Retinal hemorrhage after pediatric neurosurgical procedures

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BACKGROUND Neurosurgical procedures may occur prior to eye examination in children with suspected abusive head trauma and raise questions by child abuse physicians and ophthalmologists regarding the contribution of neurosurgery to retinal hemorrhage found postoperatively. The purpose of this study was to determine the prevalence and patterns of retinal hemorrhage attributable to neurosurgical intervention in children.

METHODS We conducted a retrospective cohort study of children undergoing neurosurgery who had postoperative ophthalmoscopy. Some children were also examined preoperatively. Primary outcome measures were the prevalence and patterns of retinal hemorrhage attributable to neurosurgical intervention. Medical records were reviewed to identify confounding coexistent diseases.

RESULTS Among 267 children undergoing 289 neurosurgical procedures, there were no cases in which children had post-procedural retinal hemorrhage that could be attributed to neurosurgery. Retinal hemorrhage was seen in 32 (12%) cases, but in every case they were either already present on preoperative examination (13 cases) or matched the pattern of a coexistent known cause of retinal hemorrhage, including head trauma with unambiguous history and/or nonocular signs (13), hydrocephalus-related increased intracranial pressure with papilledema-associated peripapillary retinal hemorrhage (5), and retinopathy of prematurity ridge-associated retinal hemorrhage (1). No retinal hemorrhage could be attributed only to neurosurgery.

CONCLUSIONS Although children undergoing child abuse evaluations may have intracranial hemorrhage requiring neurosurgery that occurs before a dilated retinal examination can be performed, our data suggest that neurosurgery independently is unlikely to produce retinal hemorrhage and therefore is not a significant confounding factor in the interpretation of retinal hemorrhage patterns in child abuse evaluations. (J AAPOS 2022;26:74.e1-5)

Some children undergoing child abuse evaluation for possible abusive head trauma (AHT) require urgent neurosurgical intervention. Ophthalmologic examination for retinal hemorrhage in these children is often delayed until after surgery.[1,2] If retinal hemorrhage is subsequently identified, questions may be raised by child abuse physicians and ophthalmologists as to whether the neurosurgical procedure itself may be considered a possible cause. If retinal hemorrhage is incorrectly ascribed to abuse, then false accusations might be made; however, if retinal hemorrhage is incorrectly ascribed to neurosurgery, then child abuse may be missed. To our knowledge, there are no published data addressing the question of whether neurosurgery is a potential confounding cause of retinal hemorrhage in children being evaluated for abusive head trauma.

The differential diagnosis of retinal hemorrhage in young children includes birth-related retinal hemorrhage in the first weeks of postnatal life; abusive or accidental head trauma; raised intracranial pressure; leukemia; sepsis; retinal vascular diseases, such as venous occlusion or hypertensive retinopathy; retinitis; and other less frequent medical causes. The cause of retinal hemorrhage may be identified by medical history; other findings on ocular and physical examination, laboratory testing, and imaging studies[1,2]; pertinent negative findings; and the specific patterns of retinal hemorrhage and other retinal findings associated with these diseases.[1-3] The effects of neurosurgery

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on the retina and possible associated patterns of retinal hemorrhage are unknown. Hypothesized mechanisms by which neurosurgery may cause retinal hemorrhage include changes in intracranial or intravascular pressure. Of particular interest may be neurosurgical procedures that result in acute increases or decreases in intracranial pressure, such as craniotomy and evacuation of intracranial hemorrhage, which might produce associated patterns of retinal hemorrhage, such as papilledema-associated peripapillary retinal hemorrhage or central retinal venous occlusion.

We sought to determine the prevalence and patterns of retinal hemorrhage attributable to neurosurgical intervention in children. To answer this question, we carefully accounted for potentially confounding coincident diseases in the study patients that may cause retinal hemorrhage, by considering the distinct patterns of retinal hemorrhage and other ocular findings that were present.

Subjects and Methods

We conducted a retrospective cohort study of children hospitalized at Children's Hospital of Philadelphia from January 1, 2013, to July 23, 2019. We included children >1 month of age, to reduce confusion with birth-related retinal hemorrhage, and <18 years of age, who had a neurosurgical procedure and at least one documented postoperative fundus examination by a pediatric ophthalmologist, preferably within 0-3 days but no more than 7 days following neurosurgery. The children were identified by searching electronic medical records. Some children were also examined preoperatively, but a preoperative examination was not a requirement for inclusion in the study. These pre- and post-operative examinations were performed as part of standard of care ophthalmology consultations requested by the primary pediatric or surgical team for varying reasons; for example, to evaluate for evidence of raised intracxranial pressure, such as papilledema, or to evaluate for retinal hemorrhage as part of a child abuse evaluation, To avoid potential selection bias, we did not exclude children based on coincident medical diseases, previous head trauma, or suspected abusive head trauma, even though these conditions may be potential causes of retinal hemorrhage. The study was approved by the Institutional Review Board of Children's Hospital of Philadelphia and conducted in compliance with the US Health Insurance Portability and Accountability Act of 1996.

Data abstracted from the medical record included patient age, type of neurosurgical procedure, clinical indication for neurosurgery, and medical history, including concurrent diseases that might cause retinal hemorrhage and supporting clinical information related to such potentially confounding diseases, such as non-ocular physical findings, laboratory test results, and imaging studies. We recorded whether there was suspected or confirmed abusive head trauma or child abuse and collected the results of ophthalmological examinations, including the type, number, locations, and laterality of retinal hemorrhage, presence of retinal folds or retinoschisis, optic disk atrophy or swelling, and other ocular abnormalities.

The primary outcomes were the prevalence of retinal hemorrhage attributable to neurosurgery and the patterns of retinal hemorrhage attributable to neurosurgery. The description of pattern of retinal hemorrhage included the laterality, number, types, locations, overall retinal geographic distribution, and presence of coincident fundus findings, such as white or yellow lesions, optic disc swelling, retinal whitening, etc. To determine if the prevalence or patterns of retinal hemorrhage attributable to neurosurgery varied according to the neurosurgical procedure performed, the neurosurgical procedures were grouped according to type, including craniotomy, burr-hole related, drain implants, spinal surgery, and other. For neurosurgical cases in which more than one procedure was performed, type of neurosurgical procedure was categorized by the most invasive procedure performed.

With regard to determining whether retinal hemorrhage could be attributable to neurosurgery, an a priori plan was established to account for potential confounding by the presence of coincident medical conditions that cause retinal hemorrhage, in the following manner. If retinal hemorrhage was identified on a post-operative examination, additional data were considered, including results of a preoperative fundus examination if available; past medical history; suspected or confirmed abusive or accidental head trauma or child abuse; nonocular physical examination findings of trauma; laboratory studies; medications; and imaging study results. The specific pattern of retinal hemorrhage on post-operative examination was compared to findings of the preoperative fundus exam if available and to known retinal hemorrhage patterns associated with coincident diseases in that child. If no coincident disease known to cause retinal hemorrhage was present in a child, the retinal hemorrhage was deemed attributable to neurosurgery. If a coincident cause of retinal hemorrhage was present in a child, but the retinal hemorrhage pattern observed did not match a pattern known to be associated with that coincident disease, the retinal hemorrhage was attributable to neurosurgery. If there was a coincident cause of retinal hemorrhage in a child, and the retinal hemorrhage pattern matched the known, reported pattern associated with that cause of retinal hemorrhage, the retinal hemorrhage for that child could not be attributed to neurosurgery alone, although neurosurgery could not be excluded as a possible contributing factor. If retinal hemorrhage was present on examination prior to neurosurgery, and the hemorrhage seen after neurosurgery matched the preoperative hemorrhage, the retinal hemorrhage could not be attributed to neurosurgery.

Results

The study included 267 children (median age, 3.9 years; IQR, 0.4-11.9 years), with adequate postoperative fundus examination results in 529 eyes. There were 5 children in whom only one eye was adequately examined due to inadequate dilation in the contralateral eye. Of the 529 eyes, 520 were examined following pharmacological pupillary dilation, and 9 were examined with sufficient natural pupillary dilation. All examinations were conducted by indirect ophthalmoscopy. Retinal examinations occurred at a mean of 3.1 days postoperatively, with 178 examinations

Table 1. Comparison of characteristics of children with and without retinal hemorrhage

RH status	Age, years, median (IQR)	Craniotomy (n = 101)	Burr hole–related (n = 57)	Ventricular CSF drain implantations (n = 103)	Spinal surgeries (n = 8)	Other neurosurgical procedures (n = 20)
Children with RH (n = 32)	0.5 (6.27)	15 (15%)	0	17 (17%)	0	0
Children without RH (n = 235)	5.8 (11.6)	86 (85%)	57 (100%)	86 (83%)	8 (100%)	20 (100%)

CSF, cerebrospinal fluid; *IQR*, interquartile range; *RH*, retinal hemorrhage.

occurring 0-3 days postoperatively, and 89 examinations occurring 4-7 days postoperatively. The study patients underwent a total of 289 neurosurgical procedures: 101 craniotomy procedures; 57 burr-hole related procedures; 103 ventricular cerebrospinal fluid drain implantations, including shunts and drains; 8 spinal surgeries; and 20 other procedures. Twenty-six children underwent more than one neurosurgical procedure.

Retinal hemorrhage was seen postoperatively in 32 (12%) of 267 children and in 53 (10%) of 529 eyes (Table 1). In 13 of the 32 cases, the retinal hemorrhage was present on a preoperative retinal examination, in the same pattern, and of same or lesser severity postoperatively. In all 19 of the remaining cases with retinal hemorrhage, there was a coexistent disease known to cause retinal hemorrhage, and the pattern of retinal hemorrhage matched the known pattern of hemorrhage associated with the coexistent disease. In 235 children, retinal hemorrhage was not present in either eye on post-neurosurgical ophthalmological examination. Overall, the prevalence of retinal hemorrhage definitively attributable to neurosurgery was 0% (95% CI, 0.00%-0.72%).

Of the 19 children with a coincident disease causing retinal hemorrhage, 13 had an unambiguous trauma history and/or nonocular signs diagnostic of trauma, and there was a retinal hemorrhage pattern consistent with trauma. In 9 of 13 cases, the child had AHT diagnosed by nonocular findings. One child had hypoxic-ischemic brain injury and otherwise unexplainable bruises in multiple areas; 6 children had acute-on-chronic subdural hematoma with other nonocular evidence of trauma, including rib fractures, bruises, oral injuries, and ligamentous injuries; 1 child with eventually fatal injury had subdural hematoma and diffuse cerebral edema with uncal herniation, bruising in multiple areas, and elevated liver function tests; and 1 child with confessed shaking by the caregiver had chronic subdural hematomas. In these cases of AHT, the retinal hemorrhage pattern was one of highly numerous, intraretinal and/or multilayered retinal hemorrhages diffusely distributed in the posterior pole and retinal periphery. The remaining 4 children had a history of accidental head trauma and consistent clinical findings. One child had diffuse intracerebral hemorrhage and edema with depressed skull fracture following a high-speed motor vehicle crash, and retinal hemorrhage in a pattern of papilledema-associated intraretinal peripapillary hemorrhages, as well as larger posterior pole intraretinal hemorrhages in both eyes; 1 child had an epidural hematoma from hitting their head on a coffee table, and a small right peripapillary intraretinal hemorrhage; 1 child had an epidural hematoma following a fall from a car and a few intraretinal posterior pole hemorrhages in both eyes; and 1 child had a large epidural hematoma, cerebral infarction, and parietal skull fracture following a fall from a bed to a hard floor, and bilateral moderately numbered, primarily intraretinal with a few preretinal hemorrhages, located in the posterior poles and retinal peripheries of both eyes.

Of the 19 children with coincident disease, 6 had no evidence or history of trauma and had retinal hemorrhages in patterns consistent with a medical disease that was also present. Five of these children had hydrocephalus-related increased intracranial-pressure and superficial peripapillary intraretinal hemorrhages around a swollen optic disk; 4 children had a brain tumor, and 1 child had congenital hydrocephalus with a shunt malfunction. One premature infant had acute retinopathy of prematurity and retinal hemorrhage along the fibrovascular ridge characteristic of the disease.

Discussion

We found no clear evidence that neurosurgery itself causes retinal hemorrhage in children. Of 289 postoperative neurosurgical cases examined, 32 (12%) cases had retinal hemorrhage after the procedure. However, in every case the retinal hemorrhage was either already present on preoperative examination and unchanged or resolving postoperatively, or the pattern of hemorrhage matched the recognized retinal hemorrhage pattern of a coexistent known cause of retinal hemorrhage, so the retinal hemorrhage could not be definitively attributed to the neurosurgical procedure, because the hemorrhage could have been caused by the coincident disease. While we cannot exclude the possibility that neurosurgery may have contributed to the retinal hemorrhage observed in the latter cases, the lack in our cohort of even a single case that was clearly attributable to neurosurgery, without a coincident potentially confounding condition present, suggests that neurosurgery is not likely to cause retinal hemorrhage.

Consideration of anticipated hemorrhage patterns that might arise from mechanisms through which neurosurgery could be hypothesized to cause retinal hemorrhage further supports the conclusion that neurosurgery is unlikely to cause retinal hemorrhage, because those patterns were not observed in our study.[4,5] One theory is that a procedural maneuver during neurosurgery could inadvertently cause a sudden, momentary hyperacute rise in intracranial pressure, such as occurs with arteriovenous malformation rupture, resulting in intraocular hemorrhage in a condition known as Terson syndrome; however, the well-described pattern of hemorrhage seen in Terson syndrome is primarily one of vitreous and preretinal hemorrhage near the optic disk and in the posterior pole, with intraretinal hemorrhage being a less prominent feature.[6-8] This pattern was not seen in any of the children in our study. A more likely effect of neurosurgery might be a sudden decrease in intracranial pressure, a therapeutic goal in many neurosurgical cases, but decreases in intracranial pressure are not known to cause retinal hemorrhage. Another theoretical mechanism might be increased resistance to outflow from the central retinal vein caused somehow by neurosurgery resulting in retinal venous occlusion and retinal hemorrhage; however, the radiating or "explosive" pattern of retinal hemorrhage associated with optic disk swelling and tortuous retinal veins that is characteristic of central retinal vein occlusion was not seen in any of the children. Finally, direct trauma to the optic nerve or stretching of the optic nerve from brain manipulation would be expected to result in optic nerve injury with optic disk changes, or central retinal artery occlusion with retinal whitening, neither of which feature retinal hemorrhage.

Based on our study results, neurosurgery does not appear to be a significant confounding factor in the clinical setting of child abuse evaluations. We found no evidence that neurosurgery independently causes retinal hemorrhage, and the patterns of hemorrhage that might be hypothesized to arise from neurosurgery, such as from Terson syndrome or venous occlusion, were not seen. The retinal hemorrhage we observed exclusively postoperatively was consistent with the patterns caused by coincident disease, including raised intracranial pressure, which causes papilledema-associated peripapillary intraretinal hemorrhages,[3,9] retinopathy of prematurity, which occurs in very young premature infants and has distinctive retinal findings, including abnormal fibrovascular growth at a border between vascularized and avascular retina,[10] and head trauma. Children with AHT without neurosurgery have retinal hemorrhages that in approximately two thirds of cases are numerous, multilayered, present throughout the posterior pole and extending into the retinal periphery.[11] The children with AHT in our study had such patterns and clear nonocular evidence of trauma. Retinal hemorrhage in AHT can be milder in severity or, in more severe cases, accompanied by circumlinear retinal folds or retinoschisis.[9,10] In cases of accidental head trauma in which the mechanism is a single blunt force impact, retinal hemorrhages are typically located in the posterior pole, few in number, and unilateral.[1,12] Retinal hemorrhage may be associated with epidural hemorrhage following accidental injury,[13] as seen in 3 of our patients, and more severe retinal hemorrhage may occur with higher severity accidental head trauma, as seen in our patient who was in a serious motor vehicle accident and in our patient with a large epidural hemorrhage resulting in brain infarction.[14,15]

Strengths of our study include ophthalmologist-performed fundus examinations and careful analysis of the potential confounding posed by coincident causes of retinal hemorrhage in children undergoing neurosurgery, facilitated by consideration of the specific patterns of hemorrhage associated with those causes. There are also limitations to consider. Intraretinal hemorrhages in children resolve over days following onset, and some examinations were performed after 72 hours, prior to which some intraretinal hemorrhages could have resolved.[16] However, the majority of examinations in the study were performed between 0 and 3 days, with 178 children examined in that interval. Preoperative examinations were performed for only 13 of the 32 children with retinal hemorrhage; had all children received pre-operative examinations, it may have enabled us to more directly identify hemorrhage attributable to neurosurgery. Cohort size is unlikely to have been a significant limitation, as the upper boundary of the 95% confidence interval for the prevalence of retinal hemorrhage attributable to neurosurgery was <1%. Selection bias is unlikely, as we did not exclude children based on type of neurosurgery procedure or coincident medical disease. Circular reasoning with regard to the presence of retinal hemorrhage and the diagnosis of trauma was not an issue, because in every case of head trauma, whether accidental or abusive, there was clear nonocular evidence of trauma.

While children undergoing child abuse evaluations may have intracranial hemorrhage necessitating that neurosurgery be performed before a retinal examination may be performed, neurosurgery does not appear to be a significant confounding factor in the interpretation of retinal hemorrhage findings. We found no cases where retinal hemorrhage could be attributed only to neurosurgery, and no retinal hemorrhage was seen in a pattern that might be expected to arise as a result of neurosurgery-induced intracranial pressure or retinal vascular related changes. In children who have had neurosurgery, when retinal hemorrhage is seen, another etiology for the hemorrhage should be sought.

References

1. Araki T, Yokota H, Morita A. Pediatric traumatic brain injury: characteristic features, diagnosis, and management. Neurol Med Chir (Tokyo) 2017;57:82-93.
2. Fong R, Konakondla S, Schirmer C, Lacroix M. Surgical interventions for severe traumatic brain injury. J Emerg Crit Care Med 2017;1:28.
3. Binenbaum G, Rogers DL, Forbes BJ, et al. Patterns of retinal hemorrhage associated with increased intracranial pressure in children. Pediatrics 2013;132:e430-34.
4. Hoving EW, Rahmani M, Los LI, Renardel de Lavalette VW. Bilateral retinal hemorrhage after endoscopic third ventriculostomy: iatrogenic Terson syndrome. J Neurosurg 2009;110:858-60.
5. Tabandeh H. Intraocular hemorrhages associated with endoscopic spinal surgery. Am J Ophthalmol 2000;129:688-90.

6. Muller PJ, Deck JH. Intraocular and optic nerve sheath hemorrhage in cases of sudden intracranial hypertension. J Neurosurg 1974;41:160-66.
7. Medele RJ, Stummer W, Mueller AJ, et al. Terson's syndrome in subarachnoid hemorrhage and severe brain injury accompanied by acute raised intracranial pressure. J Neurosurg 1998;88:851-5.
8. Khan SG, Frenkel M. Intravitreal hemorrhage associated with rapid increase in the intracranial pressure (Terson's syndrome). Am J Ophthalmol 1975;80:37-43.
9. Shi A, Kulkarni A, Feldman KW, et al. Retinal findings in young children with increased intracranial pressure from nontraumatic causes. Pediatrics 2019;143:e20181182.
10. Daniel E, Ying GS, Siatkowski RM, Pan W, Smith E, Quinn GE, e-ROP Cooperative Group. Intraocular hemorrhages and retinopathy of prematurity in the Telemedicine Approaches to Evaluating Acute-Phase Retinopathy of Prematurity (e-ROP) Study. Ophthalmology 2017;124:374-81.
11. Morad Y, Kim YM, Armstrong DC, Huyer D, Mian M, Levin AV. Correlation between retinal abnormalities and intracranial abnormalities in the shaken baby syndrome. Am J Ophthalmol 2002;134:354-9.
12. Bechtel K, Stoessel K, Leventhal JM, et al. Characteristics that distinguish accidental from abusive injury in hospitalized young children with head trauma. Pediatrics 2004;114:165-8.
13. Forbes BJ, Cox M, Christian CW. Retinal hemorrhages in patients with epidural hematomas. J AAPOS 2008;12:177-80.
14. Kivlin JD, Currie ML, Greenbaum VJ, Simons KB, Jentzen J. Retinal hemorrhages in children following fatal motor vehicle crashes: a case series. Arch Ophthalmol 2008;126:800-804.
15. Moran K, Reddie I, Jacobs M. Severe hemorrhagic retinopathy and traumatic retinoschisis in a 2 year old infant, after an 11 metre fall onto concrete. Acta Paediatr 2008;97(suppl 459):149.
16. Binenbaum G, Chen W, Huang J, Ying GS, Forbes BJ. The natural history of retinal hemorrhage in pediatric head trauma. J AAPOS 2016;20:131-5.