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Case Report ***Open Access***

FOCAL BRAIN INJURY IN A TERM NEONATE ASSOCIATED WITH HISTOLOGICAL CHORIOAMNIONITIS.

Shabih Manzar, MD, Department of Pediatrics, School of Medicine, Louisiana State University Health Science Center, USA

Corresponding author: Manzar S, Associate Professor, Department of Pediatrics, School of Medicine, Louisiana State University Health Science Center, 1501 Kings Highway Shreveport, LA 71130, USA, Tel: +1318-626-1623; E-mail: smanza@lsuhsc.edu

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ABSTRACT

White matter injury (WMI) has been described in preterm infants in association with chorioamnionitis (CA). We report a case of term neonate with both gray and WMI to the frontal lobe in association with CA. The case presentation is followed by literature review.

Keywords: *Term, Neonate, Brain injury, White matter, Chorioamionitis*

CASE PRESENTATION

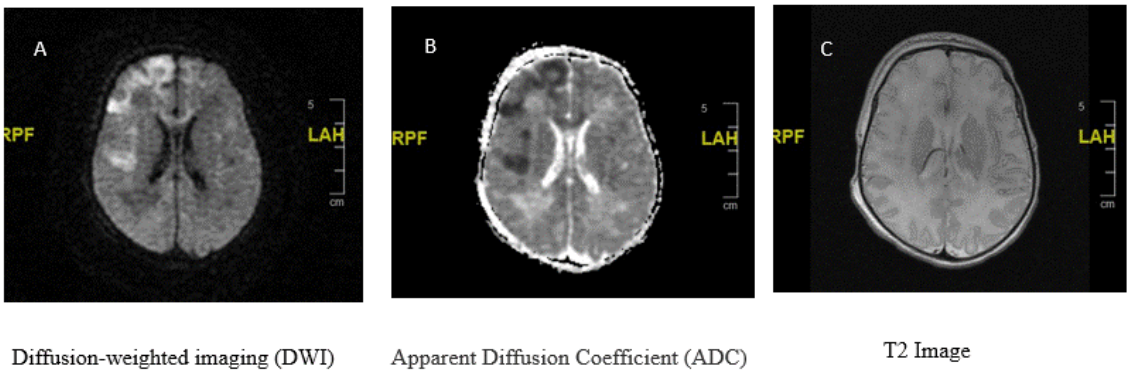
A male infant was delivered via vaginal delivery at $39^{3/7}$ weeks of gestation. Mother was 18 years old gravida 1, para 1. She had history of elevated blood pressures. Pregnancy medication included prenatal vitamins and no other medications. All her prenatal labs were negative including RPR, HIV, hepatitis B, chlamydia, and gonorrhea. Significant history revealed rupture of membrane for 19 hours prior to delivery, foul smelling amniotic fluid and fever with highest temperature of 102^{o}F (38.9°C), suggestive of chorioamnionitis.

At delivery, the infant had no cry, poor tone, and poor respiratory effort. However, the heart rate (HR) was above 100 beats per minute. He was taken to the preheated warmer, dried, stimulated and bulb suctioned. He was then placed on continuous positive airway pressure

(CPAP), oxygen saturations improved and then the infant was transported to neonatal intensive care unit (NICU). Apgar score was 5 (2 for HR, 1 for respiratory effort, 1 for color, 1 for tone and 0 for reflexes) and 8 (2 for HR, 2 for respiratory effort, 2 for color, 1 for tone and 1 for reflexes) at 1 and 5 minutes respectively. Infant's physical examination was significant for tachycardia and abnormal muscle tone. No dysmorphic features were noted. Vital signs showed a temperature of 100.9 °F (38.3 °C) and heart rate of 191 beats per minute. Cord blood gas showed a pH of 7 with base excess of – 17.

HOSPITAL COURSE

In the NICU, while stable on CPAP, the infant developed seizure. He was started on anticonvulsant and hypothermia therapy was instituted as per unit protocol. A complete work up including CBC, serum electrolytes, blood, and CSF bacterial cultures and HSV (herpes simplex virus) was obtained. Infant was treated with ampicillin, gentamicin, and acyclovir. All his labs came normal. Antibiotics were stopped. Brain MRI with DWI-ADC was obtained on day 6 of life that showed regional gray and white matter injury (Figure 1).



Diffusion-weighted imaging (DWI) Apparent Diffusion Coefficient (ADC) T2 Image

FIGURE 1
NEONATAL BRAIN MRI SHOWING EXTENSIVE AREAS OF RESTRICTED DIFFUSION INVOLVING GRAY AND WHITE MATTER ON THE RIGHT FRONTAL LOBE (A-DWI, B-ADC, C-T2 IMAGE).

Electroencephalogram (EEG) revealed abnormal prolonged interburst intervals of about 40 to 45 seconds and the presence of bursts of intermittent rhythmic discharges mostly over the central head regions, consistent with non-specific global neuronal dysfunction. Initial metabolic screen including serum pyruvic acid and ammonia was normal. Follow up state metabolic screen panel for fatty acid profile, amino acid profile, organic acid profile was all normal. Gross placental pathology showed a placental disc measuring 16 x 15 x 3 cm and weighing 528 grams with no grossly visible lesions suggestive of infarct or neoplasia while the histological examination showed stage 2, grade 2 chorioamnionitis and funisitis.

Infant transitioned well post warming and started of PO feeds, which he tolerated well. The neurological exam at discharge was normal. He passed pre-discharge hearing screen test. Infant was assessed by the pediatric neurologist and was sent home on phenobarbitone with follow up with primary physician, neurology clinic, developmental clinic, and early steps intervention. A plan was made to obtain MRI with DWI-ADC as an outpatient.

DISCUSSION

Inflammation has been implicated in the pathogenesis of neonatal brain injury. The potential mechanisms include pro-inflammatory cytokines release related to the fetal inflammatory response (FIR) (Kallapur, et al., 2014). Acute chorioaminiotis (CA) incites FIR leading to neuronal injury and edema (Pacora, et al., 2002; Dammann, et al., 2002; Nedelcu, et al., 1999, Gavilanes, et al., 2009). The sequence of events leading to brain injury in the case presented could be explained by the gross and histological findings on the placenta. Stage 2 with grade 2 CA signifies severe infiltration of neutrophils that led to a cascade of FIR resulting in gray (GMI) and white matter injury (WMI). A detailed investigation to look for other causes of infection or inflammation in this infant was negative. The blood and CSF HSV PCR were also negative. However, a negative work up for infection does not preclude CA as a triggering factor for FIR. Recently (Kim, et al., 2015) elucidated on the concept of sterile CA and FIR.

The abnormal area of GMI and WMI was seen on the diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) while T2 images were normal (Figure 1). Brain MRI is a sensitive tool to detect the inflammation. DWI detects random movements of water proton. When inflammation happened, the water move into the cell and have restricted movement which results in bright signal on DWI. DWI in neonate can identify early injury after an insult owing to its ability to detect changes in brain water. (Granger, et al., 2018) have shown a correlation between MRI findings and CA in preterm infants. DWI with corresponding ADC map, as observed in the case (Figure), provided the ability to differentiate edema associated with increased extracellular space, metabolic compromise or evolving necrosis (Granger, et al., 2018; Rodrigues & Grant. 2011; Tocchio, et al., 2015).

The involvement of both gray and white matter in a term neonate has not been reported earlier. The exact pathogenesis is unknown. A multi-hit model for brain inflammation in neonate has been proposed by Korzennieswski, et al., 2014. Different regions of brain have different susceptibility to injury at different maturational stages. For example, developing oligodendrocytes are more susceptible to oxidative stress than mature oligodendrocytes. The regions involved in asphyxia are basal ganglia while in stroke it is the area in the territory supplied or drained by the artery or vein (Ferriero, 2004). We noted a regional involvement precluding stroke or asphyxia as the main cause of damage.

(Li, et al., 2009) described eleven cases of WMI in term newborn with focal findings out of which ten had restricted diffusion on apparent diffusion coefficient maps. None of the cases had any documented history of histological severe CA.

In summary, CA is a potential risk factor for neonatal brain injury. The case highlights on the value of DWI MRI in neonates. We suggest obtaining DWI MRI in all newborn infants affected by CA. Further studies are needed to investigate the etiologies and pathogenesis of localized gray and white matter injury in neonates.

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