



The role of prothrombotic factors in the ocular manifestations of abusive and non-abusive head trauma: A feasibility study[☆]

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ARTICLE INFO

Article history:

Received 1 February 2011

Received in revised form

12 September 2011

Accepted 22 November 2011

Available online 8 May 2012

Keywords:

Shaken Baby syndrome

Retinal hemorrhage

Feasibility study

Prothrombotic factors

Thrombophilia

Head trauma

ABSTRACT

Objectives: Retinal hemorrhage is a cardinal manifestation of abusive head injury. Thrombophilia is relatively common in the general population and in adults can be associated with retinal hemorrhage. The specificity of retinal hemorrhage for abusive head trauma in the presence of prothrombotic factors, in particular following non-abusive head trauma, has not been investigated. Our objective was to determine whether the hypothesis that prothrombotic factors affect specificity of retinal hemorrhage to AHT can be tested. This may have important ramifications both for diagnosis and expert witness testimony.

Methods: To investigate the feasibility of studying this issue, we conducted a prospective cohort study of children with abusive and non-abusive head trauma. Thrombophilia screening and ophthalmic examinations were performed.

Results: Six of 30 admitted children were fully enrolled. Enrollment obstacles included caregiver stress, animosity towards allegations of abuse, child protection services involvement, and research phlebotomy coordination. Prevalence of thrombophilia was high in children with retinal hemorrhage and in 1 case the question of hemorrhage adjudicated as abuse was considered in light of a history of a fall.

Conclusion: We estimate that to answer the critical question of retinal hemorrhage specificity for abuse in the presence of thrombophilia will require 53 centers for a 1 year study or 18 centers for a 3-year study. We identify potential obstacles and interventions.

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[☆] Funded in part by Brandon's Eye Research Fund, Vision Science Research Program of the Toronto Western Hospital, Ontario Graduate Scholarship, Institute of Medical Science of the University of Toronto, the Research Training Centre of the Research Institute of the Hospital for Sick Children, and the Foerderer Fund.

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Introduction

Retinal hemorrhages are found in approximately 85% of children younger than 3 years old subjected to abusive head trauma (AHT) characterized by repeated severe acceleration-deceleration forces with or without blunt impact (Shaken Baby syndrome) (Levin, 2000; Ludwig & Warman, 1984; Morad et al., 2002). Aside from retinal hemorrhages attributed to birth trauma in the neonatal period (Committee for the Classification of Retinopathy of Prematurity, 1984), retinal hemorrhages in healthy children that are multilayered, too numerous to count, and extend to the edge of the retina (ora serrata) are suggestive of AHT; these features distinguish AHT from non-abusive head trauma (non-AHT) (Bechtel et al., 2004; Christian, Taylor, Hertle, & Duhaime, 1999; Duhaime et al., 1992; Duhaime et al., 1987; Gilliland, Luckenbach, & Chenier, 1994; Jenny, Hymel, Ritzen, Reinert, & Hay, 1999; Levin, 1990; Vinchon, Noizet, Defoort-Dhellemmes, Soto-Ares, & Dhellemme, 2002). Misclassifying a child's injuries as caused by abuse when the child was not abused can have significant adverse consequences, namely family separation, legal proceedings and/or incarceration (Hymel & Hall, 2005). To increase the accuracy of head trauma classification we must consider underlying conditions that may cause a child to present with clinical findings mimicking abuse after a non-abusive incident.

Retinal vein occlusion is a recognized cause of hemorrhagic retinopathy in adults (Klein, Klein, Moss, & Meuer, 2000), and has been associated with thrombophilia (Arsene et al., 2005; Bashshur et al., 2004; Behbehani, Sergott, & Savino, 2004; Bressler & Bressler, 1993; Hattenbach, Beeg, Kreuz, & Zubcov, 1999; Janssen, den Heijer, Cruysberg, Wollersheim, & Bredie, 2005; Mintz-Hittner, Miyashiro, Knight-Nanan, O'Malley, & Marlar, 1999; Miserocchi, Baltatzis, & Foster, 2001; Suvajac, Stojanovich, & Milenkovich, 2007; Yesim et al., 1998). As some have hypothesized (Brinker et al., 1997; Emerson, Jakobs, & Green, 2007; Levin, 1990; Muller & Deck, 1974; Mushin, 1971), venous stasis may result from increased intracranial pressure transmitted to the optic nerve sheath with compression of the central retinal vein that travels within. In childhood head trauma, the uniquely strong vitreo-retinal attachments may predispose children to shearing-induced vascular endothelial disruption or loss of retinal autoregulation. If a child with non-AHT possesses thrombophilia, which is present in approximately 5% of the general Caucasian population (Bauer et al., 2002; Bertina, 1999; Lee, Henderson, & Blajchman, 1996; Reitsma & Rosendaal, 2007; Rosendaal, 1999a, 1999b; Seligsohn & Lubetsky, 2001) and is associated with a higher risk for developing thrombosis, there may be an increased risk for retinal vein thrombosis leading to retinal hemorrhage. Thus, thrombophilia could potentially lead to a child being misclassified as having AHT.

A large sample is required to study if thrombophilia truly decreases the specificity of retinal hemorrhage as an indicator of AHT because (1) only an estimated 5% of the general population has a prothrombotic risk factor, (2) only a small proportion of children with prothrombotic risk factors actually experience a thrombotic event (Tormene et al., 2002), and (3) there will likely be obstacles to enrolling from a vulnerable population of children (Duhaime, 2007), specifically those with possible AHT (Amaya-Jackson, Soclar, Hunter, Runyan, & Colindres, 2000; Barlow, Thomson, Johnson, & Minns, 2005; Bradley & Lindsay, 1987; Tormene et al., 2002).

Legal criteria for admissibility of medical diagnosis and expert medical testimony in court proceedings consider the reliability of the foundational data used in formulating judgments on the subject matter. The Daubert criteria for the admissibility of scientific evidence in court, ask, in part, (a) whether the particular subject matter is capable of being tested, (b) whether it has been tested, (c) what the methodology is for testing the theory, and (d) what the "error rate" is for the particular testing process (Annas, 1994; Berger, 2005; Daubert v Merrel Dow Pharmaceuticals Inc., 1993). If a theory fails to meet the Daubert criteria, then it may be considered less reliable and therefore less likely to be admissible. If the presence of prothrombotic factors lowers the diagnostic specificity of retinal hemorrhages for AHT, in legal terms this would be perceived as raising the potential "error rate" of the opinion that such hemorrhages are specific for AHT. Given the potential obstacles to test the hypothesis that prothrombotic factors may influence the presentation and diagnostic sensitivity of hemorrhagic retinopathy, a single-centre feasibility study was conducted as an indication of how successful a larger multi-centre prospective cohort study might be and thus the potential admissibility and weight of prothrombotic factors as evidence used in court for adjudicating cases of suspected AHT.

Methods

Children were recruited from The Hospital for Sick Children (Toronto, ON Canada) from December 1, 2006 to August 1, 2007 according to the following inclusion criteria: inpatient between 1 month and 7 years of age, head injury confirmed by diagnostic imaging (skull fracture[s], contusions, intracranial hemorrhage, increased intracranial pressure, cerebral edema), informed consent by substitute decision maker fluent in English, and responsible staff physician approval (consideration given to factors such as substitute decision maker anxiety level, enrollment in concurrent research studies, and clinical stability to allow research blood samples to be obtained). Exclusion criteria were: presence of underlying disorders which may affect hemostatic balance (e.g., liver disease, cancer, hemophilia, von Willebrand disease), presence of underlying disorders which may affect ocular manifestations (e.g., retinopathy of prematurity), use of drugs which may affect hemostatic balance (e.g., heparin, warfarin, aspirin, non-steroidal anti-inflammatory agents), or blood transfusions during current illness prior to intended blood draw. Children with mild transient coagulopathy attributed to traumatic brain injury were included.

The assignment of children as having suffered AHT or non-AHT was based on the decision made by the multi-disciplinary Suspected Child Abuse and Neglect (SCAN) Team of The Hospital for Sick Children; all clinical, laboratory, and historical findings were thoroughly evaluated before coming to a conclusion about the nature of the child's injuries. A classification of

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