Raised intracranial pressure and retinal haemorrhages in childhood encephalopathies

[original article; 1 table, 2 figs; 1 table online]

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PUBLICATION DATA

Accepted for publication 25th January 2017.
Published online 00 Month 2017.

ABBREVIATIONS

ATBI Accidental traumatic brain injury
CPP Cerebral perfusion pressure
ICP Intracranial pressure
ITBI Inflicted traumatic brain injury
NTE Non-traumatic encephalopathy
PICU Paediatric intensive care unit
PTIcpp Pressure-time index of cerebral perfusion pressure
PTIicp Pressure-time index of intracranial pressure
RICP Raised intracranial pressure

[abstract]

AIM To explore the relationship between raised intracranial pressure (RICP) and retinal haemorrhages in traumatic and non-traumatic childhood encephalopathies.

METHOD A prospective study of 112 children, 35 females and 77 males, with an age range of 0.01mo–17y8.3mo, (mean 5y8.6mo; median 4y5.6mo) included 57 accidental traumatic brain injuries (ATBI), 21

inflicted traumatic brain injuries (ITBI), and 34 non-traumatic encephalopathy cases. Measurements included intracranial pressure (ICP), cerebral perfusion pressure, pressure-time index of ICP, and number, zone and layer of retinal haemorrhages on retinal imaging.
RESULTS Group I had measured elevated ICP (*n*=42), Group II had clinical and/or radiological signs of RICP (*n*=21), and Group III had normal ICP (*n*=49). In the combined Groups I and II, 38% had retinal haemorrhages. Multiple logistic regression confirmed that the presence of retinal haemorrhages was significantly related to the presence of RICP independent of age and aetiology; however, the occurrence and overall numbers were not significantly related to the specific ICP level. The numbers of intraretinal (nerve-fibre layer and dot blot) retinal haemorrhages were significantly greater in those with RICP. The ITBI population was significantly different from the other combined aetiological categories.
INTERPRETATION The study results indicate a complex RICP/retinal haemorrhage relationship. There was no evidence of existing retinal haemorrhages being exacerbated or new retinal haemorrhages developing during periods of confirmed RICP.

DOI:

What this paper adds

- Generally, Raised intracranial pressure (RICP) predicts retinal haemorrhages after adjusting for age and aetiology.
- Specific intracranial pressure level (mmHg) was not correlated with retinal haemorrhage numbers.
- No evidence of new retinal haemorrhages during acute admission with RICP.
- Retinal haemorrhage–RICP association is different in inflicted traumatic brain injury compared with other aetiologies.

[main text]
Retinal haemorrhages occur in 85.71% of children with inflicted traumatic brain injury (ITBI),[1] and in 12.2% with accidental traumatic brain injury (ATBI).[1] It is not known for certain whether these haemorrhages represent a primary injury from impact and/or rotation, or alternatively result from secondary

brain injury, either systemic (e.g. hypertensive) or intracranial (such as raised intracranial pressure [RICP], seizures, or hypoxia or coagulopathy, etc.).[2] This lack of certainty has sometimes led to debate about the origin of retinal haemorrhages in ITBI.

There are relatively few publications where some direct measure or assessment of intracranial pressure (ICP) has been used to investigate the ICP–retinal haemorrhage relationship.[3–10]

This 6-year prospective sequential observational study at the Royal Hospital for Sick Children, Edinburgh, aimed to explore one possible secondary brain insult, namely RICP, defined as a value above age-specific norms[11] in three patient groups (Group I with ICP invasively measured at the bedside, Group II with radiological/clinical signs of RICP, and Group III with normal ICP), and its relationship to retinal haemorrhage characteristics – number, layer, and distribution – acquired by retinal imaging.

METHOD

Participants

Ethical approval was granted by the Lothian research ethics committee (LREC 2004/6/2) and parents/carers gave informed consent to the research.

From a sequentially admitted cohort of 112 acutely ill children who had retinal imaging, 57 were children with ATBI managed in the paediatric intensive care unit (PICU) (age range 0.2mo-15y9mo; median 8y11mo, mean 7y10mo). Twenty-one (21 out of 112) children had a diagnosis of ITBI (age range 1.25mo-2y5mo, median 3.12mo; mean 5.64mo), confirmed at child protection case conference. Of these ITBI, 10 required physiological support in PICU and the remainder were managed in a high dependency unit or paediatric neurology ward. A further 34 out of 112 children had other non-traumatic encephalopathies (NTEs), necessitating intensive care (age range 0.01mo-17y8.3mo, median 11.60mo; mean 5y5.2mo) Patients in this study all had neuroimaging (computed tomography [CT] and/or magnetic resonance imaging [MRI]) and other investigations as clinically appropriate.

Monitoring of physiological variables

ICP was monitored using an intraparenchymal transducer-tipped catheter (Camino Laboratories, San Diego, CA, USA). The duration of monitoring was determined by clinical need. Systolic, diastolic, and mean arterial blood pressure were monitored continuously using an intra-arterial line, referenced to the right atrium. The cerebral perfusion pressure (CPP) was a derived value (from mean arterial pressure and ICP) and displayed along with continuous monitored values of oxygen saturation, heart rate, and core and peripheral body temperature, on bedside monitors. Data from these variables were recorded at 1-minute time resolution and then transferred into the Edinburgh Monitor and Browser©; Computer Programme 1994 for later offline validation, review, and analysis as previously described.[12]

The ICP measurements for Group I (n=42) included the following: (1) direct measurement of the ICP (a) as a single opening pressure measurement via a cerebrospinal fluid access device (n=4) and (b) opening

pressure and ongoing mean ICP measurements over the first 24 hours of monitoring (35 via Camino, one via external ventricular drain, and two via subdural catheters; *n*=38). Values of ICP derangements are age-dependent and above the accepted range of normal values – that is, 5.5–6 mmHg for infants, increasing gradually to 12 mmHg for 12-year-olds, and beyond 15 mmHg for adolescents.[11]

(2) A pressure-time index for ICP (PTIicp) and CPP (PTIcpp) was undertaken in 30 of the Camino-measured patients (*n*=30 out of 35). This is a cumulative index measuring combined duration and amplitude of values above age-related normal thresholds for the whole ICP or CPP recording, and therefore quantifies the total burden of secondary brain ICP or CPP insult.[12,13]

Retinal imaging

Hand held RetCam imaging (Clarity Medical Systems, Irvine, CA, USA), was undertaken where clinically feasible on ventilated children within 24 hours of admission and sequentially (78 out of 112), as previously described.[14] All suspected ITBI cases were seen by a paediatric ophthalmologist. All non-ITBI cases (ATBI and NTE cases) if possible, were seen after direct or indirect ophthalmoscopy, or by consultant neurology staff instructed in the use of RetCam. A standard set of images was downloaded to a dedicated computer for morphometry, counting, layer attribution, and retinal 'zoning'. Zonal classification and retinal layer of the retinal haemorrhages was made as previously described.[14,15]

Statistical analyses

Non-parametric tests were used as some of the variables were skewed. Quantitative variables were compared between groups by Mann–Whitney or Kruskal–Wallis tests, χ^2 tests were used to test for association between categorised factors, and the association between two quantitative variables was tested by Spearman's rank correlation. The significance of predictors of retinal haemorrhages adjusted for one another was tested by multiple logistic regression, with age included on a logarithmic scale because of its extreme skewness. Bonferroni correction for multiple testing was used when specific choices had been made of which groups to compare. Analyses were performed using SPSS version 19 (IBM Corp., Armonk, NY), using a significance level of 0.05.

RESULTS

The study population (112 children) is detailed in Table I, and comprises three groups: Group I, those with objectively measured and elevated ICP; Group II, those with clinical signs or radiological evidence of RICP but without objective pressure measurement; and Group III, those with normal ICP. Retinal haemorrhages were present in Groups I, II, and III in 10 out of 42, 14 out of 21, and 9 out of 49 children respectively.

Pressure measurement methods and aetiology

Group I

The 42 children with opening pressure values comprised 31 ATBI, five ITBI, and six NTEs. For the 31 ATBI children in PICU who required ICP monitoring, all had their ICP measured by means of a Camino System. For the ITBI children (n=5), the ICP was measured via a Camino System in PICU (n=1), or by a strain gauge transducer (Gaeltec) connected to a subdural catheter on admission (n=2), or during evacuation of subdural collection (n=2). The six children with NTE had ICP measured via subdural measurement, ventricular access device or Camino system.

Group II

Twenty-one children had clinical and imaging evidence of RICP. RICP results from enlargement of the ventricular compartment (hydrocephalus), the brain compartment (cerebral oedema), or as a result of space occupation (from tumour, clot, cyst, or abscess). RICP may be indicated by periventricular lucencies, brain shifts, ventricular or cisternal compression, etc. A radiologist confirmed 20 out of 21 cases with brain imaging evidence of pathology and RICP. Often, children had several brain compartments involved: 15 out of 20 children had a space occupation from subdural haemorrhage, tumour, extradural haemorrhage, or other cerebral haemorrhage; 6 out of 20 had brain swelling; and 8 out of 20 had ventricular enlargement.

Clinical signs of pressure, such as disproportionate head expansion (enlarging occipito–frontal circumference), tense non-pulsatile fontanelle, scalp vein distention, etc., in infants, fits or decerebration in older encephalopathic children, or observed elevated pressure at operation were noted in 13 children. Twelve of these had imaging signs of RICP.

Group III

The remaining 49 children had no RICP directly measured or implied by imaging or clinical signs or symptoms.

Retinal haemorrhages and raised ICP

In Group I with measured ICP, 10 out of 42 patients (23.8%) had retinal haemorrhages. In Group II with radiological and/or clinical signs of RICP, 14 out of 21 (66.6%) had retinal haemorrhages. In Group III patients with normal ICP, 9 out of 49 (18.36%) had retinal haemorrhages.

In Groups I and II combined (i.e. all cases with either measured, or radiological or clinical signs of RICP), 24 out of 63 (38.09%) had retinal haemorrhages.

Of all the patients in this study (ATBI, ITBI, and NTEs), 33 out of 112 (29.5%) had retinal haemorrhages.

Multiple logistic regression showed that the ICP group remained significant (p=0.023) as a predictor of retinal haemorrhage after adjusting for both aetiological group and age.

In terms of the presence or absence of retinal haemorrhages with RICP, the ITBI population is significantly different (14 out of 14) from the other two aetiological groups combined with raised pressure (10 out of 49; Fisher’s exact test p<0.001).

Occurrence of retinal haemorrhages in children with directly measured elevated ICP

In those children with directly measured ICP (*n*=42), the opening pressure was elevated in all cases and 10 (23.8%) had retinal haemorrhages. All of the ITBI subjects in this group had retinal haemorrhages (5 out of 5) while the ATBI cases had retinal haemorrhages in 5 out of 31 (16.1%). The association between ICP opening pressure level and the presence (*n*=10) or absence (*n*=32) of retinal haemorrhages was non-significant (Mann–Whitney Test, *n*=42; *p*=0.329, Fig. 1).

Relationship of the total number of retinal haemorrhages with the ICP opening pressure level

The total number of retinal haemorrhages in both eyes in relation to the ICP opening pressure for the 10 patients in Group I with haemorrhages, ranged from 2 to 327 retinal haemorrhages with a corresponding range of ICP opening pressure values from 7 to 58mmHg. This relationship was not significantly correlated (Spearman's rho correlation=0.176, 95% confidence interval –0.51 to 0.72).

Numbers of retinal haemorrhages in groups with and without RICP

Combining those children with measured RICP and those with clinical/radiological signs of RICP (*n*=63), and comparing them with the group without any signs of RICP (*n*=49), significantly greater total number of retinal haemorrhages was found in the former (Mann–Whitney *U* test, *p*=0.027 [Bonferroni Correction]). However the total number of retinal haemorrhages was significantly different (Kruskal–Wallis test, $p<0.001$) among the three groups described above. In this study those cases who had clinical or radiological signs of RICP, without objective pressure measurement (Group II), had the largest number of retinal haemorrhages (*n*=14) and 64.3% of these were ITBI cases.

Other indices of ICP

Additionally, the ICP was measured using indices other than the opening pressure (i.e. mean ICP value in the first 24 hours; PTIicp and PTIcpp), and the relationship between these unique pressure values and the number of retinal haemorrhages was further investigated.

The average intracranial pressure over the first 24 hours following admission in five ATBI and two ITBIs was 16.75mmHg (range 7.8–31.9). In this same group the average PTIicp (minutes times mmHg) values for the total duration of ICP monitoring in intensive care was 52 524 (range 11 890–139 257). A PTIicp value above zero indicates some degree of age-specific ICP derangement. The average PTIcpp (minutes × mmHg) was 4660 (range 0–10 805). Any PTIcpp value above zero indicates a degree of cerebral perfusion pressure derangement. The measurement of the total burden of ICP and CPP (PTIicp and PTIcpp) for the whole duration of monitoring, and the mean ICP value over the first 24 hours of monitoring, for these seven cases with retinal haemorrhages, showed no relationship with the total number of retinal haemorrhages seen (Spearman's rho correlation coefficient).

Relationship between intracranial pressure level and retinal haemorrhage type (layer) and retinal zone

The total number of retinal haemorrhages counted in the 112 patients was 3922, which included six eyes with retinal haemorrhages 'too numerous to count' (estimated as a mean of 303 retinal haemorrhages per eye),[1] and which were distributed according to ICP category and then subdivided according to the retinal layer involved. The numbers of pre-retinal haemorrhages, flame-shaped haemorrhages (nerve fibre layer), dot/blot haemorrhages, subretinal or vitreous haemorrhages, and total haemorrhage numbers were recorded. In Group I (with measured ICP) the numbers of different retinal haemorrhages were 22, 322, 769, 4, and 1117 respectively. Similarly, the numbers in Group II (with clinical or radiological signs of pressure) were 50, 243, 1970, 1, and 2264 respectively, and in Group III (normal, ICP) were 9, 17, 515, 0, and 541 respectively. The dominant retinal haemorrhage type in all groups was intra-retinal (dot blot and flame) retinal haemorrhage.

There were significantly more intra-retinal retinal haemorrhages in those with RICP (n=63, p=0.015; Mann–Whitney test). Separately there were significantly more flame haemorrhages in those with RICP (p=0.002; Mann–Whitney test). There were few subretinal or vitreous layer haemorrhages.

The analysis of the different retinal zones in relation to the presence or absence of RICP was not statistically possible in those cases of ATBI because there were too few cases without elevated pressure, neither was this analysis possible in some cases of ITBI which had retinal haemorrhages described as 'too numerous to count', because confluent and extensive haemorrhages obscured the markers of the different zones.

NTE cases with RICP (n=4) had more dot-blot retinal haemorrhages in the posterior pole and retinal periphery (86 and 58, respectively) than those without RICP, n=4 (12 and 5, respectively).

Qualitative and quantitative changes in retinal haemorrhages during ongoing simultaneous ICP measurements

From the continuous recordings of ICP in 31 cases, it was possible to calculate the mean values every 6 hours for the duration of monitoring. In a small number of cases, this allowed exploration of the relationship between the changing ICP level and the retinal haemorrhages (numbers and types) from sequential retinal images. Examples are shown in Figures 2a and 2b, giving case details, along with the graphed 'mean ICP' level every 6 hours, and changing total and differential retinal haemorrhage count. Figure 2c shows the first and last simultaneous pressure and retinal haemorrhage count. There was no change in retinal haemorrhage count or retinal haemorrhage type with changing ICP levels.

DISCUSSION

A comprehensive review of the literature concluded that, in general, elevated ICP did not cause extensive haemorrhagic retinopathy, but isolated cases were recognised.[16] The present study revisits this relationship and sets out to investigate with advanced pressure measurements and retinal imaging in a prospective study,

whether in childhood encephalopathies, raised ICP is associated with retinal haemorrhages or is a factor in their origin.

Clinical experience and evidence from the literature point to RICP as causal of certain types of retinal haemorrhages in some conditions, for example idiopathic intracranial hypertension, and in unrelieved cerebrospinal fluid shunt blockage, which both have RICP as the fundamental and sole pathology. Severe crush injuries with extensive retinal haemorrhages have transient very high intravascular pressure.

The concept of 'secondary brain insult' and its management in the neurointensive care of traumatic brain injury is well established, and RICP is one of the major secondary brain insults which causes ischaemic brain injury and 'brain shifts', and has led to the concept of the 'golden hour' which emphasises the requirement for urgent pressure management in the prevention of early death and severe injury.[17] Whether RICP, as a secondary insult, also could be causally responsible for retinal haemorrhages in traumatic brain injury is unknown.

A synopsis of the existing literature, in which an assessment of RICP with retinal haemorrhages has been reported, is seen in Table SI (online supporting information).

Studies that have attempted to relate retinal haemorrhages and RICP have done so by indicating the frequency of retinal haemorrhages in series of cases with RICP, as has this paper. However, comparisons across the literature are of limited value, given the different group numbers and aetiological makeup of the groups. The frequency of retinal haemorrhages in the present study, in cases with measured ICP, together with cases where there were radiological or clinical signs of RICP, was 24 out of 63 (38%) and multiple logistic regression showed a significant difference between the ICP groups (p=0.027) as a predictor of retinal haemorrhages after adjusting for aetiology and age. This dichotomous relationship between RICP and retinal haemorrhages provides a basic level of association.

In the study group with directly measured pressure (n=42), there was no correlation between the opening pressure level and the presence or absence of retinal haemorrhages. There was also no significant correlation between the total number of retinal haemorrhages seen in each patient with their ICP opening pressure (mmHg). The reason for non-significance in this association (Fig. 1) is that the ITBI cases all had RICP and many retinal haemorrhages, whereas cases with no retinal haemorrhages in this group could have an opening pressure ranging from 3 to 30mmHg. It was also found that the total burden of pressure insult or ischaemic insult over the first 24 hours showed no relationship with the total number of retinal haemorrhages.

ITBI is a group of special clinical interest given that retinal haemorrhages are often part of the diagnostic criteria. The ITBI population with RICP is significantly different (in terms of percentages with retinal haemorrhages) from the other two combined aetiological groups with RICP – that is, 14 out of 14 versus 10 out of 49 (Fisher's exact test p<0.001). Morad et al.[6] retrospectively found no correlation between imaging signs of pressure and retinal findings. By comparison, the present small sub-group (n=9) with similarly diagnosed raised pressure all had retinal haemorrhages (9 out of 9).

Preliminary observations of sequential imaging and pressure measurements in a number of patients (Fig. 2a and 2b) point to a declining number of retinal haemorrhages regardless of the ICP measurement level. Additionally, separate measurement of the first and last values of pressure and haemorrhage counts (Fig. 2c) showed no increase in the retinal haemorrhage count. It is unlikely therefore that over the course of the acute illness, RICP has exacerbated the retinal haemorrhage count or moderated the type of retinal haemorrhage seen, and therefore in ITBI, it is reasoned that the retinal haemorrhages occurred at the time of the traumatic acceleration/deceleration injury (shaking), which causes vitreous traction of the retina and increased intraocular venous pressure.

The dominant retinal layer of the retinal haemorrhages was intra-retinal across the study population, and significantly more were seen in those with RICP than those without. Interestingly, there were more dot blot haemorrhages in the posterior pole and in the retinal periphery in the present study, in those cases with NTE (not including any idiopathic intracranial hypertension cases) and RICP, than in those without RICP.

In this study, as in previously published studies, an attempt was made to show a statistical relationship between ICP and retinal haemorrhages. However, even with some highly significant statistical values (at the 1% level), one can do no more than describe a relationship between the retinal haemorrhages and RICP, but cannot because of the purely observational nature of such studies, and without a hypothesis-driven clinical trial, prove causality.

A major methodological limitation to an ideal clinical investigation is the absence of immediate and continuous pressure measurement and retinal imaging from the moment of accidental or non-accidental trauma. Whether raised pressure, at what level, and over what time span can induce retinal haemorrhages following trauma is not known. However, papilloedema, indicative of RICP, can occur at various times after acute head injury in adults,[18] but it may not occur at all, or is rare in infants or young children,[19] because of the pressure compensatory mechanism of head expansion with open anterior fontanelle,[20] etc., and it is at this age (<18mo) that ITBIs mostly occur. A further limitation in this study is that not all ITBI patients are managed in PICU with physiological monitoring because of the different types of clinical presentation, for example acute encephalopathic or chronic extracerebral presentation.[21] This prospective study has attempted to ameliorate some of these difficult requirements, and the inferences are based on actual pressure measurements and concomitant retinal imaging. Lastly, an increase in case numbers might have strengthened any statistical relationship, because in the present data there tend to be few retinal haemorrhages in relatively many cases of ATBI, and the converse in ITBI.

SUPPORTING INFORMATION

The following additional material may be found online:

Table SI: Summary of literature related to the association of raised intracranial pressure and retinal haemorrhages.

ACKNOWLEDGEMENTS

We are grateful to Dr Rob Elton for statistical advice; the medical and nursing staff in the PICU and the neurology ward at RHSC. We are indebted to the patients and parents/carers for consenting to participate in this study. The staff of the department of Child Life and Health in University of Edinburgh. Funding was obtained from the RS Macdonald Charitable Trust Edinburgh, from the Royal College of Surgeons Edinburgh (Ophthalmology Grant), and from the Friends of The Sick Kids Foundation, Edinburgh, Scotland. The authors have stated that they had no interests which might be perceived as posing a conflict or bias.

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Table I: Study population (*n*=112)

	GROUP I. *n*=42 With measured opening ICP (% RICP)			GROUP II. *n*=21 With radiological/clinical signs RICP			GROUP III. *n*=49 Normal (no clinical signs of RICP or measurement of		
	Retinal haemorrhages	No retinal haemorrhages	Total Group I	Retinal haemorrhages	No retinal haemorrhages	Total Group II	Retinal haemorrhages	No retinal haemorrhages	Total Group II
NTE (*n*=34)	0	6	6 (100%)	4	5	9	4	15	19
ITBI (*n*=21)	5	0	5 (100%)	9	0	9	4	3	7
ATBI (*n*=57)	5	26	31 (30/31; 96.8%)[a]	1	2	3	1	22	23
Total (*n*=112)	10	32	42 (97.6%)	14	7	21	9	40	49

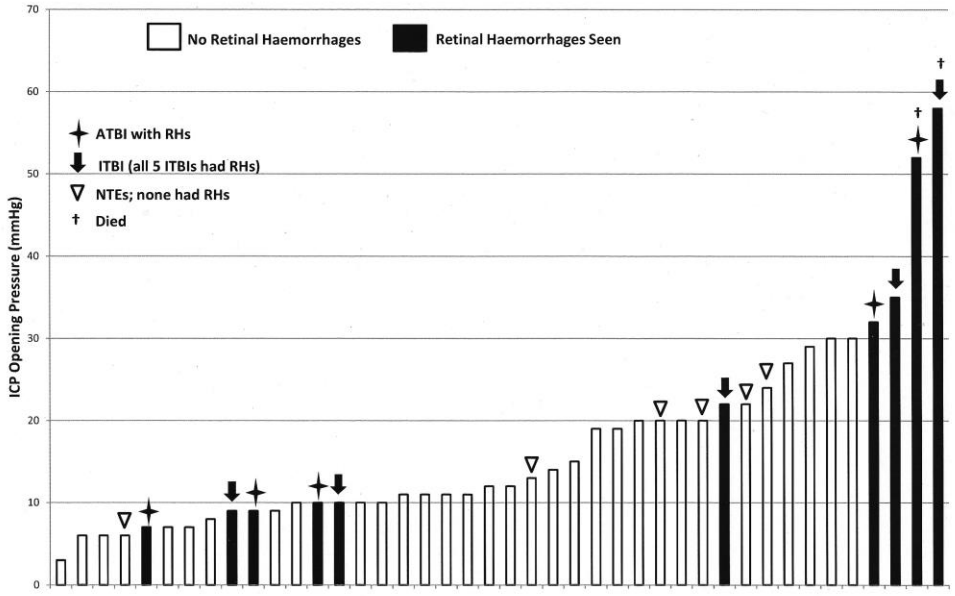
[a]Only one ATBI had measured ICP, which was borderline raised. ICP, intracranial pressure; RICP, raised intracranial pressure; NTE, non-traumatic encephalopathy; ITBI, inflicted traumatic brain injury; ATBI, accidental traumatic brain injury.

Figure 1: Individual cases on x-axis with their respective opening CSF pressure on the y-axis (mmHg). The 10 cases with retinal haemorrhages are shown in black bars, and these are further subdivided in those caused by inflicted traumatic brain injury (ITBI, black arrows) and those caused by accidental traumatic brain injury (TBI, stars). Six cases of non-traumatic encephalopathy (NTE) had measured pressure and none had retinal haemorrhages (open triangle).

Figure 2a and 2b: (a) Repeated retinal imaging and sequential intracranial pressure (ICP) measurements in 18-month-old child with inflicted traumatic brain injury (ITBI). Findings included subdural haematoma and intracranial haemorrhage, rt occipital fracture, lt greenstick fracture of radius and ulna, lt supracondylar fracture of humerus, fracture of rt 10th rib, and epileptic seizures. Craniotomy and evacuation of clot, sedation/paralysis/ventilation and ICP monitoring. Child Protection Team involvement. Flames, flame retinal haemorrhage; D/Bs, dot/blot retinal haemorrhages. (b) Repeated retinal imaging and sequential ICP measurements in a 10-year-old child hit by a car wing mirror while playing in the street. Child was thrown in the air and landed near the kerb. Findings included right comminuted fracture of the temporo-parietal region, left contra-coup injury and left fronto- parietal haemorrhagic contusions, small right frontal extra-axial collection (without significant mid-line shift and with patent basal cisterns), probable base of skull fracture, pulmonary contusion, renal bruising, and limb grazes. Raised intracranial pressure (RICP; monitored via a Camino bolt), was initially difficult to control. Good recovery at 6 months post injury.

Figure 2c: A number of cases with retinal haemorrhage counts from the first and last imaging session along with corresponding intracranial pressure values at those times. In the six cases shown (two of which were inflicted traumatic brain injury [ITBI], cases 2 and 6; the other four were accidental traumatic brain injury [ATBI]) where the intracranial pressure (ICP) level has remained virtually static (case 1), has decreased (cases 2, 5, and 6) or increased (cases 3 and 4), the total retinal haemorrhage numbers have either declined or remained unchanged. Importantly, in all cases with sequential retinal haemorrhage counts, none show any increase in retinal haemorrhage numbers.

Figure 1



42 children with and without retinal haemorrhages arranged in ascending order of measured ICP Opening Pressures.

Figure 2a

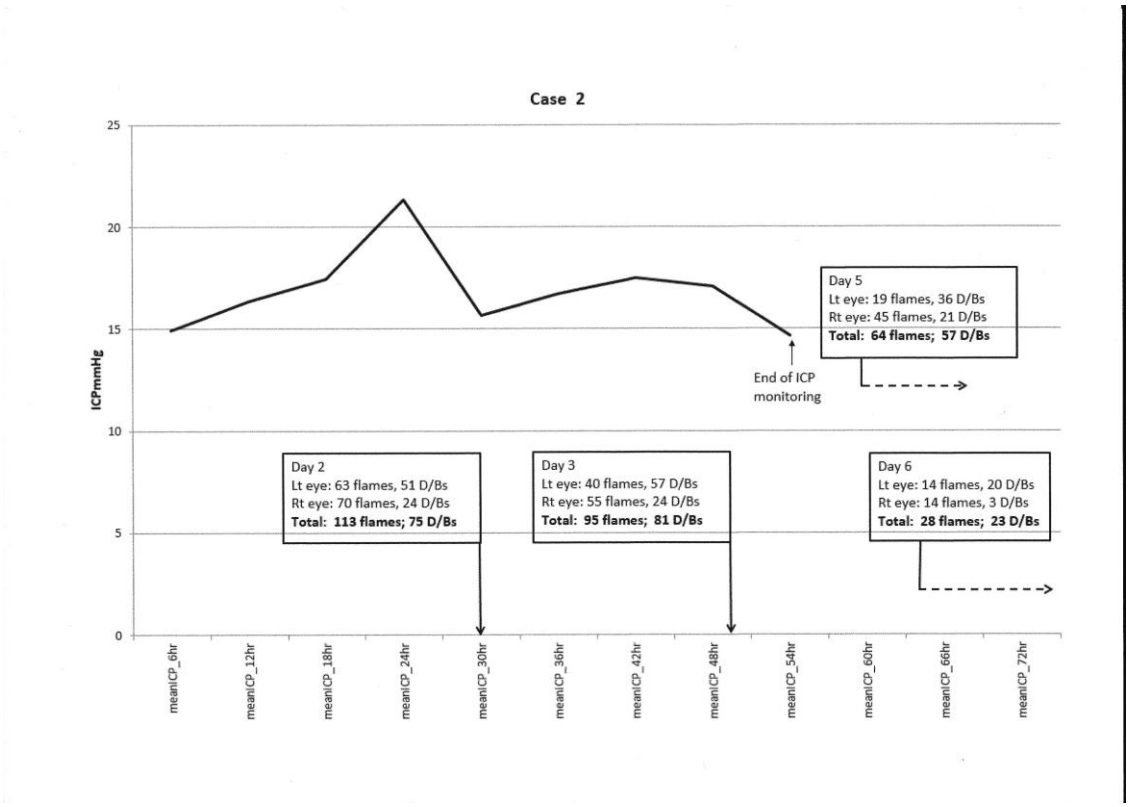


Figure 2b

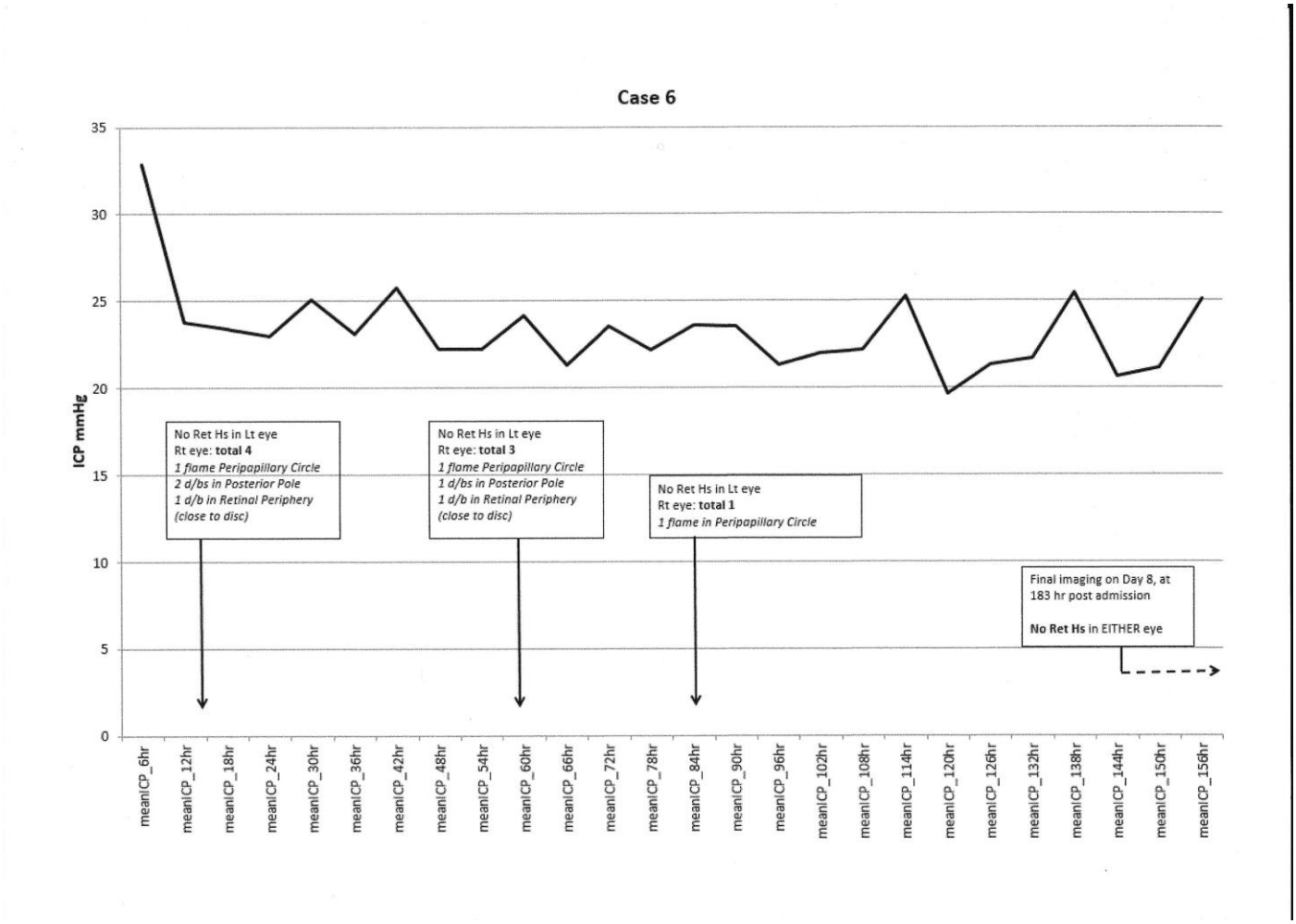


Figure 2c

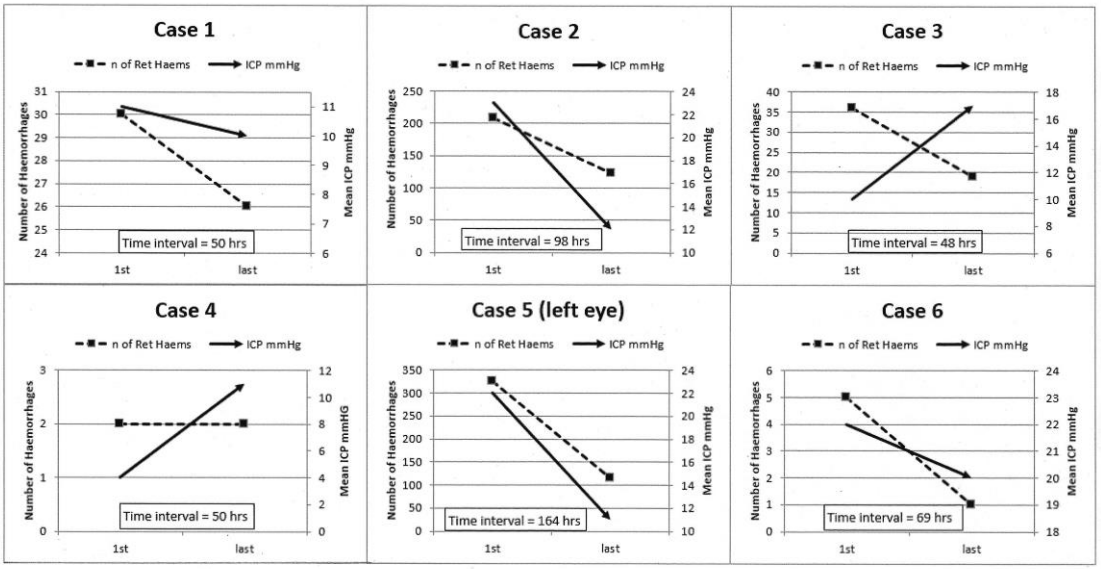

Case 1
n of Ret Haems
ICP mmHg
Number of Haemorrhages
Mean ICP mmHg
Time interval = 50 hrs
1st
last
Case 2
n of Ret Haems
ICP mmHg
Number of Haemorrhages
Mean ICP mmHg
Time interval = 98 hrs
1st
last
Case 3
n of Ret Haems
ICP mmHg
Number of Haemorrhages
Mean ICP mmHg
Time interval = 48 hrs
1st
last
Case 4
n of Ret Haems
ICP mmHg
Number of Haemorrhages
Mean ICP mmHG
Time interval = 50 hrs
1st
last
Case 5 (left eye)
n of Ret Haems
ICP mmHg
Number of Haemorrhages
Mean ICP mmHg
Time interval = 164 hrs
1st
last
Case 6
n of Ret Haems
ICP mmHg
Number of Haemorrhages
Mean ICP mmHg
Time interval = 69 hrs
1st
last

Table SI:

Reference	Detail Pressure measurement	RHs	Results	Conclusion
Binnenbaum G. et al 2013. Pediatrics; 132 (2): e430 – e434	Measured lumbar CSF in 100 children	16/100 with RH (15 due to IIH; 1 Guillian Barré)	8/16 with splinter RHs had mean OP of 40cmH2O (29.42mmHg); 8/16 had superficial IR RHs adjacent to a floridly swollen optic disc, & higher mean pressure of 44cmH2O (32.36mmHg)	Raised pressure is associated with superficial and centrally located RHs in 16% with raised LP pressure.
Weisberg LA 1975; Medicine 54(3): 197-207	Measured Lumbar CSF in 120 IIH adults	27% had RHs or exudate (usually centrally located)	15% (n=11) with RHs with CSF pressure 22-29mmHg. 50% (n=15) with RHs if CSF pressure 29-37mmHg; 100% (n=6) with RHs if CSF pressure >37mmHg	Incidence of RH increased with increasing CSF pressure.
Bhadwaj 2010* Abstract: Clinical and Experimental Ophthalmology; 38, (Suppl 2) p19-20	Prospective case series of 17 infants and children, with conditions associated with RICP (11/17 were obstructive hydrocephalus; 3 with spontaneous ICH and 3 with cerebral oedema), determined by measurement or neurosurgical or radiological assessment, together with RetCam imaging.	Intraocular H seen in 3/17 (18%);		Concluded “that pressure was NOT an apparent cause of haemorrhagic retinopathy in this group.
Bhardwaj G et al. 2010** 2010 Clinical and Experimental Ophthalmology; 38, (Suppl 2) p18	Prospective case series of 93 head injuries in infants and children (9 with no evidence of direct impact) with retinal imaging		IOH was seen in a higher proportion 7/9 (78%) and with greater severity in non-impact (all abusive) than 8/84 with impact head injuries (10%).	Head injury with RICP had significantly higher rate of RH than those with normal ICP. RICP may contribute to, or exacerbate the retinal findings.
Muller PJ and Deck JH, 1974; J Neurosurgery. 41(2):160-166	Intraocular and optic nerve sheath haemorrhages in cases of sudden intracranial hypertension	Post mortem; eyes of 23 patients with ICHT (pathological confirmation of cerebral compression from trauma, massive spontaneous ICH, 9 ruptured berry aneurysms, and 2 internal carotid occlusions causing massive post-	In the 23 patients with ICHT, intraoccular haemorrhage found in 37% and optic nerve sheath H in 87%.	

		infarction cerebral swelling without haemorrhages) and 24 eyes of patients with no evidence of ICHT.		
Vanderlinden RG & Chisholm LD. 1974. J Neurosurgery 41(2)167-176	6 clinical case studies of vitreous haemorrhages accompanying SAH (4) and craniocerebral injury (2), i.e. Terson's Syndrome		Clinically recognised raised ICP accompanying subhyaloid (and subsequent vitreous) R H.	
Gnanaraj L et al. 2007. Eye; 21(1): 5-10	Retrospective study of Crush head injuries in children	Autopsy findings: 4/9 had Retinal Hs in posterior pole; 3 with SILM, and 1 had more extensive RHs extending to the ora serrata.		Intraretinal and pre-retinal haemorrhages predominantly in the posterior pole. Haemorrhages under the ILM or extending to the oro serrata were only seen where the crush was a fatal MVA.
Lueder GT et al. 2006. Archives of Ophthalmology. 124 (12):1782-3	4month old child with very rapid rise in ICP following crush injury who died.	Perimacular retinal folds, retinoschisis and 4-quadrant multi-layer RHs		Postulated that very rapid massive increase in ICP in severe head crush injury resulted haemorrhage within perineural sheaths and separation of retinal membranes at the outer nuclear layer.
Kivlin JD et al. 2008. Archives of Ophthalmology; 126 (6) 800-804.	Post Mortem study; 10 children < 3, fatally injured in MVA, i.e. extremely high force injuries	8/10 had severe and extensive RH extending to the periphery (in 13 eyes); bilateral in 7/10; 3 patients had retinal folds; 6/10 patients had RH below the ILM, and 9/10 patients had ONS haemorrhages		They postulated rapid deceleration with rotation as the cause of the RHs. An association of extensive severe ocular haemorrhage with fatal major accidental trauma, and presumed RICP.
Vinchon M et al. 2002; 37(5):245-253	Retrospective review of 18 cases <24 months who suffered MVAs, with clinical picture of RICP	3/16 had flame Hs at the posterior pole. 2 of these 3 patients with RHs had collapsed arachnoid spaces and clinical signs of RICP.		Occurred in association with intracranial hypertension
ForbesBJ et al. 2008. AAPOS; 12(2) 177-180	Retrospective study; 9 children <3 years, with accidental epidural haematomas and ophthalmological review	5/9 (all <8mo of age) had a few retinal haemorrhages which were superficial and in the posterior pole		" A rapid change in ICP associated with EDH leads to the development of RHs" (forces are generally low with EDH)
Minns RA et al 2012. Pediatrics;	Case 1. A newborn with huge co-natal brain tumour; CT at 6hrs after birth showed fresh	Severe bilateral haemorrhagic retinopathy	bulging fontanelle, and very large head (OFC=40.5cm at birth), dilated ventricles. Markedly RICP and brain	and high forces in birth canal -> RHs. … see notes in file of RH040

130(5):e1227-e1234	blood haemorrhaging from tumour. baby died a few days later.		shift. No SDH	
	Case 2. An adolescent girl with a blocked ventriculo-peritoneal shunt presenting with symptoms of headache, vomiting and neck pain	ophthalmologist-confirmed extensive vitreous and subhyaloid haemorrhages	Confirmed RICP	Clear association between RICP and RHs, as no other pathology.
Morad 2002. Am J Ophthal. 134 (3):359	29 ITBI cases with one or more retrospectively assessed radiological signs of RICP and retinal haemorrhages.		There was a relationship between the Total Cranial Trauma Score and Total Retinal Haemorrhage Score (severity of both) was correlated, p=0.032.	No correlation between radiological signs or RICP and retinal abnormality findings
Galvin and Sanders 1980. B J Ophthal. 64 (4): 262	Descriptions of 2 cases with severe intracranial hypertension, papilledema and haemorrhagic peripheral retinopathy		Case 1. LP Opening Pressures >460mmH2O. Treated with steroids Case 2. LP Opening Pressure > 400mmH2O. Treated with repeated LP, steroids, acetamolozide and glycerol, and subsequently a theco-peritoneal shunt	Multiple punctate peripheral retinal haemorrhages can occur in association with marked disc swelling from severe intracranial hypertension.
Patrick Watts et al. JAAPOS 2013, 17 (1): 70-78	Systematic review of new-born retinal haemorrhages. 13 studies, and 1777 infants.	25.6% of newborns after SVD had RH; Infants delivered by vacuum extraction 42.6% RH; Infants delivered (forceps + vaccuum) had 52% RH	Predominantly intraretinal and posterior; mostly resolved by 6 weeks	Hypothesized mechanisms include (i) increased intracranial pressure (suction on chignon) or (ii) duration of 2nd Stage or (iii) rapid descent or compression/decompression of the head.
Mena OJ et al. 2010. Am J Forensic Med Pathol. 32(1):55-57	A fatal case of Terson's Syndrome in 7 mo infant.	Aneurysm of MCA and diffuse SAH of brain and spinal cord. Bilateral optic nerve sheath haemorrhage and extensive RH extending to ora serrata.		The PM reasoning was that a rise in ICP caused marked optic nerve sheath haemorrhage + intra- and preretinal haemorrhages.
McCasland B. 1999. BJO; 83 (7): 883-884 Letter to Ed.	An infrequently reported subretinal (bilateral peripapillary) haemorrhage in IIH in a 41 year old woman.			Elevated ICP was responsible for the Subretinal haemorrhages but only mild disc oedema, and

* Bhardwaj G. 2010 Abstract: Retinal findings in infants following non-traumatic acute rise in intracranial pressure. Clinical and Experimental Ophthalmology; 38, (Suppl 2) p19-20

**Bhardwaj G et al. 2010 Intraoccular haemorrhages assessed objectively in paediatric head injuries in Sydney; Clinical and Experimental Ophthalmology; 38, (Suppl 2) p18