Is “Shaken Baby Syndrome” The Malignant Peak of a “Benign Hydrocephalus of Infancy” Iceberg?

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Abstract

In cases where carers have been convicted of Shaken Baby Syndrome the infant is twice as likely to be male as female. A similar 2:1 overrepresentation of males exists in Benign Hydrocephalus of Infancy, also known as Normal Pressure Hydrocephalus (NPH).

It has previously been shown that excessive intra-abdominal pressures, occurring in paroxysmal coughing, retching or vomiting, can be communicated to intracranial veins. It is proposed that the missing pressure in NPH is this transient cerebral venous hypertension, in particular that caused by violent retching and vomiting in pyloric stenosis which also shows a 2:1 MF ratio.

Distension of intra cranial veins and capillaries would temporarily increase brain volume which would stimulate the dura to signal suture growth to the dimensions occurring during, and just after, the transient pressure surge. The pressure surge in capillaries throughout the brain would force water out through their walls into the interstitium. This water would then diffuse out through the brain surface, producing subarachnoid collections. At higher pressures the capillary endothelial cell tight junctions would separate, exposing the porous basement membrane, through which proteins could escape. At higher pressures still, some capillaries and veins would burst, producing the symptoms of Shaken Baby Syndrome.

Keywords: Shaken baby syndrome; External hydrocephalus; Benign hydrocephalus; Pyloric stenosis; Venous hypertension; Vomit

Abbreviations: BHI: Benign Hydrocephalus of Infancy; CNS: Central Nervous System; CSF: Cerebrospinal Fluid; IJV: Internal Jugular Vein; IVC: Inferior Vena Cava; MRI: Magnetic Resonance Imaging; TVHH: Transient Venous Hypertension Hydrocephalus

Introduction

When Miller and Miller [1] searched MEDLINE using the Keywords "Shaken Baby Syndrome", "Retinal Hemorrhage", and "Subdural Hematoma" to select SBS convictions, they found male infants outnumbered female infants by about 2:1. They then searched MEDLINE selecting for External Hydrocephalus. This refers to fluid collecting outside the brain but inside the skull. It is associated with Macrocephally (large heads). They found that in External Hydrocephalus 68.8% were male, again approximately a 2:1 ratio.

Pyloric Stenosis blocks the outflow from the stomach into the intestines causing violent (projectile) vomiting. It has been shown [2] that the transient intra-abdominal pressures involved can, in some circumstances, arrive in the intracranial venous circulation, causing many haemorrhages currently assumed to indicate SBS. Here again males are significantly overrepresented (typically about 4:1) [3,4].

This raises the question “Is the gender bias found in Shaken Baby Syndrome, External Hydrocephalus, and Pyloric Stenosis a coincidence, or could it be a consequence of that in pyloric stenosis?” This is the subject of this article.

Forms of hydrocephalus

There is no lymphatic system in the brain, instead there is an analogous system, cerebrospinal fluid, (CSF), Figure 1. Most (80% [5]) of this fluid is produced in the brain ventricles, particularly the lateral ventricles, where Choroidal Epithelial cells draw surplus fluid from the brain’s interstitium. The CSF then leaves the lateral ventricles through the interventricular foramina and enters the third ventricle. From there CSF passes through the cerebral aqueduct into the fourth ventricle and out into the subarachnoid space through its medial and lateral apertures. The subarachnoid space is the space between the pia and arachnoid membranes. The pia lies close to the cerebral surface and follows it into sulci etc. whereas the arachnoid wraps around the organs bulging against them. Those formed between the hemispheres are known as Inter-hemispherial cisterns and those at the base of the brain as basal cisterns. Both can be seen in MRI scans. CSF from the various subarachnoid cisterns flows superiorly through the sulci and fissures on the medial and superolateral surfaces of the cerebral hemisphere [6]. The main site of absorption into the venous system is through the arachnoid granulations, especially those that protrude into the Superior Sagital Sinus.

The interventricular foramina and the cerebral aqueduct (Figure 1) are physically vulnerable to closure, blocking flow and causing pressure to build in ventricles upstream. This all occurs within the brain and the resultant forms of hydrocephalus are classed as internal hydrocephalus.

Hydrocephalus which appears not to originate within the brain, is described as external hydrocephalus. Zahl et al. in their extensive study...
review of the current knowledge of Benign Hydrocephalus of Infancy (BHI) [7] note a subgroup, “external hydrocephalus”. (In the following direct quotes are shown in italics) They say:

It is usually defined as a rapid increase in head circumference, combined with enlarged subarachnoid spaces as seen on neuroimaging – especially overlying the frontal lobes – and normal or only moderately enlarged ventricles. It occurs mainly during infancy. The word "benign" is often used together "external hydrocephalus" to reflect the common view that this is a self-limiting condition, occurring during infancy, and resolving spontaneously during childhood.

This subgroup is also referred to as Normal Pressure Hydrocephalus (NPH) because nowhere in the head has raised pressure been found. Nevertheless, it produces abnormal skill growth (macrocephaly) and other abnormalities typical of other forms of hydrocephalus. There appears to be some genetic factor involved. Zahl et al. [7] noted that around 40% of children with external hydrocephalus have at least one first degree relative with a large head (> 95th to 98th percentile).

Recently it has been proposed that external hydrocephalus is actually produced by pressure like other forms of hydrocephalus, but that the pressure is transient, Transient Venous Hypertension Hydrocephalus (TVHH) [2]. It is produced when blood is forced retrograde up the IVC, through the sinus venarum of the right atrium [9], and up the SVC to the jugular veins. If these valves are weak, or the pressure too high, blood at high pressure will overcome them and produce extreme cerebral venous hypertension [2]. The cerebral venous hypertension is thus extreme but transient. Although its effects can be observed, it is very unlikely that the pressure itself will occur in clinic.

Spontaneous Recovery

Spontaneous recovery from pyloric stenosis is possible and may be more common than supposed. Figure 2 shows plots of measurements made on an infant at visits to the infant’s paediatrician. At about two and a half months there is an abrupt halt to head and length growth but weight increases. This suggests that there was a temporary blockage of the alimentary tract, with widespread edema. This would be accounted for by inability of the pylorus to open. Two weeks later the pyloric muscle thickness/circumference ratio seems to have improved and all three parameters began to move towards normal. Such an event would have been classed as a benign “tummy upset”.

In the following the nature and consequences of the vascular damage are described, followed by derivation of the origin of various neuroimaging features in this form of external hydrocephalus.

Venous Hypertension

Transient Venous Hypertension Hydrocephalus (TVHH) differs
from other forms of hydrocephalus in that the relevant pressure is generated outside the head. Injury results from excessive cerebral venous pressure. There may be increases in intracranial pressure but they are secondary to vascular distension.

Capillaries in the brain and lung are formed of a tube of endothelial cells, whose edges are joined by watertight junctions (Figure 3).

These form the blood-brain barrier. This inner tube is surrounded by a fibrous basement membrane which is porous, but provides mechanical strength. At intervals pericytes lie between the endothelial cells and the basement membrane but they do not significantly affect the following considerations.

West et al. [10] showed that such capillaries respond to increased lumen pressure in three basic steps (Figure 4). For mild increases of lumen to interstitium pressure (LOW) water outflow through capillary walls increases resulting in local edema.

Next, in MEDIUM the tight junctions tear apart and endothelial cells start to peel back from the basement membrane. As these basement membranes are porous small proteins start to leak out into the interstitium. With further pressure rise small tears appear in the basement membranes allowing larger proteins to escape. These are described as "pressure sensitive pores" since they tend to close up when pressure returns to normal. Up to this stage the damage is reversible, rendering the process "benign".

With further increase in lumen pressure, (HIGH), the capillary wall ruptures allowing erythrocytes to escape forming petechiae and hematomas. Analogous apply to veins.

**CSF High protein content location**

Chazal et al. [11] studied the distribution of the protein content in the CSF of two infants showing excessive skull growth. Both had dilated pericerebral spaces. In a 2.5 month old female CSF in the ventricles contained 0.42 g/l, 0.5 g/l in a lumbar sample but 12.0 g/l in that withdrawn from the region of the cranial convexity. The corresponding figures for the four month male infant were 0.2 g/l from ventricles, 1.60 g/l from lumbar dural, but 10 g/l from cranial convexity. Chazal et al. [11] proposed that these remarkably higher protein concentrations above the anterior convexities compared to those in the ventricles and lumbar spine were due to stagnation of flow. The TVHH hypothesis predicts protein release between endothelial cells and through the capillary basement membranes.

**Rapid increase in head circumference**

A feature of Zahl’s definition of external hydrocephalus, quoted above, is a rapid increase in head circumference [7].

Figure 5 shows 3 SBS cases in which such a benign phase of rapid growth preceded the terminal event, (marked by a red star).

This would suggest that these cases had passed through the high protein leak stage figure 4 to capillary rupture.

**Occiput physiology and development**

Skull bones form in two ways. The primary mechanism follows the evolutionary process of initially producing a model of the future bone in cartilage. This cartilage model is then impregnated with calcium, converting it to bone. The bones of the occiput develop in this way. The second form of bone development bypasses the cartilage model and forms bone directly from mesenchyme at the site. This, described as dermal bone, is how the rest of the cranium develops.

**Cerebral Artery Hydrodynamics**

As early as in the embryo, two vascular subsystems can be seen in the head, that supplied by internal carotid arteries and that supplied by the vertebral arteries (Figure 6). Vertebral arteries supply the spine, the occipital lobe, and lower brain centres right round to the Posterior Communicating Artery, which links the two systems [12].
Neuroimaging patterns as evidence of transient venous hypertension

TVHH provides explanations of neuroimaging patterns in external hydrocephalus which confirm a venous hypertensive origin of this disorder.

Zahl et al. [7] describe the neuroimaging characteristics of external hydrocephalus as:

Frontal subarachnoid spaces that are enlarged beyond the upper limit together with normal to moderately enlarged ventricles. A concurrent finding is often a wide interhemispheric fissure and enlarged third ventricle and basal cisterns....The enlarged basal cisterns often were seen in external hydrocephalus but not in subdural hematomas.

So why are the frontal lobes in particular enlarged whereas in other forms of hydrocephalus there is fore/aft asymmetry? TVHH provides an explanation based on protection of the occipital lobe by the physiology of its vasculature. Occipital lobe venous drainage differs from that of the other lobes giving it some protection from venous pressure surges.

The vertebral vascular system dates back to the time when vertebrate fish were the highest forms of life. Eyes and cerebral pattern recognition were highly developed long before land vertebrates evolved. The occipital lobe retains this function and its connection to the vertebral vascular system. Most of the other arteries in the head and body developed later from vessels of the gill arches as they became redundant when land, air breathing, vertebrates evolved [13]. The internal carotid arteries which supply the other brain lobes are of this later origin. Both systems have a common supply from subclavian arteries and so are subject to same arterial pressure surges if they occur.

Cerebral Venous Hydrodynamics

Blood from lobes of the brain’s anterior circulation arrives in the sigmoid sinuses at the base of the brain, becoming internal jugular veins (IJV) as they leave the cranium [14] (Figure 7).

The Internal Jugular Veins are low resistance vessels that drain directly into the appropriate brachiocephalic vein. Jugular vein valves are just above this junction.

Blood from the occipital lobe has a much more tortuous path. From the occipital sinus it drains through the atlas bone into the top of the vertebral venous plexus. This plexus consists of many small anastomosing vessels which also receive blood from small veins from many other tissues [15]. Blood flows down through this dense venous plexus, passing through the transverse foramina of successive cervical vertebrae. When it reaches the level of the 6th vertebra it flows out into a vertebral vein (Figure 7). Like the jugular veins the vertebral veins also drain into the ipsilateral brachiocephalic vein and have a valve just above this junction. Thus at their lower ends both jugular and vertebral veins are subject to the same pressure (that in the brachiocephalic vein) and any superimposed pressure surge coming up the SVC. The critical factor in the present context is the time taken for sufficient blood to reverse flow through these veins to distend their respective intracranial venous beds if their valves fail. Lobes connected to the jugular veins will fill rapidly. Retroflow between the brachiocephalic veins and the vertebral circulation within the skull is impeded by the section of the vertebral venous plexus between vertebra 6 and the atlas. This flow has to deliver sufficient blood to distend vessels in the top of the spine, the brain stem, part of the scalp, neck etc. in addition to those in the occipital lobes, before a hypertensive surge can occur in the occipital lobes. In fact pressure in the occipital lobe may not even have time to rise sufficiently to cause significant transient oedema, let alone any damage, before the venous pressure surge has ceased. Thus the occipital lobes are protected by their more primitive vascular connections.

So it is not that the frontal lobes that are abnormal, their capillaries are behaving as expected when subjected to high lumen pressure, it is that the occipital lobes that are protected.

Frontal Subarachnoid Fluid Collections

It was previously mentioned that 80% of CSF is formed by chorionic plexuses in the brain ventricles. The rest comes from interstitial fluid exuded from brain capillaries (Figure 1). Cormack [16] puts it thus:

*Interstitial Fluid Formed within the CNS contributes to cerebrospinal fluid. As in any other vascularised tissue fluid is formed by brain capillaries. Instead of draining into lymphatics, the excess tissue fluid moves through the network of intercellular channels and leaves the brain by way of the pemeascular spaces that accompany its vasculature, and also directly its outer and inner surfaces, thereby entering the sub arachnoid space and brain ventricles. This fluid serves as an auxiliary*
source of cerebrospinal fluid, contributing approximately 10% to 20% of the total volume.

This direct outflow is independent of chorionic villus behaviour. It normally results from the small difference of pressure across capillaries. Surge pressures may 10 to 100 times this, and the resulting flow will add a significant increment to subarachnoid fluid volume.

Macrocephally

It is well known that if cerebrospinal fluid is overproduced, or its outflow is obstructed, cranial growth becomes excessive (Hydrocephalus). It is commonly assumed that the skull is simply “stretched” by the excessive CSF pressure, but actually skull growth is regulated to respond to increased brain volume. Those interested in the details of this process are referred to the excellent review article by Opperman [17]. In brief, the cranium starts in the embryo as a mesenchyme derived membranous half “balloon” lined with a primitive dura mater [18]. As the brain grows the dura mater gets stretched and responds by diffusing signaling material into the cranial membrane which stimulates chondrogenesis but inhibits osteogenesis. Ossification centers develop within this cranial membrane, typically at the positions of the centre of future skull bones. Ossification stiffens the cranium, so the dura under these newly forming skull bones no longer gets stressed and no longer stimulates local growth. The remaining spaces between these bone plates are designated “sutures”. Beneath sutures the dura continues to stimulate chondrogenesis keeping the edges of these nascent bone plates apart. If the ossified edges meet, the underlying dura is no longer stretched and local skull edges will unite prematurely. In the mouse it has been shown that if the dura is stripped off the cranial membrane the bone plates develop abnormally and unite prematurely [18]. In normal skull development, the dura under the sutures continues to be stretched, maintaining the sutures in their plastic state, and allowing the nascent skull bones to expand.

This process does not require continuous stretch. Tholpady et al. [19] maintained posterior intrafrontal sutures of the rat in vitro at a tension of 3 mN for 30 minutes per day and found that they remained patent after 14 days whereas those maintained under no tension had fused. This shows that the chondrogenesis augmentation and osteogenesis inhibiting signaling materials remained active for some time after removal of the stress. Thus the continuous stretch in internal hydrocephalus and the intermittent but repeated stretch occurring in TVHH would be expected to result in similar excessive cranial growth. In infants the Monroe-Kelly doctrine does not apply because the skull is growing faster than the brain for some time, i.e. it is macrocephalic (Figure 8a).

This is consistent with Zahl et al. [7] comment: “Some have even suggested that the skull is growing faster than the brain for some time, giving a transient subarachnoid CSF accumulation”.

Assuming jugular veins on both sides are equally overcome by pressure surges the skull will become symmetrically macrocephalic. If only the valve on one side fails, the other hemisphere would be expected to develop normally. On the valve failure side excessive osteogenesis and chondrogenesis signalling materials would stimulate accelerated growth. This would cause a bulge in the skull, figure 8b, which might be described as a form of plagiocephaly.

Incidence

Hydrocephalus

Zahl et al. [7] define Hydrocephalus as a relatively common neuropsychiatric condition, with an incidence of about 0.9 per 1,000 births. It is defined as the abnormal accumulation of cerebrospinal fluid (CSF) within the ventricles and/or subarachnoid spaces, leading to an increase in intracranial pressure.

The subtype “external hydrocephalus” is usually defined as a rapid increase in head circumference, combined with enlarged subarachnoid spaces as seen on neuroimaging, especially overlying the frontal lobes – and normal or only moderately enlarged ventricles. It occurs mainly during infancy, and the subarachnoid space gradually decreases and disappears over the next years.

Miller and Miller [1] searched MEDLINE for macrocephally (enlarged heads) associated with Intracranial Extraxial Fluid Spaces (also known as External Hydrocephalus, Benign Subdural Collections of Infancy, Benign Subdural Hygroma etc.). Those reporting gender ratios found a mean of 68.8% were males a ratio of 2.2:1.

This is consistent with Zahl et al. [7] comment that: “It seems that about two thirds of children with external hydrocephalus are boys.

Pyloric stenosis

Pyloric Stenosis, the malady proposed here as producing the cerebral venous hypertension surges, is also more common in boys. Estimates vary from four to six males for each female case [3,4,21,22]. Of course this is only the pyloric stenosis detection rate, not the hydrocephalus rate, but it does predict a strong gender bias in the production venous hypertension surges.

Shaken Baby Syndrome

Miller and Miller [1] studied Traumatic Brain Injury of Infancy, (TBII). Relevant scientific articles published between 1966 and 2005, were found by searching MEDLINE with the keywords “Shaken Baby Syndrome”, “Retinal Hemorrhage”, and “Subdural Hematoma”. Relevant articles referenced in these articles and published before 1996, were also included.

If there were no association of gender with TBII or with macrocephaly, the expected percentage of males would be 51.4%. Out of 1,609 cases where the carers were convicted of Shaken Baby
 Syndrome, 62.6 % were males, again roughly twice as many male as female infants.

Conclusions

The concept that transient abdominal pressure surges during violent retching or vomiting may be sufficient in some infants to overcome jugular venal valves and arrive in the cerebral venous circulation is consistent with the imaging patterns seen in external hydrocephalus. It supplies the missing pressure component in "Normal Pressure Hydrocephalus". The factors seen on imaging, (fluid collections of high protein content over the frontal convexities, enlarged and sometimes distorted heads etc) further support this concept. It follows that the overrepresentation of males in Pyloric Stenosis, which is the source of the pressure, should also appear in External Hydrocephalus; and it does. The elevated concentration of protein found by Chazal et al. [11] in fluid in the subarachnoid space above frontal convexities in cases of benign hydrocephalus indicates that capillary endothelium was peeling off the basement membrane. At this stage damage would not be visible and would be reversible, i.e. the situation would appear benign. However if lumen pressures increased further the capillaries would burst as the basement membranes failed. This would allow whole blood to escape, producing the haemorrhages of "Shaken Baby Syndrome". Furthermore, if SBS conviction cases are actually simply External Hydrocephalus at higher pressure, SBS would also be expected to show a similar 2:1 male dominance, which Miller and Miller [1] did find.

Thus it would seem that some cases of apparent Shaken Baby Syndrome may merely be the malignant pressure peak of a benign hydrocephalus iceberg (Figure 9).

Figure 9: The External Hydrocephalus Iceberg. Stages in failure of brain capillary walls with increasing lumen squeeze pressure.

It is further concluded that a considerable proportion of convictions for SBS must be due to this high pressure version of external hydrocephalus, (TVHH), for it to dominate the male/female ratio.

Summary

1. External Hydrocephalus (Normal Pressure Hydrocephalus (NPH)) involves pressure like other forms of hydrocephalus but the source of pressure is outside the head and is transient.

2. If this transient pressure is sufficient to break through the jugular vein valves the resulting cerebral venous hypertension produces hydrocephalus, Transient Venous Hypertension Hydrocephalus (TVHH). If the pressure surge is high enough SBS-like damage will also occur.

3. Because the origin of this pressure is Pyloric Stenosis the incidence of this form of "SBS" will mirror that of Pyloric Stenosis, explaining the 2:1 male overrepresentation in "SBS" convictions.

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