An infant with subdural hematoma and retinal hemorrhages: does von Willebrand disease explain the findings?

Arne Stray-Pedersen · Sigrid Omland · Bård Nedregaard · Sjur Klevberg · Torleiv Ole Rognum

Abstract An 11-month-old girl presented to hospital with a massive subdural haematoma and bilateral retinal haemorrhages following an allegedly minor fall. There were no external signs of bruising and no prior bleeding tendency was reported. Although initial analyses were normal, repeated testing of the coagulation-fibrinolysis system led to a diagnosis of mild von Willebrand disease (vWD) Type I. It was concluded that minor head trauma as described by the parents, in the presence of such a coagulation disorder, could explain the findings. Police charges against the parents, initially accused of child abuse, were withdrawn. Retinal haemorrhages in infants with vWD have not been previously reported. This case highlights the importance of considering vWD as a possible contributory factor in cases of infant head injury.

Keywords Von Willibrand disease · Retinal hemorrhage · Child abuse · Subdural hematoma

Introduction

Non-accidental head injury in infants (NAHI) is a major cause of death and brain morbidity in early childhood [1]. Common manifestations are intra-cranial, most often subdural, hematoma and retinal hemorrhages, often accompanied by encephalopathy (hypoxic ischemic/diffuse axonal injuries), as well as various degrees of external bruising and fractures of the ribs and long bones [2, 3]. The injuries in NAHI are most likely caused by violent shaking of the infant and/or blunt force violence [2, 4]. In contrast, based on clinical evidence, subdural hematoma and retinal hemorrhages are unlikely to occur after a fall from low height [5, 6]. However, both metabolic and soft tissue disorders as well as coagulation defects may increase an infant’s vulnerability to mild head trauma and must be ruled out [7]. Accuracy in the diagnosis of NAHI may have significant implications in possible civil and criminal proceedings.

Von Willebrand factor (vWF) is a multimeric glycoprotein which mediates platelet adhesion and serves as a carrier of coagulation Factor VIII. Von Willebrand Disease (vWD) is characterized by an abnormality or deficiency of vWF resulting in varying degrees of bleeding tendency [8]. The most common variant of vWD is Type I, a partially quantitative defect in vWF having a prevalence of approximately 1% in the general population [9, 10]. Patients with mild Type I vWD may not have clearly impaired clotting and may lead a nearly normal life. They may, however, present clinically with mild gastrointestinal,
cutaneous and mucosal bleeding, or with hemorrhage following surgery [8].

**Case report**

An 11-month-old girl of Norwegian ethnicity was admitted to hospital from her home. Her parents explained that the girl had been standing on her feet, holding on to a shelf, when she suddenly fell backwards and hit her head on a carpeted wooden floor. She immediately cried, but shortly afterwards while lying on her mother’s lap, stiffened with neck hyperextension and closure of the eyes. She was not reacting to her parents’ attempts to establish eye contact. Upon admission to hospital she had reduced consciousness and a dilated left pupil. No external sign of trauma was observed. A CT examination of the head shortly after admittance revealed an extensive acute subdural hematoma (SDH) with high attenuation over the left cerebral hemisphere along the frontoparietal area. The hematoma extended to the interhemispheric subdural space, lateral to the superior sagittal sinus. There was an obvious mass effect with a midline shift to the right and partial compression of the left lateral ventricle. In addition, there was also a subdural fluid collection in the left frontal area, ventral to the acute SDH. The attenuation of this compartment was low, but significantly higher compared to that of the cerebrospinal fluid. Thus it was suggestive of SDH in the chronic stage. Additionally, there was fluid around the right frontal lobe including the interhemispheric fissure, probably representing an enlarged subarachnoid space (Fig. 1).

Emergency neurosurgery followed and a brownish red hematoma was removed. A blood transfusion (300 ml) was administered during the operation. The following day, an MRI examination of the head was performed. Apart from the postoperative changes, including an epidural fluid collection along the left hemisphere, there was a remnant of the acute subdural hemorrhage in the parietal region. A small collection of subdural fluid could be seen in the posterior fossa along the occipital bone, probably extending a short distance along the tentorium cerebelli. The signal of this fluid was highly suggestive of hemorrhage in a subacute or more chronic stage. Apart from the finding of a probable micro-hemorrhage in the right cerebellar hemisphere, there were no signs of diffuse axonal injury in the brain parenchyma. Diffusion imaging gave no indication of hypoxic-ischemic injury to the brain. Fundoscopy with indirect ophthalmoscope through medically-dilated pupils was performed shortly after surgery. The findings were photographically recorded using a Ret-Cam retinal camera. Numerous hemorrhages in all retinal layers, of all sizes, and in all visualized sectors were observed in both eyes, with several of them having a whitish center, a Roth spot [11]. In the left eye both a preretinal hemorrhage and several optic disc hemorrhages were observed. (Fig. 2).

Clinical forensic examination was performed the day after admission. No external evidence of trauma was disclosed, no extracranial swelling was observed on the pre-operative CT-scan and no fractures were evident on full body radiography. Laboratory analyses on the day of admission showed: Hb—8.3 gr/100 ml, platelets—397 $\times$ 10^9/l and leucocytes—22.4 $\times$ 10^9/l. The bleeding time (Cephotest) was within normal range, and fibrinogen was 2.0 gr/l. Later, metabolic screening of urine was performed with negative results. Coagulation factors were found to be within normal range (Table 1).

Due to the inconsistency between the reported trauma and the severity of the injuries, the case was reported to the police, and the parents were accused of abuse. Medical experts concluded that the infant probably had undergone two traumatic events, one occurring 1–2 weeks earlier, and

![Fig. 1 CT scan shortly after admittance: a Axial (slightly oblique) image level near vertex shows extensive acute SDH over the left cerebral hemisphere (black arrows) and enlarged subarachnoid spaces (white asterisks) along the right frontal lobe. b Axial image, level of the top of the side ventricles and c coronal image show subdural fluid of both high and low attenuation, suggestive of acute (black arrow) and chronic (white arrow) SDH](image-url)
the other shortly before hospital admission. The findings of retinal hemorrhages combined with subdural hematoma were suggestive of an acceleration-deceleration injury mechanism, most likely due to episodes of violent shaking. One or more minor falls from a standing height were an unlikely mechanism of injury, with repetitive events of abusive violent shaking a more likely explanation of the injuries.

The girl made a slow, but apparently full recovery. Child Protection Services (CPS) concluded that the parents should be allowed continued caretaking of the child under CPS guardianship. The following year the girl had not sustained injuries or displayed further bleeding symptoms.

Six months after the incident, further analysis of coagulation parameters suggested that the girl suffered from Type 1 vWD. Due to this new finding, the case was re-evaluated and medical conclusions were modified. As a result of the presence of vWD type 1, the possibility that minor head traumas causing the injuries could not be ruled out. The police charges were subsequently withdrawn. The parents also underwent laboratory testing, but displayed normal vWF antigen and activity tests.

**Table 1** Laboratory analyses of coagulation parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Initial laboratory analyses</th>
<th>Laboratory analyses 6 months later</th>
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<tbody>
<tr>
<td>INR</td>
<td>1.1 (1–2)</td>
<td>1.0</td>
</tr>
<tr>
<td>Cephotest</td>
<td>35 s (30–42)</td>
<td>31 s</td>
</tr>
<tr>
<td>F VIII</td>
<td>76% (50–150)</td>
<td>48%</td>
</tr>
<tr>
<td>F IX</td>
<td>101% (50–150)</td>
<td>64%</td>
</tr>
<tr>
<td>vWF:Ag</td>
<td>80% (50–200)</td>
<td>33% control test: 43%</td>
</tr>
<tr>
<td>vWF:RCo</td>
<td>81% (50–200)</td>
<td>47% control test: 42%</td>
</tr>
<tr>
<td>vWF multimeric analysis</td>
<td>Reduced quantity, normal pattern</td>
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**Discussion**

Subdural hematoma and retinal hemorrhages in infants are strongly suggestive of NAHI [2]. SDH is often extensive and most prominent along the posterior parts of the brain. It arises from rupture of bridging veins, which extend from the cortical surface to the dural venous sinuses resulting in hemorrhage into the subdural space. Stretching and tearing of the bridging veins may occur when the head is subject to abrupt acceleration-deceleration injury mechanisms such as a fall from a height or in violent, abusive shaking [4]. Interhemispheric extension of the SDH is clearly suggestive of an anterior-posterior shaking mechanism, but may also appear with high force accidental trauma.

Retinal hemorrhages found in infants with NAHI are typically extensive, located in several layers of the retina and extending to the ora serrata [4, 12]. The injury mechanism behind such retinal hemorrhages is most likely rapid acceleration-deceleration motion creating shearing forces which in turn directly or indirectly cause tearing of capillary membranes in the retina [12]. Additional findings of injury to the brain parenchyma will further increase the suspicion of NAHI. It may present as brain contusion and diffuse axonal injury (DAI), or diffuse edema/hypoxic-ischemic injury, the latter often with diffuse, large areas with restricted diffusion but no hemorrhage. In infants and small children with serious non-accidental injury, the diffuse hypoxic-ischemic pattern is much more common than diffuse axonal injury [13, 14]. While contusion and DAI are trauma specific findings, hypoxia-ischemia is not, and other causes must be ruled out.

Subdural hematoma and in particular retinal hemorrhages are rare in infants and small children suffering witnessed accidental trauma [1]. Lyons and Oates reported in a retrospective study of 207 small children who fell out of bed (0.6–1.35 m) while in hospital, that none sustained life-threatening injuries such as intracranial hemorrhage. There is in fact abundant evidence that minor head trauma, in the absence of underlying medical conditions, is extremely unlikely to be associated with severe intracranial injury or retinal hemorrhages [1, 15, 16]. However,
sporadic cases, including a fatal video-taped short fall in a 23-month old child have been reported [17]. Extensive retinal hemorrhages have been described in victims of accidental high-energy deceleration trauma such as motor vehicle crashes, as well as in NAHI [18].

Centrally located retinal hemorrhage combined with vitreous hemorrhage may occur secondary to an abrupt increase in intracranial pressure i.e. subarachnoidal bleeding, a finding described as Terson syndrome in adults. Whether this can be found in children is uncertain [19]. In a suspected case of NAHI, both birth injuries as well as metabolic disorders and diseases of the hematopoietic system such as anemia, leukemia, polycythemia and hemophilia must be ruled out. Recent studies have shown that small SDH and retinal hemorrhages may be seen in asymptomatic newborn infants, especially after instrumental vaginal deliveries. However, such hemorrhages appear to heal spontaneously and are unlikely to be present after 2 months of age [20, 21].

The widely used term NAHI does not depict the mechanism of injury but includes both inflicted impact trauma and violent shaking. Whether inflicted or accidental, blunt impact to the head usually requires a certain amount of force which normally leads to visible skin lesions such as bruising or abrasions. In the case presented, the absence of such lesions indicates that the applied force might have been comparatively low. A fall from a major height or inflicted blunt impact to the head thus seems implausible. CT scan showed both high and low attenuation subdural fluid, suggestive of hematoma of new and older ages (acute and chronic SDH). The exact timing of subdural hemorrhage at different ages with MRI is uncertain and is often not possible to determine. The combination of MRI and CT can, however, give complementary information regarding the different stages of blood-degradation products that may be highly relevant to the dating of hemorrhages [22]. In NAHI infants allegedly subject to abusive shaking, the subdural hematoma is typically of such mixed density and is often localized interhemispherically along the falcotentorial membranes [23]. However, in the present case the acute SDH were predominantly located unilaterally, which might favour a blunt impact to the head rather than shaking.

Type I vWD is a coagulation disorder characterized by a partial, quantitative deficiency of vWF and may lead to various degrees of bleeding tendency. Laboratory investigations may reveal normal international normalized ratio (INR) and normal or slightly prolonged bleeding time (Activated partial thromboplastin time—Cephotest), but reduced vWF concentration (vWF:Ag) and reduced ristocetin cofactor activity (vWF:RCo). Factor VIII coagulant may be normal or slightly reduced. The vWF multimeric pattern is normal. Much of the genetic variation in vWF levels is due to blood type, and patients with Type O have levels 25% lower than non-Type O. The patient presented in this report had Type O blood.

Patients with Type I vWD may show no signs of bleeding tendency. Hemorrhage usually involve mucous membranes and skin, and are of mild to moderate severity. Life-threatening bleeding is rare in persons who have type I vWD, but may occur in Type II and III [27]. In the literature we have only found three patients, aged 13, 19 and 33 years, with retinal hemorrhages associated with vWD [27, 28]. Although analysis for vWD in most countries is routinely carried out in cases suspicious of NAHI, no cases have been presented in the literature thus far. In the present case, the coagulation parameters, vWF:Ag and vWF:RCo, were normal initially. The slight reduction in both vWF:Ag and vWF:RCo as well as in FVIII was first detected 6 months later in a follow-up control at the local hospital. The test results were confirmed in a third test performed 3 weeks after (Table 1). Shortly after admission the girl received two units of red blood cell transfusions (300 ml) as part of the initial life-preserving treatment in supplement of the neurosurgery. Prior to the transfusion, vWF:Ag and vWF:RCo were unfortunately not tested, the first test being performed 7 days later. We question whether the blood transfusion may have contributed to the initial false negative test results.

The possibility of a chronic SDH spontaneously rebleeding is considered unlikely [4]. However, it is generally assumed that less traumatic force is needed for acute SDH to occur in patients with an enlarged subdural space i.e. due to chronic SDH. The enlarged space may lead to stretching of the bridging veins which hypothetically may increase the susceptibility to rupturing [24, 25]. Healing of SDH is by formation of a granulating membrane with thin-walled capillaries, and it has been postulated that these capillaries may be prone to bleed after a minor event [26]. The presence of a vWD coagulation disorder may further enhance the susceptibility for rebleeding. Reviewing the present case in light of this knowledge, the presented explanation that the infant suffered a fall on the head from a standing position cannot be ruled out as a possible injury mechanism initiating the acute SDH. However, the chronic SDH still needs to be explained as well as the retinal hemorrhages. Multi-layered extensive retinal hemorrhages are strongly indicative of a shaking event. It might be argued that the intensity of violence sufficient to cause rupture of bridging veins and retinal capillaries is unaffected by the vWD coagulation disorder. On the other hand, slight venous or capillary ruptures may possibly occur after minor trauma, but are in the case of a normal platelet adhesion ability promptly sealed. The presence of Type I vWD may indeed cause extensive bleedings, but it remains questionable...
whether this coagulation disorder may increase the susceptibility for intracranial and retinal hemorrhages.

In fatalities, coagulation disorders are extremely difficult to diagnose. Doctors appearing as medico-legal expert witnesses should bear this fact in mind, especially when other signs of abuse are lacking. Without the full triad of subdural hematoma, retinal hemorrhages and encephalopathy (the latter was not present in the current case), the conclusion that observed injuries are caused by shaking must be made with great caution.

Key Points

1. Subdural hematoma and retinal hemorrhages in an infant are findings suspicious of abuse.
2. Such injuries may be caused by shaking or other physical abuse, but accidental injury as well as various rare pathological conditions, i.e. metabolic and coagulation disorders must be considered.
3. Repeated laboratory testing may be necessary in order to reveal minor coagulation disorders such as von Willebrand disease Type 1.
4. The significance of von Willebrand disease as a possible contributory factor in infants with subdural and retinal hemorrhages should be further addressed.

References