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Ocular and Associated Neuropathologic Observations in Suspected Whiplash Shaken Infant Syndrome

A Retrospective Study of 12 Cases

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We examined the eyes of 12 infants who died with the clinical and pathologic diagnosis of the shaken baby syndrome. The ocular histopathologic findings and the neuropathologic findings were compared. Preretinal, intraretinal, and subretinal hemorrhages were observed; hemorrhages of the superficial retinal layers and subsensory retinal space predominated. Retinal hemorrhages were found in 12 cases, intracranial hemorrhage was found in 11 cases, and cerebral edema was found in 10 cases. The intraretinal and periretinal hemorrhages were most prevalent at the posterior pole. Five cases had retinal folds. There was a low incidence of optic disc edema and choroidal hemorrhage.

Key Words: Ocular histopathology—Ocular neuropathology—Shaken baby syndrome.

The term "whiplash shaken infant syndrome" was coined by Caffey in 1974 to describe the whiplash-induced subdural and retinal hemorrhages, brain damage, and mental retardation found in casually or vigorously shaken infants (1). Subsequently, it became appreciated that only vigorous shaking elicited this constellation of findings, often in the absence of external signs of bodily injury. The whiplash shaken infant syndrome, or shaken baby syndrome, has become a recognized manifestation of child abuse caused by vigorous shaking of infants by the extremities, shoulders, or thorax (2). It has been suggested that the brain damage is exacerbated by the disproportionately large size of the infant's skull, weak cervical musculature, and susceptibility of the incompletely myelinated brain to trauma (3). The subdural and subarachnoid hemorrhages have been attributed to the shearing of bridging veins and direct contusion (2,4).

Retinal hemorrhages occur frequently in the shaken baby syndrome, but are neither invariably present nor pathognomonic of the syndrome. The pathogenesis of these hemorrhages remains controversial and there is a paucity of literature that documents the detailed ocular histopathology of the shaken baby syndrome. Retinal, vitreous, subdural optic nerve, and intrascleral hemorrhages were observed in seven of ten cases of suspected child abuse, all of which had external signs of blunt trauma (5). In this study, we undertook the systematic evaluation of 12 pairs of eyes from infants who died subsequent to suspected violent shaking.

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MATERIALS AND METHODS

Method of Selection

The eyes from all infants who died between 1985 and 1990 with the clinical and pathologic diagnosis of established or suspected shaken baby syndrome and who upon autopsy demonstrated retinal hemorrhages were obtained through the Office of the Chief Medical Examiner of the State of North Carolina. Of the 12 cases, four were categorized as having a "definitive shake injury"; that is, a specific history of shaking was elicited. The remaining eight cases were categorized as "presumptive shake injury"; that is, no history of shaking could be elicited, but the available evidence strongly suggested shaking as the cause of the brain injury. Time of survival following hospital presentation ranged from 0 (dead on arrival) to 480 h, with a mean survival time of 91 h.

Handling of Tissues

Eyes were immersion fixed in 15% unbuffered formalin for 48 h, washed with water for 3 h, and maintained in 60% ethanol. Following gross external examination, removal of a superior calotte, and internal examination with a dissecting microscope, portions of the globes were embedded in paraffin and processed for light microscopy. Horizontal sections of the globes and transverse sections of the optic nerves were stained with hematoxylin–eosin (H&E), luxol fast blue–periodic acid Schiff (LFB–PAS), and Prussian blue for microscopic evaluation. The ocular histopathologic findings were correlated with the pathologic findings of the central nervous system (CNS) as recorded in the medical examiners' final autopsy reports.

RESULTS

Clinical Findings

Of the 12 infants, 83% (10 of 12) were limp and unresponsive and 17% (2 of 12) were having seizures at the time of hospital admission. Male infants comprised 66.7% (8 of 12) and female infants comprised 33.3% (4 of 12) of the study group. The racial distribution was 66.7% (8 of 12) black and 33.3% (4 of 12) white. The age range was 1–21 months, with a mean of 7.6 months and a median of 4 months.

CNS and Ocular Findings

At autopsy, two of the four definitive cases demonstrated evidence of external head trauma (both with scalp contusions, one with a skull fracture); two of the eight presumed cases had scalp contusions, and one of these also had a facial bruise. Table 1 summarizes CNS and ocular pathology findings by case. The most common pathologic findings in the CNS were hemorrhage and edema, with 10 of 12 infants having acute subdural hemorrhage; 10 of 12 having acute cerebral edema as evidenced by increase in age-adjusted brain weight, swollen gyri, compressed sulci, and collapsed ventricles; and nine of 12 having acute subarachnoid hemorrhage. Acute ischemic neuronal necrosis and herniation of the cerebella tonsils were less common observations. The subdural hemorrhages ranged in volume from 6 to 50 ml and were located over the hemispheres. The subarachnoid hemorrhages were slight.

Schematic normal retina anatomy and distribution of hemorrhages are depicted in Fig. 1. Hemorrhages were most frequently located in the superficial layers (nerve fiber and ganglion cell layers) and beneath the sensory retina (Fig. 2) and were bilateral and approximately symmetric in all cases. Separation of the internal limiting membrane by red blood cells was observed in all of the globes with retinal hemorrhage (Fig. 3). Hemorrhage around the retrobulbar optic nerve was observed in nine of 12 cases; six were bilateral. Of these, all showed subdural hemorrhage and five of the nine showed subarachnoid hemorrhage (Fig. 4). Areas of hemorrhagic retinal detachment with formation of retinal folds were found in five of 12 cases. These folds were located in the posterior pole (Figs. 5 and 6). Macular edema involving primarily the outer plexiform layer was found in the five cases with retinal folds and in one additional case (Fig. 6). Peripapillary disruption of the retinal pigment epithelium was associated with subretinal hemorrhage in three cases (Fig. 7). Less common ocular lesions were

TABLE 1. *Central nervous system and ocular lesions*

Intracranial hemorrhage				Acute ischemic	Optic nerve									
SAH	SDH	SAH or SDH	Cerebral edema	neuronal necrosis	SAH	SDH	SAH or SDH	Retinal hemorrhage	Tonsillar hernia-tion	Optic disc edema	Macular edema	Hyphema	Posterior retinal folds	Optic nerve infarcts
9/12	10/12	11/12	10/12	7/12	5/12	9/12	9/12	12/12	3/12	2/12	6/12	2/12	5/12	2/12

Fractions are the number of cases with a specific finding per 12 total cases. SDH, subdural hemorrhage; and SAH, subarachnoid hemorrhage.

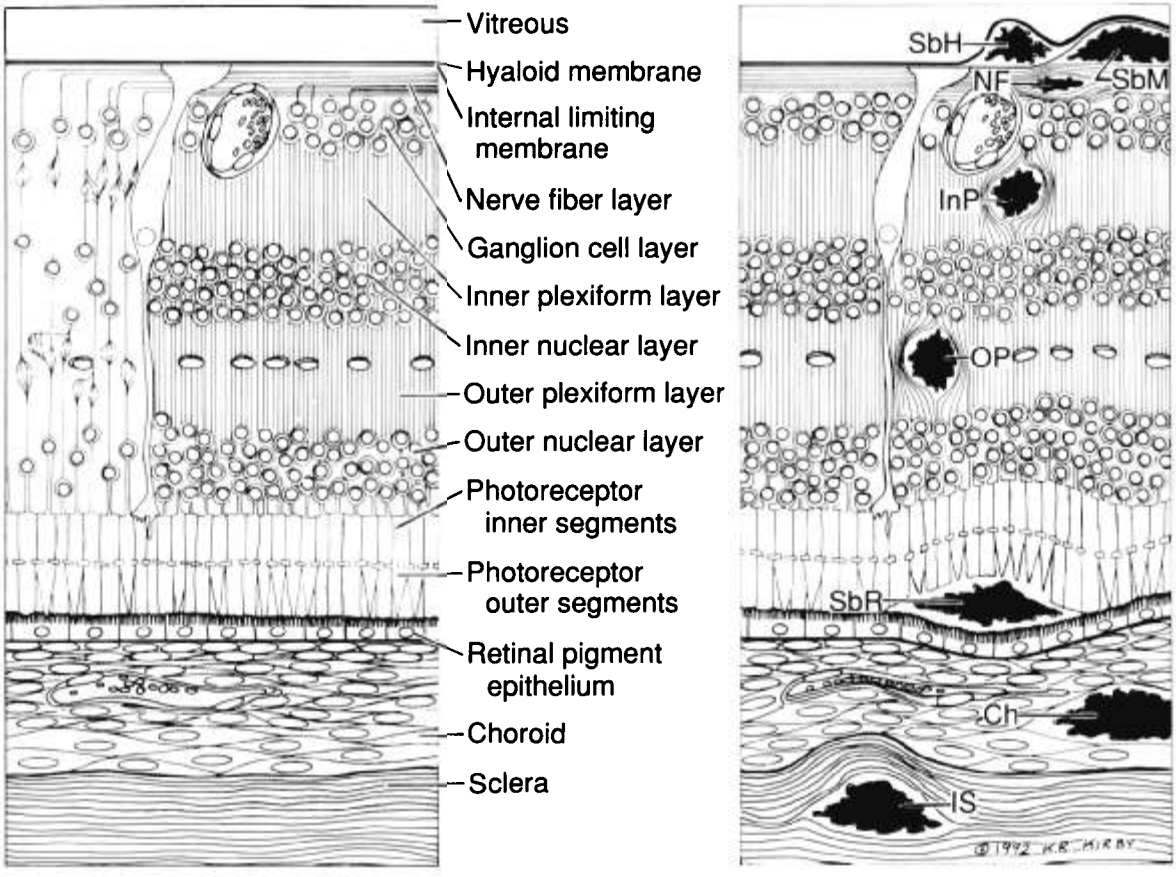

FIG. 1. Schematic anatomy of the retina **(left)** with associated schematic representation of the location of hemorrhages encountered in the shaken infant syndrome. SbH, subhyaloid hemorrhage; SbM, submembranous hemorrhage; NF, nerve fiber layer hemorrhage; InP, inner plexiform layer hemorrhage; OP, outer plexiform layer hemorrhage; SbR, subretinal hemorrhage; Ch, choroidal hemorrhage; and IS, intrascleral hemorrhage. In actuality, hemorrhages were likely to extend from one layer into another, with involvement of nuclear layers as well. Intrascleral hemorrhages were encountered only in the peripapillary area.

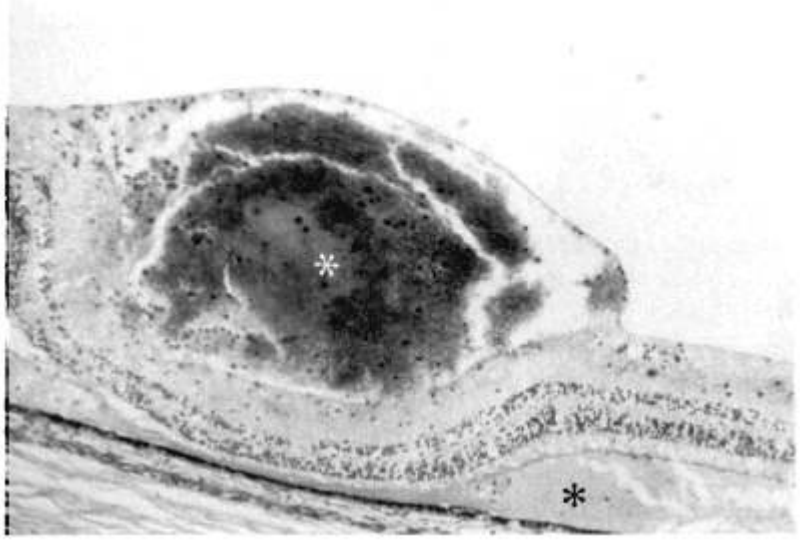

FIG. 2. Submembranous hemorrhage (white asterisk) and subretinal hemorrhages and protein (black asterisk) were seen in the posterior pole. LFB/PAS, original magnification ×100.

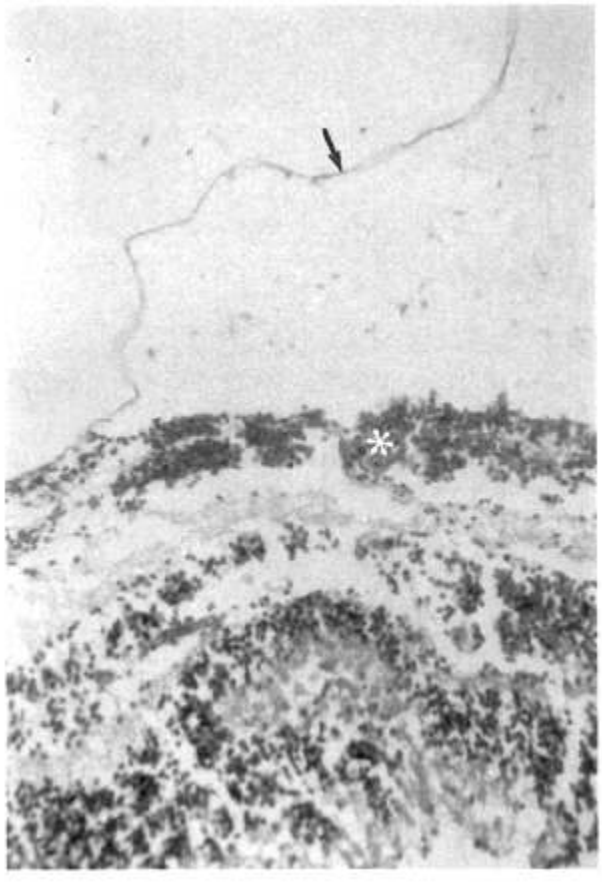

FIG. 3. Separation of the internal limiting membrane (arrow) was observed in this case associated with nerve fiber layer hemorrhage (asterisk). H&E, original magnification ×400.

optic disc edema, hyphema, and infarction of the optic nerve. The two cases with optic disc edema were also the two with optic nerve infarcts. One globe demonstrated optic atrophy and was one of the two cases that demonstrated previous hemorrhagic events of retina and optic nerve, as indicated by the presence of iron-positive macrophages.

Retinal Hemorrhages

Table 2 summarizes the locations of the retinal hemorrhages. Although the majority of hemorrhages were located in the superficial layers of the retina, hemorrhages were also frequently found in the middle and deep layers of the retina and in the subretinal space. When present in the outer plexiform layer, hemorrhages tended to aggregate and form cystic spaces (Fig. 8). Hemorrhage was occasionally found in the vitreous. More hemorrhages were seen posterior than anterior to the equator. All of the retinal hemorrhages were recent. Small choroidal hemorrhages were present in six of 12 cases, and five eyes from four cases demonstrated peripapillary intrascleral hemorrhage.

Retinal Hemorrhages and Associated CNS Events

Table 3 illustrates the frequency in which retinal hemorrhages appeared concomitantly with subdural and/or subarachnoid hemorrhages, cerebral edema, and acute ischemic neuronal necrosis of the brain. Two cases with retinal hemorrhages did not have subdural hemorrhage. Cerebral edema was associated with retinal hemorrhages in 10 of 12 cases.

DISCUSSION

The clinical findings reported in this study are similar to those observed by others (6). The shaken baby syndrome is an entity primarily observed in infants <2 years of age. All of the subjects in our study presented with signs of significant CNS dysfunction, as evidenced by unresponsiveness or seizures.

Hemorrhage around the retrobulbar optic nerve was seen in 75% of our cases. It has been suggested

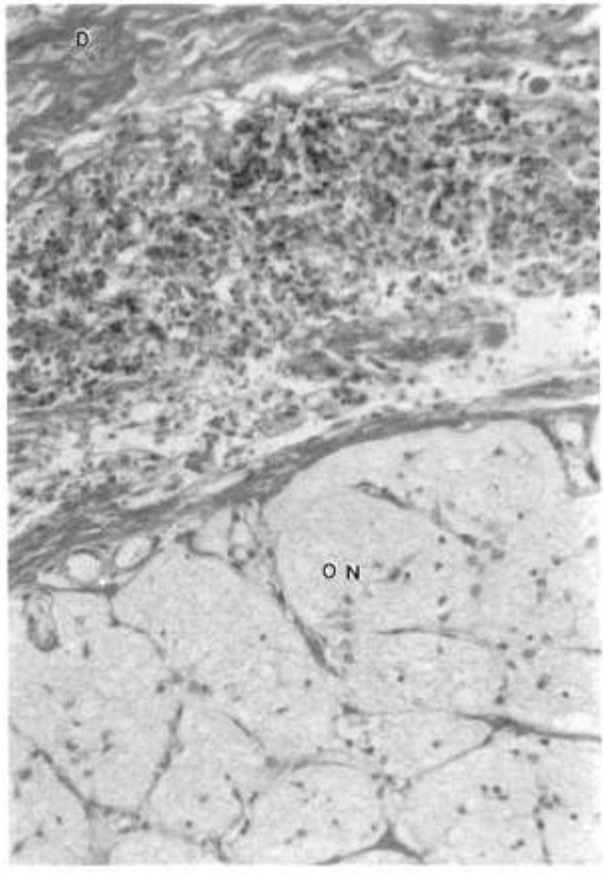

FIG. 4. Subdural and subarachnoid hemorrhages were present in nine of 12 cases. D, dura mater; and ON, optic nerve. H&E, original magnification ×400.

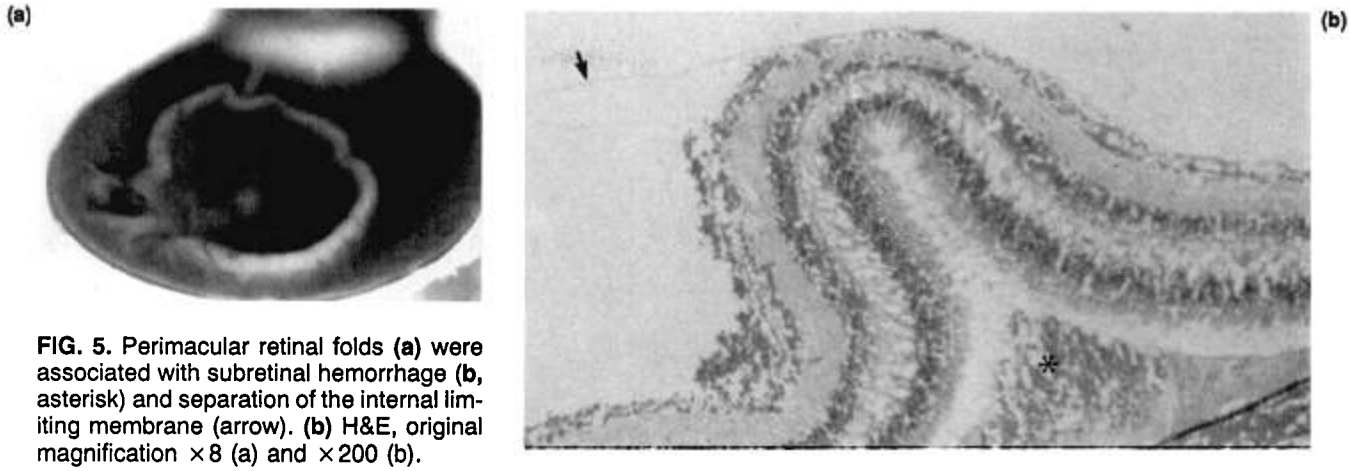

FIG. 5. Perimacular retinal folds **(a)** were associated with subretinal hemorrhage **(b,** asterisk) and separation of the internal limiting membrane (arrow). **(b)** H&E, original magnification ×8 (a) and ×200 (b).

that this hemorrhage may contribute to optic disc edema and, over time, to optic atrophy through direct mechanical compression of the optic nerve (7). In our series, however, these hemorrhages were small and thus seem an unlikely cause of nerve compression. A pathogenetic mechanism for these hemorrhages has been proposed by Lambert et al. (8), who observed that optic nerve sheath hemorrhages are seldom extensions of subdural or subarachnoid hemorrhages, and suggested that these hemorrhages occur subsequent to an acute increase in intracranial pressure, which suddenly distends the subarachnoid space, damaging the dural and bridging vessels embedded in the optic nerve vaginal sheath. Posterior retinal folds were present in 42% of our autopsied shaken baby syndrome infants. In each case, the retinal folds were associated with subretinal hemorrhages and macular edema. The macular edema was probably the result of separation of the internal membrane or vitreous traction. An interesting finding is that all of the retinal folds were perimacular; an explanation for the perimacular occurrence has been proposed by Greenwald et al. (9), who suggested that the area surrounding the macula is relatively sensitive to vitreoretinal tractional forces induced during shaking. While retinal folds may be commonly identified in normal infant eyes, presumably due to fixation artifact, the contention that the retinal folds are real and not postmortem artifacts is supported by (a) previous visualization in live infants (10) and (b) the association of these folds with subretinal hemorrhage. However, the incidence of retinal folds in our study was less than that reported in smaller studies and therefore not as likely to be a hallmark of shaking injuries as has been previously suggested (10).

Our findings agree with other reports that hemorrhage is most often in the superficial retina, notably the nerve fiber and ganglion cell layers (2,8). Our data indicate that the space between the sensory

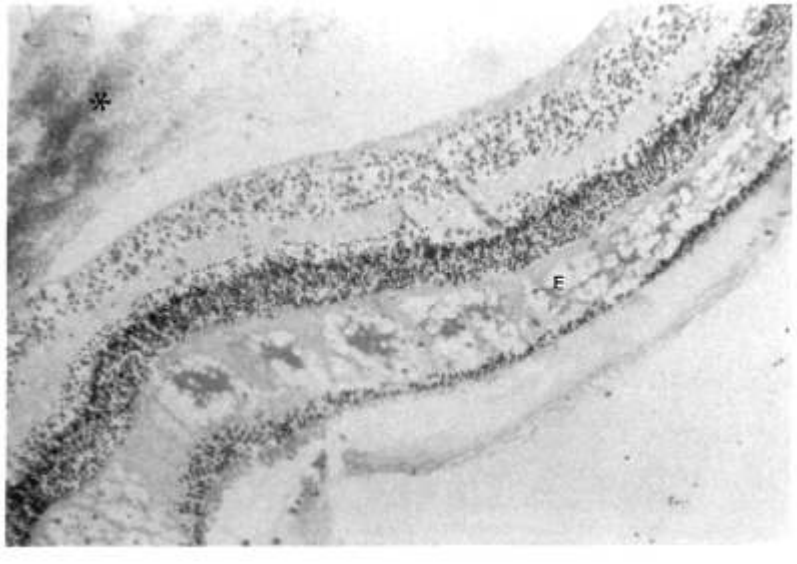

FIG. 6. Macular edema (E) was associated with retinal folds and in this case with preretinal hemorrhage (asterisk). H&E, original magnification ×200.

TABLE 2. *Patterns of intraocular hemorrhages by case*

Case no.	Vitreous		SHL		SML		NFL		GCL		IPL		INL		OPL		ONL		SRS		Choroid	
	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L
1	+	+				++	++	++	++	++	++	+	+	+	+	+	+	+	+	+		
2		+	+	+	++	++	++	++	++	++	+	+	+	+	+	+	+	+	+	+	+	+
3	+	+				++	++	++	+	+	+	+	++	+	++	+	++	+	+	+	+	+
4	++	+++	++	++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	++	++	++	+++	+++	++	+
5					++	+							+	++	++	++	+	+	+	+		
6	++	++			+	+	++	++	++	++	+	+	+	+	+	+	+	++	++	++	+	+
7	+		+		+++		+++		+++		+++		++		++		++		+++		++	
8						+	+	+	+	+	+											
9	+	+					++	++	++	++	+	+	++	++	+	+	+	+	+	+	+	
10	+	+			+	+	++	++	++	++	+	+	++	++	+	+	+	+	+	+		
11	+	+			++	++	++*	++	+	++	+	+	++		+				+			
12		+				+		++		++		+		++		+				+		

Case 2, perimacular retina fold, both eyes; case 3, perimacular retinal fold, right eye; Case 7, subfoveal hemorrhage, perimacular retinal fold and hemorrhagic necrosis of retina, right eye (left eye unavailable for examination); case 9, perimacular retinal fold, both eyes; case 10, perimacular retinal fold, both eyes; and case 12, right eye unavailable for examination.

R, right eye; L, left eye; SHL, subhyaloid layer; SML, submembranous layer; NGL, nerve fiber layer; GCL, ganglion cell layer; IPL, inner plexiform layer; INL, inner nuclear layer; OPL, outer plexiform layer; ONL, outer nuclear layer; and SRS, subretinal space.

+, mild; ++, moderate; and +++, severe hemorrhage.

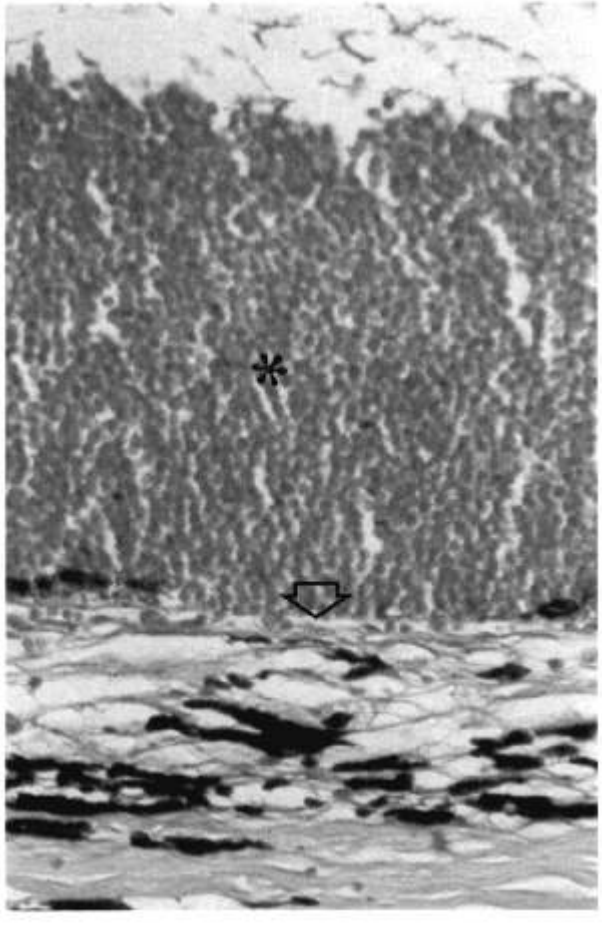

FIG. 7. Peripapillary absence of the retinal pigment epithelium (arrow) was associated with subretinal hemorrhages (asterisk) in three cases. H&E, original magnification ×400.

retina and retinal pigment epithelium is also a frequent site of retinal hemorrhage in shaken baby syndrome; this observation is supported by Lambert et al. (8), but disputed by Rao et al. (7). Subretinal hemorrhage could be secondary to choroidal hemorrhage via breaks in Bruch's membrane and the retinal pigment epithelium, or might also be due to intraretinal hemorrhage dissecting through the outer retina, as after rupture of arterial macroaneurysms (11). We observed breaks in the choroid associated with subretinal hemorrhages in three cases, suggesting a choroidal source. However, the disparity between choroidal and subretinal hemorrhages in our cases suggests that the hemorrhages located in the deeper retinal layers and subretinal space rep-

TABLE 3. *Cerebral lesions associated with retinal hemorrhage*

Case no.	SDH	SAH	Cerebral edema	Acute ischemic neuronal necrosis
1	+	+	+	+
2	+	+	+	
3		+*	+	+
4	+	+	+	+
5	+			+
6	+	+	+	
7	+**	+	+	
8			+	+
9	+	+		+
10	+*		+	+
11	+**	+		
12	+**	+	+	

SAH, subarachnoid hemorrhage; and SDH, subdural hemorrhage.

+, presence of a given lesion; *, lesion only present in right hemisphere; and **, lesion only present in left hemisphere. All other lesions were found bilaterally.

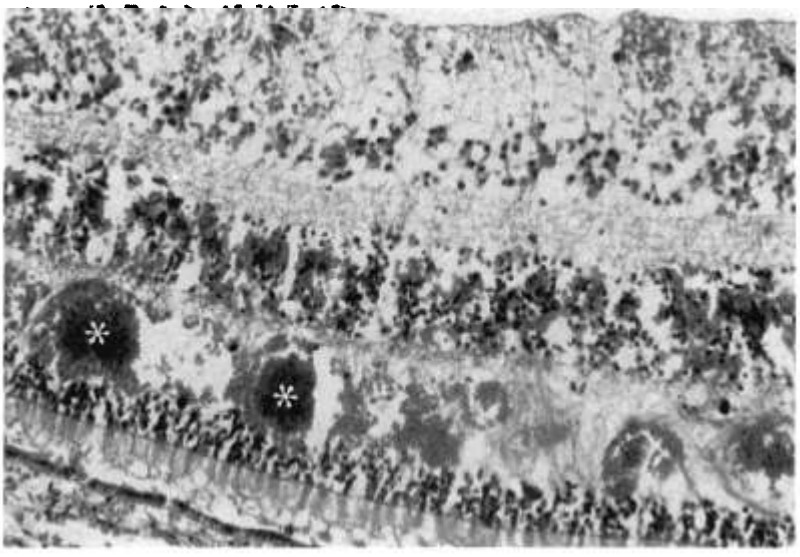

FIG. 8. Hemorrhage within the outer plexiform layer (asterisk) tended to accumulate within cystic spaces compartmentalized by Mueller cells. H&E, original magnification ×400.

resent dissection of hemorrhage from more superficial retinal layers.

Our observations fail to define further the pathogenesis of retinal hemorrhages in the shaken baby syndrome, which have been postulated to result from hemodynamic forces elicited by the compression of the infant's thorax (Purtscher's retinopathy) (12), central retinal vein obstruction from disc edema (13), vitreoretinal traction causing retinoschisis (14), an increase in intracranial pressure via cerebral edema or hemorrhage (Terson's syndrome) (14,15), or direct head trauma (5,16).

Purtscher's retinopathy is thought to be etiologically similar to Valsalva retinopathy, which is produced by increases in intravascular pressure (8). These syndromes are associated predominantly with superficial retinal and preretinal, but not subretinal or choroidal, hemorrhages. Thus, this mechanism is unlikely to explain the distribution of the hemorrhages seen in our study, which included 11 cases of subretinal and six cases of choroidal hemorrhages. The low incidence of disc edema noted in our cases obviates optic nerve swelling as a major cause of the retinal hemorrhages.

The subdural hematomas and diffuse axonal injury found in cases of the shaken baby syndrome have been attributed to the acceleration–deceleration forces causing shearing of vessels and axons (2). Likewise, the retinal hemorrhages found in this syndrome have been attributed to the vitreoretinal tractional forces induced by the shaking, causing retinoschisis and shearing of intraretinal blood vessels (9). While retinal folds and separation of the internal limiting membrane are likely to be caused by vitreous traction, which might well result in retinal hemorrhage, it is difficult to attribute the choroidal and intrascleral hemorrhages present in our cases to vitreous traction.

The parallel incidence of intracranial hemorrhages and cerebral edema with retinal hemorrhages (intracranial hemorrhage was seen in 11 and cerebral edema was seen in 10 of the 12 cases of retinal hemorrhage) implicates an increase in intracranial pressure as a possible pathogenetic mechanism of the retinal hemorrhages. Intracranial pressure would be increased by subdural hemorrhage and cerebral edema. It should be noted that we did not observe vitreous hemorrhage to the degree typically observed in Terson's syndrome. This is possibly because the superficial hemorrhages, or vitreoretinal tractional forces, were not sufficient to rupture the internal limiting membrane. Support for this suggestion is provided by case 4, where all retinal layers exhibited massive hemorrhage, the internal limiting membrane was ruptured, and vitreous hemorrhage was severe.

The observation that direct head trauma is seen in a high percentage of cases of fatal child abuse attributed to shaking (5,7) has led to the hypothesis that shaking alone may not be adequate to induce the observed ocular lesions, and that cases attributed to shaken baby syndrome may in fact be due to blunt head trauma by itself or in combination with shaking. Our data suggest otherwise, in that necropsy evidence of head trauma was seen in only five of 12 cases. However, two of four cases that were categorized as "definitive shaken baby syndrome" had evidence of head trauma, indicating that it may well be common for the two to coexist. We believe that the acceleration–deceleration injury of shaking is accurately attributed to a clinical syndrome, but we cannot dispute that other forms of

injury (such as blunt trauma) may manifest in a similar fashion. Increase in intracranial pressure arising from subdural hemorrhage and cerebral edema correlates highly with retinal hemorrhages, but is just as likely to represent a direct effect of trauma upon an adjacent tissue as a causal relationship. □

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