.

(2) Department of Neurosurgery, West Wing, John Radcliffe Hospital, Headley Way, Headington, Oxford, OX3 9DU, United Kingdom.

None of the authors have any financial interest in any product, method or material or lack thereof mentioned in this article.

Journal of Glaucoma – Case Report

Manuscript word count: 592

Abstract: 227

Figures: 2

References: 6

Keywords

Glaucoma; normal tension glaucoma; low cerebrospinal fluid pressure; translaminar cribrosa pressure; intraocular pressure; CSF pressure; CSF shunt; ProGAV; optic disc hemorrhage

Abstract

Introduction: The evidence for low cerebrospinal fluid (CSF) pressure as a key parameter in the pathogenesis of glaucoma is increasing. Primate models have demonstrated the onset normal tension glaucoma (NTG) from experimentally induced chronic intrathecal hypotension; an approach not possible in human subjects.

Case Presentation: A 27-year old male presented with a central scotoma in his left eye. He had undergone 8 CSF shunt revision procedures over a 25-year period secondary to recurrent low CSF pressure following surgical excision of a pinealoblastoma, aged 2. A focal nerve-fibre layer defect was detected in the left eye associated with reduced retinal sensitivity on microperimetry. Three adjacent optic disc haemorrhages had been documented in the same position over an 18-month period. A diagnosis of left-sided NTG was made; the patient was started on Latanoprost 0.005%. A new generation CSF shunting device (ProGAV) - which neutralises CSF pressure fluctuations analogously to trabeculectomy surgery for intraocular pressure - was considered necessary in this patient to alleviate persistent headaches and reduce the risk of progressive glaucomatous visual loss.

Conclusion: This exceptional case illustrates how premature onset NTG may occur as a result of chronic, recurrent intrathecal hypotension – a “pure” human model. We describe an original management approach of implanting an adjustable, programmable CSF shunt valve (ProGAV) to reduce fluctuations in the translaminal cribrosa pressure difference, and reduce the risk of glaucomatous visual loss.

Case History

A 27-year-old male presented with a 6-month history of a persistent scotoma above fixation in his only seeing left eye. At 2 years of age, he had undergone primary excision and adjunctive radiotherapy for a malignant pinealoblastoma. Post-operatively, he developed hydrocephalus for which ventriculo-peritoneal, ventriculo-pleural, then ventriculo-atrial shunts were consecutively established. Over a 25-year period since primary resection, he underwent 8 shunt revision procedures, with formal documentation of recurrent low CSF pressure (CSFP) (**Figure 1**), although remained asymptomatic between CSFP measurements. He had no family history of juvenile-onset glaucoma. He did not take medications or recreational drugs.

On examination, unaided visual acuity was 20/200 OD and 20/16 OS. He had long-standing right amblyopia with right relative afferent pupillary defect and optic disc pallor (noted during childhood). Intraocular pressure (IOP) was 14mmHg bilaterally (normal <21mmHg). Anterior segment examination was unremarkable and gonioscopy revealed open drainage angles bilaterally. Fundal examination revealed a left optic disc hemorrhage (**Figure 2A**).

Functional testing using automated visual field analysis revealed a scotoma at fixation superiorly in the left eye (**Figure 2B**). Structural testing of the left macula using Scanning Laser Ophthalmoscopy revealed an arcuate distribution of maculopapillary retinal nerve fibre layer loss (**Figure 2C**), adjacent to the disc hemorrhage, corresponding to an area reduced retinal sensitivity on microperimetry (**Figure 2D**). Two further optic disc hemorrhages at the same position had been noted three years prior to presentation (**Figure 2E**), and by his optometrist 18 months earlier.

A diagnosis of juvenile-onset normal tension glaucoma was made secondary to chronic low CSFP, affecting his only seeing eye. He commenced topical Latanoprost 0.005% to each eye, reducing IOP to 10mmHg. He underwent implantation of the ProGAV® 2.0 programmable CSF shunt. Four weeks post-operatively, CSFP had stabilized at 6-13mmHg with resolution of headaches **(Figure 1)**.

Discussion

Over the past 10 years, the evidence for low CSFP as a novel risk factor in glaucoma is growing. Case-control studies have documented a lower CSFP in glaucoma patients (9.2mmHg) versus controls (13.0mmHg)¹. Experimental reduction of CSFP in monkeys is associated with glaucoma, yet reducing the IOP concurrently is protective². This case describes a unique, “pure” human model of juvenile-onset low CSFP glaucoma, in which all other non-IOP dependent pathophysiological mechanisms have been excluded.

The lamina cribrosa forms a collagenous meshwork, separating the intraocular and CSF spaces. Recurrent optic disc hemorrhages signify structural damage at the lamina cribrosa as a result of glaucoma. The translaminar cribrosa pressure difference (TLCPD) describes the disparity between IOP (normal: 10-21mmHg), and CSFP (normal: 8-15mmHg):

$$TLCPD = IOP - CSFP$$

Whilst IOP measurements dominate glaucoma management, TLCPD may be more significantly associated with glaucoma than IOP or CSFP alone³. A higher TLCPD was identified in patients

with NTG (6.6mmHg) and POAG (12.5mmHg) versus controls (1.4mmHg)³. TLCPD in this patient had been 12-23mmHg prior to surgery, lowering to +4 or less following surgery. Normalization of the TLCPD has been demonstrated protective against glaucoma⁴. The TLCPD may be influenced therapeutically by reducing IOP, or increasing CSFP:

$$\downarrow TLCPD = \downarrow IOP - \uparrow CSFP$$

Conventional glaucoma management aims to reduce IOP through topical agents, laser trabeculoplasty, or glaucoma drainage surgery⁵. This is the first report to describe the novel therapeutic approach of implantation of the ProGAV® CSF shunt with an adjustable, programmable valve⁶ to increase CSFP and reduce the risk of glaucoma progression. The ProGAV® CSF shunt features a “gravitational unit” using a ball valve to prevent CSF pressure troughs on standing. Additionally, a magnetic “adjustable valve” placed under the scalp can be rotated by an external magnetic key to adjust the CSF measurement post-operatively according to clinical need. The pressure of the ProGAV® valve can be confirmed by a plain radiograph. Glaucoma drainage surgery eliminates IOP spikes, and the ProGAV® CSF shunt may prevent CSFP troughs: stabilising the TLCPD analogously.

This report highlights glaucoma as a possible aetiology of visual loss in a patient with documented low CSFP. As the strength of the evidence implicating low CSFP in the pathogenesis of glaucoma evolves, novel therapeutic approaches to increase the CSF pressure may be sought.

References

1. Pasquale LR, Willett WC, Rosner BA, Kang JH. Anthropometric measures and their relation to incident primary open-angle glaucoma. *Ophthalmology*. 2010;1178:1521-9.
2. Yablonski M RR, Pokorny KS. Effect of decreased intracranial pressure on optic disc. *Investigative Ophthalmology & Visual Science*. 1979;18 (Suppl):165.
3. Ren R, Jonas JB, Tian G, et al. Cerebrospinal fluid pressure in glaucoma: a prospective study. *Ophthalmology*. 2010;1172:259-66.
4. Ren R, Zhang X, Wang N, et al. Cerebrospinal fluid pressure in ocular hypertension. *Acta Ophthalmologica*. 2011;892:e142-8.
5. The effectiveness of intraocular pressure reduction in the treatment of normal-tension glaucoma. Collaborative Normal-Tension Glaucoma Study Group. *American Journal of Ophthalmology*. 1998;1264:498-505.
6. Sprung C, Miethke C, Schlosser HG, Brock M. The enigma of underdrainage in shunting with hydrostatic valves and possible solutions. *Acta Neurochirurgica Supplement*. 2005;95:229-35.

Figure Legends

Figure 1. Formal CSF pressure measurements recorded in this patient over a 25-year period. The normal CSF pressure range for age is indicated by black dots (upper and lower thresholds). CSF measurements are indicated by red squares: the first four readings are single values based on opening pressure recordings on lumbar puncture, and the remainder are CSF pressure ranges recorded with a CSF pressure monitor. This figure presents objective evidence of chronic low CSF pressure over a 25-year period. The final CSF pressure measurement identifies stabilisation of the CSF pressure within the normal range following implantation of ProGAV CSF shunt device.

Figure 2. (A) Hemorrhage at the infero-temporal margin of the left optic disc at presentation. **(B)** Humphrey automated visual field analysis of the left eye demonstrating a superior split fixation visual field defect. **(C)** Nerve fibre layer defect identified on scanning laser ophthalmoscopy (SLO) inferiorly (from inferotemporal optic disc to the parafovea) **(D)** Reduced (red shading) or absent (black shading) retinal sensitivity, detected by microperimetry (MP; Maia, CentreVue, USA) within nerve fibre layer defect. These figures illustrate the correlation of structural and functional defects. **(E)** Hemorrhage at the infero-temporal margin of the left optic disc, three years prior to presentation.