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Apparent Diffusion Coefficient (ADC) of the vitreous humor and Susceptibility Weighted Imaging (SWI) of the retina in abused children with retinal hemorrhages☆,☆☆,☆☆☆

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ABSTRACT

This study speculated that the apparent diffusion coefficient (ADC) of the vitreous humor might be altered in the setting of abusive head trauma (AHT) with retinal hemorrhages (RH). Fourty-four subjects were analyzed ($n = 20$ AHT cases; $n = 24$ controls). There was no statistically significant difference in normalized ADC values between the cases and controls (-0.14 and -0.08 respectively, $p = 0.46$), but analysis of RH by susceptibility weighted imaging (SWI) compared to dilated funduscopic exam demonstrated statistically significant correlation ($p = 0.003$ and 0.012). Our results suggest that SWI serves as a more sensitive diagnostic tool for detection of ocular injury in AHT than ADC.

1. Introduction

The vitreous humor is a transparent, delicate gel composed of a highly-hydrated network of collagen type II fibrils and hyaluronic acid. By weight, the vitreous humor is composed approximately by 99% of water and 0.9% salts [1]. The network of collagen fibrils and the biochemical properties of hyaluronic acid are considered responsible for the mechanical properties of the vitreous because of the load-bearing capacity of collagen and because the vitreous does not fully collapse with enzymatic removal of hyaluronan [1].

Preliminary evidence in support of trauma-induced breakdown of the blood retinal barrier with subsequent alterations of the biochemical profile of the vitreous humor is based on open globe injuries such as rupture, penetration, perforation, or intraocular foreign body [2]. The biochemical mechanisms in open globe injury are postulated, but in closed globe injury unknown. A retinal tear or ocular penetrating injury can disrupt the integrity of the tight junctions between the sensory retina and the underlying retinal pigment epithelium. This leads to rupture of blood retinal barrier and influx of immune cells into the vitreous cavity triggering the production of growth factors and cytokines [2]. Even with 1 mm of retinal break, moreover, the influx of serum proteins, vitreal cells, and blood through the retinal break can recruit proinflammatory cytokines and lead to proliferative vitreoretinopathy [3].

A number of approaches have been devised to measure the mechanical properties of the vitreous humor in animals, encompassing bulk measurements [4], magnetic microrheology [5], visual tracking [6], as well as acoustic procedures [7]. Diffusion weighted imaging (DWI) has been a complementary technique useful in the differential diagnosis of various orbital pathologies including orbital cellulitis and inflammation, as well as optic nerve infarction [8–11]. Diffusion can be quantitatively evaluated by using the apparent diffusion coefficient (ADC) map which is expressed in square millimeters per second. The ADC reflects diffusion properties within the tissue and depends on many physiologic parameters such as volume fractions, extracellular tortuosity, intracellular restrictions, membrane permeability, active processes across membranes, spin relaxation rates, and anisotropic morphology [12].

It should be noted, however, that the presence of retinal hemorrhage rather than vitreous hemorrhage is the most common ophthalmological finding of abusive head trauma (AHT)[13]. In fact, the most frequent etiology of retinal hemorrhages in infants

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and children is AHT [14,15]. In one study of 560 AHT cases, retinal hemorrhageswere observed in 74% (range: 51–100%) of clinical exams and 82% (range: 63–100%) of autopsy cases [16]. Of the different subtypes of retinal hemorrhages, peripheral and macular traumatic retinoschisis, splitting of the retinal layers, are highly associated with AHT. In some cases, dome-shaped retinal hemorrhages can cross into the vitreous and cause deteriorate visual development in young children [17]. Since retinal hemorrhages can resolve quickly, it is imperative to obtain prompt ophthalmologic evaluation in children highly suspected for AHT.

In this study, we thereby selected patients with AHT and associated ocular injury based on the presence of retinal hemorrhages. With the previous evidence that even a small retinal disruption can lead to vitreal influx of inflammatory markers, we hypothesized that the biochemical properties of the vitreous will be altered as measured by vitreous ADC values in this patient cohort. More specifically, we hypothesized that low ADC value (or higher diffusion restriction from trauma induced structural or biochemical alteration) would be correlated with the presence of RH, a marker for ocular injury in our case. A comparison was made of the vitreous ADC values in patients with AHT-associated RH versus controls. We also evaluated the diagnostic sensitivity of susceptibility weighted imaging (SWI) in the detection of RH in AHT. To our knowledge, no studies have examined the imaging changes in the vitreous compartment in the setting of AHT.

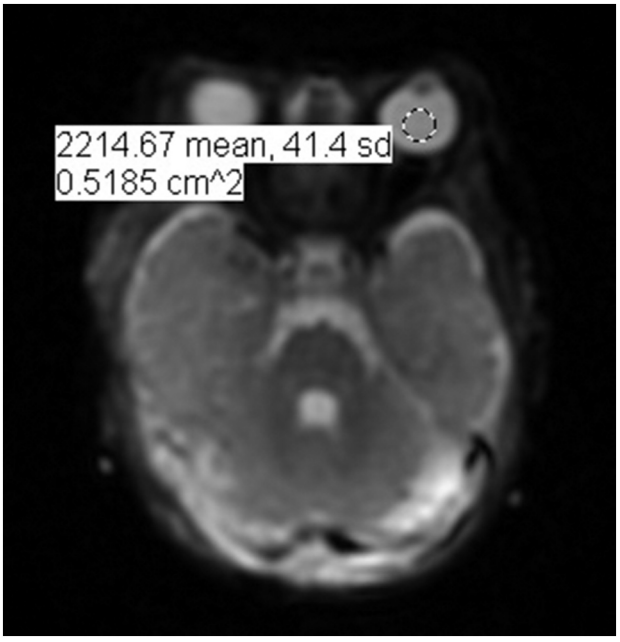

Fig. 1. An ROI with an area of 1 cm2 was drawn in the right and left eye as shown.

2. Materials and methods

The study was approved by our Institutional Review Board as part of a larger study related to the identification and evaluation of children at risk for AHT. A total of 20 brain MR images from March 1, 2011 to June 1, 2012 obtained at Children's Hospital of Pittsburgh of UPMC from children with AHT and RH were retrospectively evaluated. All AHT patients had documented intracranial hemorrhage on brain MR imaging and all underwent a dilated funduscopic exam (DFE) as part of clinical care. As controls, MR imaging obtained from 24 patients of similar age with varying clinical indications for the exam including seizure, and non-traumatic neurologic complaints, developmental delay were studied. None of the controls had intracranial hemorrhage and none had a DFE as there was no clinical indication. ADC values of the right and left eye were obtained of both cases and controls.

2.1. MR Imaging evaluation

MR imaging was conducted on either a 1.5 T or 3 T magnet (Signa, HD platform HDxt 16.0, GE Healthcare, Milwaukie, WI) using a standard brain protocol that included brain DWI and ADC sequences. For the standard DWI and ADC sequences, the image parameters were as follows: repetition time/echo time (TR/TE) = 50.0/78.3 ms, slice thickness 5 mm, field of view (FOV) = 200 mm, flip angle = 15, matrix 288 × 224, in-plane resolution = 0.6 mm on the 1.5 T magnet; and TR/TE = 46.9/26.0 ms, slice thickness 3 mm, FOV = 200 mm, flip angle = 15, matrix = 320 × 224, in plane resolution = 0.6 mm on the 3 T magnet, respectively. For the standard MR imaging brain protocol, the DWI was acquired with 5-mm slice thickness that specifically included the orbits. The ADC images were quantitatively analyzed for ADC values by the primary author of this paper and the images were confirmed by two experienced neuroradiologists (GZ and AP). An ROI with an area of 0.5 cm2 was drawn in the right and left eye directly on the imaging software (Fig. 1). For internal control, an ROI with an area of approximately 0.5 cm2 was drawn in frontal horn of the right lateral ventricle. For susceptibility weight imaging (SWI) analysis, RH was determined by the presence of low signal intensity in at least two slices of the retina in the axial plane. Two neuroradiologists (GZ and AP), blinded to the results of the DFE, qualitatively analyzed the images for presence of RH.

2.2. Ophthalmological evaluation

Written documentation of the DFE was used to collect the following data: side of RH (right, left, or both), extent of RH (posterior pole or beyond the posterior pole), and layers of the retina (preretinal, intraretinal, and subretinal). In each case, photos of the RH were taken using a RetCam (Clarity MSI, Pleasanton CA). Timing of the DFE was recorded as the number of days between the MR imaging and the eye exam: positive numbers referred to subjects in whom DFE was performed before the MR imaging, and negative numbers referred to subjects in whom the MR imaging was performed first.

2.3. Statistical analysis

ADC values of the eye were compared between controls and RH subjects using the nonparametric Wilcoxon Rank-Sum test. ADC values were then normalized to the ADC values of the frontal horn of the right lateral ventricle. Analysis was then repeated for ADC values normalized as percent difference from ADC values of the right frontal horn. If RH was bilateral, the right eye was selected for analysis [18]. Retinal hemorrhage evaluation (positive or negative) by SWI in right and left orbit was compared to the presence of hemorrhage in the corresponding retina by DFE using Fisher's Exact test. Data from SWI analysis were compared to the extent of retinal hemorrhage by DFE using the Wilcoxon Rank-Sum test. A significance value of $p < 0.05$ was selected.

3. Results

There were a total of 44 subjects analyzed ($n = 20$ cases, $n = 24$ controls). The median age was 4.6 months (quartiles: 2.6, 7.4) in controls and 5.5 months (quartiles: 4.5, 20) in cases ($p = 0.25$). There was no difference in the proportion of females in cases vs controls (35% vs. 46%, $p = 0.47$). The median number of days between MR imaging and DFE in cases was 2.5 days (quartiles: 1.0, 5.3). Of the patients with RH, 32% ($n = 6$) also had retinoschisis and 10% ($n = 2$) had coexistent vitreal hemorrhage. In both of the patients with vitreal hemorrhage, the extent of vitreal hemorrhage was not severe with discrete localization overlying the pre-retinal hemorrhage. The median Glasgow Coma Scale Score in cases was 13.5 (quartiles: 10.5, 15) with a minimum of 3 and a