Status Epilepticus and Capillary Leak Syndrome in a Neonate Related to Perinatal Hypoxic-ischemic Encephalopathy

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ABSTRACT

Hypoxic-ischemic cerebral injury that occurs during the perinatal period is one of the most commonly recognized cause of long-term neurological deficit in children, often referred to as cerebral palsy. We describe a case with capillary leak syndrome and seizures to co-morbid status epilepticus related to perinatal hypoxicischemic encephalopathy in newborn period. **[Indian J Pediatr 2010; 77 (4) : 439-441]** *E-mail: belmakaragol@ yahoo.com*

Key words: Hypoxic-ischemic cerebral injury; Capillary leak syndrome; Status epilepticus; Inflammatory mediators

Hypoxic-ischemic cerebral injury that occurs during the perinatal period is one of the most commonly recognized cause of long-term neurological deficit in children, often referred to as cerebral palsy.¹ Expression of inflammatory mediators has been demonstrated in the pathogenesis of hypoxic-ischemic brain injury.² Inflammatory cytokines also appear to exert in capillary leak syndrome, which may progress to end organ dysfunction and result in death by extravascular fluid accumulation with severe edema.³ We describe a case with capillary leak syndrome and seizures to co-morbid status epilepticus related to perinatal hypoxic- ischemic encephalopathy in newborn period.

REPORT OF CASE

A male infant was born by vaginal delivery at 40 wks gestation to a 23-yr-old primigravida woman after an uneventful pregnancy. The mother was brought to the hospital after the contractions had started, and the child was delivered by using vacuum extraction because of prolonged labour and fetal distress. The

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neonate was bradycardic and Apgar scores were 2 and 7 in 1 and 5 min respectively. Seizures developed 6 hrs after birth and did not respond to intravenous diazepam, so that the patient was transferred to the neonatal intensive care unit (NICU). On admission at our NICU, he was lethargic with generalized muscle rigidity and physical examination revealed cephal hematoma with 4x4 cm. Deep tendon reflexes were hyperactive and plantar reflexes were flexor. An electroencephalogram (EEG) on the day of admission was markedly abnormal, with low-voltage and disorganized background activity. A cranial computed tomography (CT) scan demonstrated manifest cephal hematoma but no brain edema or hemorrhage. On day 3, neurological symptoms of severe asphyxia presented with generalized clonic seizures. Antiepileptic therapy with phenytoin was started as initial therapy. On the following days, phenobarbital, midazolam and lidocain were additionally required in order to control seizures expressed as status epilepticus. A repeat CT scan on 10th day showed generalized ischemia with hypodansity in all areas. Brain magnetic resonance imaging on day 13 showed abnormally high signal intensity in the cortical areas involving the basal ganglia and thalamus on T1 weighted images secondary to asphyxia (Fig. 1). On day 14, severe generalized edema appeared (Fig. 2A). His actual weight was 4670g. Capillary leakage syndrome with generalized edema and decrease of plasma protein concentrations (serum albumin level: 2.2 g/dL) existed. Prerenal insufficiency due to fluid restriction with blood

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Fig. 1. Magnetic resonance imaging revealed abnormally high signal intensity in the cortical areas involving the basal ganglia and thalamus on T1 weighted images secondary to asphyxia.

urea nitrogen as 69 mg/dL, creatinin 0.67 mg/dL and normal serum sodium level (Na: 143 mEq/L) accompanied capillary leak. There was not any positive clinical and hematological septic score. Liver function tests were also normal. Generalized severe edema increased within following three days and concentrations of inflammatory mediators as TNF-a, IL-6, and IL-8 were reported as 14.3, 3.2 and 63.4 pg/mLrespectively. Methylprednisolon therapy with 2 mg/ kg/day dose was started intravenously on day 17. On the same day, the antiepileptic drug regimen was changed into monodrug treatment with valproate and all other drugs were ceased because of intractable seizures that could have not been controlled with the drugs. After the initiation of methylprednisolon treatment, generalized edema decreased day by day and the patient became stable with monodrug antiepileptic treatment on the 22nd day (Fig. 2B). TNF-a, IL-6 and IL-8 concentrations decreased to 3.6, 1.2 and 8.7 pg/mL respectively after the corticosteroid use. The patient was discharged from hospital with full oral feeding and oral valproate treatment on the 26th day.

On follow up examination at 3 month of age, he had not experienced any seizure activity during his home stay. On physical examination, he expressed truncal hypotonicity and exhibited mild rigidity of the lower extremities. Eye movements were normal and there was no muscle weakness or fasciculation in extremities. The response to sound stimuli was normal.



Fig. 2. (A) Capillary leakage syndrome with generalized odema manifested in the patient on 14th day. (B) Physical appearence of the patient changed almost to normal after generalized odema disappeared.

DISCUSSION

The existence of capillary leak syndrome and status epilepticus related to perinatal hypoxic-ischemic encephalopathy in our patient prompted us to consider relationship between brain injury and expression of inflammatory mediators. Cardiopulmonary bypass and sepsis related capillary leak syndrome in pediatric patients have been previously reported.³⁻⁵ Nevertheless, hypoxic-ischemic encephalopathy related capillary leak syndrome has not been described in literature in newborns. Our patient with capillary leak syndrome significantly decreased plasma protein had concentrations and developed generalised edema, which were the criteria used to define the syndrome in other studies.³⁻⁶ All other ethiologies of edema were excluded.

IL-6, IL-8 and TNF-a are important inflammatory mediators and have been reported to increase capillary permeability.⁵⁻⁹ Inflammatory cytokines appear to exert both beneficial and deleterious effects following ischemia. This dual effect may complicate the task of developing hypoxic-ischemic brain injury and capillary leakage against the inflammatory response. Activation of these cytokines in our patient were also supportive clues for capillary leak syndrome determination. However, data reported on the inflammatory response induced by these concentrations of inflammatory mediators is not sufficient. Additionally, there aren't defined normal ranges of these cytokins belonging to the neonatal period. Elevated concentrations of these

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inflammatory mediators on the 14th day and decreased concentrations on the 22nd day might be a clue for diagnostic approach to capillary leak syndrome in our patient.

Suzuki et al reported the high incidence of cytokinerelated disease as the cause of death in children with perinatal hypoxic-ischemic encephalopathy sequelae. They also emphasized that the pathogenesis of this disease needed to be clarified.¹⁰ However, they concluded that cytokine-related disease with perinatal hypoxic-ischemic encephalopathy sequelae occur in childhood period whereas our patient suffered from capillary leak syndrome and status epilepticus in the neonatal period. Furthermore, limited data about the time of release and activation of inflammatory mediators from cells in hypoxia ischemia are available. Hagberg et al reported that expression of inflammatory mediators in the pathogenesis of hypoxicischemic brain injury has been demostrated within 1-4 hour following hypoxia ischemia in neonatal rats.²

Inflammatory mediators seem to play a critical role in the pathogenesis of hypoxicischemic brain injury.² Various patterns of hypoxic encephalopathy occur in asphyxiated neonates.¹ We conclude that inflammatory mediators may play a role in the development of the present case clinic situation. However, understanding the pathogenesis of perinatal hypoxia may clarify the relationship between capillary leak syndrome and hypoxic-ischemic cerebral injury in future.

Contributions: The manuscript has been written and prepared by BSK; OE and SA have revised the manuscript; BA has attended the progress of this case together with all other authors in NICU. The patient has been consulted for pediatric Nephrology by ME. The patient has been also consulted for pediatric Neurology for drug choice by ST and GD.

The case was carried out in the NICU. All authors followed the case in NICU.

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