Severe Newborn Encephalopathy Unrelated to Intrapartum Hypoxic Events: 3 Case Reports

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Abstract

***Introduction**: Newborn encephalopathy is an important clinical problem associated with considerable morbidity and mortality and is pertinent in the assignment of blame in obstetrics litigation. **Clinical Picture**: We report 3 babies with severe neonatal encephalopathy. **Outcome**: In all 3 cases, intrapartum hypoxic insult was unlikely to be a significant contributing factor towards the development of neonatal encephalopathy. The aetiology was unclear in the first 2 cases and there was antecedent antenatal cause of feto-maternal haemorrhage in the last case. **Conclusion**: Prevention of neonatal encephalopathy was not possible in these 3 cases. We recommend that umbilical cord blood gases be clearly documented in such cases to reduce unnecessary obstetrics litigation of intrapartum asphyxia as the significant contributing factor to the poor neonatal outcome. Clinicians must have a high index of suspicion of antecedent causes and perform the necessary investigations to elucidate the aetiology of the neonatal encephalopathy.*

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Key words: Antepartum, Idiopathic, Obstetrics litigation, Severe newborn encephalopathy

Introduction

Since Little's article of 1862, it was popularly believed that brain damage in the majority of cases of cerebral palsy occurs during labour and delivery.[1] However, the growing evidence in literature has refuted this belief. Similarly, newborn encephalopathy is an important clinical problem associated with considerable morbidity and mortality and is pertinent in the assignment of blame in obstetrics litigation.

There were a total of 78,826 deliveries in our hospital in the study period from 1998 to 2002. As the incidence of severe newborn encephalopathy is rare in our institution, we do not have data on the prevalence and the proportion of severe encephalopathy due to intrapartum events. We report here 3 cases which were graded severe encephalopathy according to the criteria modified from Sarnat and Sarnat.[2] They fulfilled one or more of the following criteria: ventilation >24 hours, two or more anticonvulsant treatments, comatose or stuporous and died in the neonatal period.

As in many other studies, we noted that umbilical arterial pH <7.0 as being the most predictive of the development of neonatal complications.[3,4] The definition of metabolic acidosis as pH <7.0 in an umbilical arterial cord sample also concurs with 1 of the 3 essential criteria for defining an acute intrapartum hypoxic event.[5]

Case Reports

Case 1

A 32-year-old primigravida presented with no significant maternal or family history. She was well antenatally. Screening scan at 19 weeks' gestation was normal.

She was admitted at 31 weeks' gestation with complaint of decreased fetal movement of 2 days' duration. Admission cardiotocogram (CTG) showed fetal tachycardia at 170 bpm, with extreme poor variability and no accelerations (Fig. 1).

The couple was counselled on the poor prognosis of baby but they elected to have an urgent delivery. A baby girl

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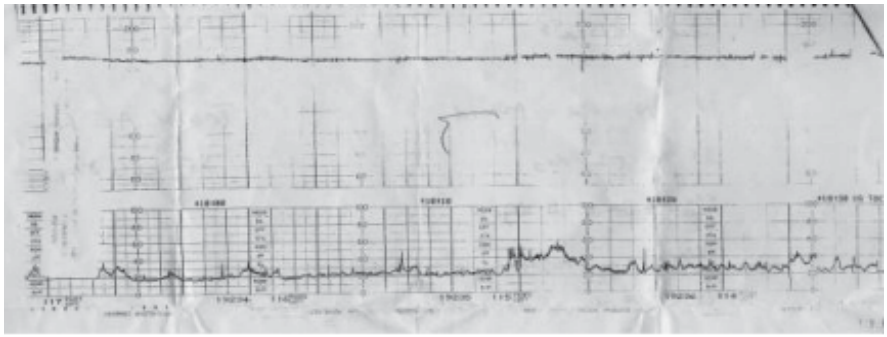

Fig. 1. Admission CTG.

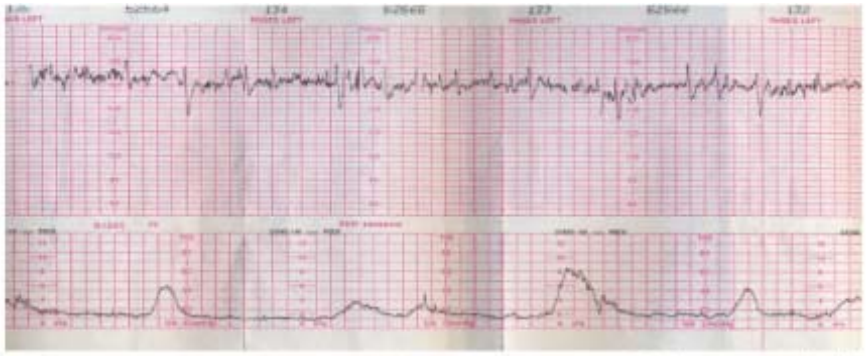

Fig. 2. Admission CTG.

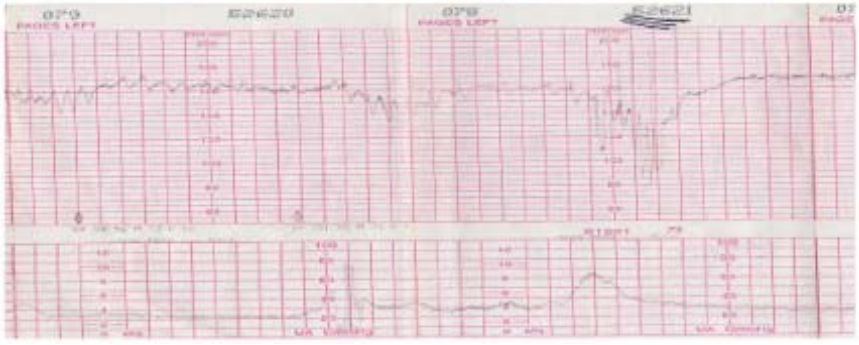

Fig. 3. CTG at 8 hours later.

weighing 1549 g was delivered abdominally. The Apgar scores were 2 and 4 at 1 minute and 5 minutes, respectively, and the baby was intubated as there was no spontaneous respiration.

The umbilical arterial blood gas showed no metabolic acidosis with a pH of 7.28 and base excess of -6.2. Cranial ultrasonography on day 1 showed bilateral subependymal cystic spaces adjacent to the frontal horns with cerebral oedema. Infective and metabolic screen was negative.

The baby remained comatose and flaccid, with fixed and dilated pupils. There was no response to pain and no spontaneous respiration. The neurologist counselled the parents that the baby was already brain dead and, subsequently, the parents agreed to reduce the ventilator settings. The baby became asystolic on day 8.

Postmortem autopsy showed no congenital abnormalies and the cause of death was hypoxic-ischaemic encephalopathy. Histology of the placenta showed no evidence of infarcts, haemorrhage or infection. There were no chromosomal abnormalities.

Case 2

A 24-year-old primigravida was booked at 11 weeks' gestation and had no significant family or medical history. Screening scan at 19 weeks' gestation was normal and a subsequent scan at 32 weeks' gestation showed growth at 50% with adequate liquor volume.

She was admitted at 37 weeks' gestation in labour at 2110 hours. Admission CTG showed no accelerations or cycling pattern (Fig. 2). Eight hours later at 0510 am the next day, the CTG showed fetal tachycardia at 160 bpm with reduced variability and recurrent variable decelerations (Fig. 3). There was no sentinel hypoxic event noted.

Subsequently, there were no further decelerations seen in

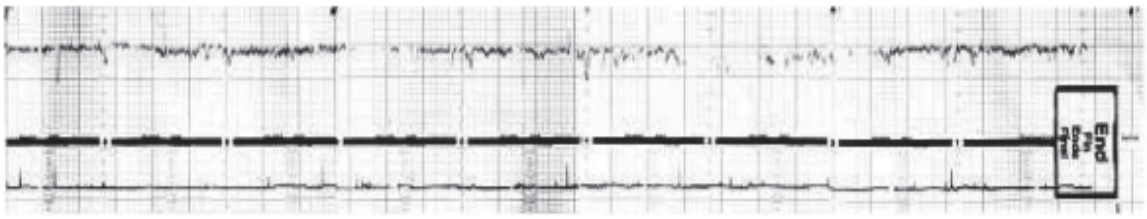

Fig. 4. Admission CTG.

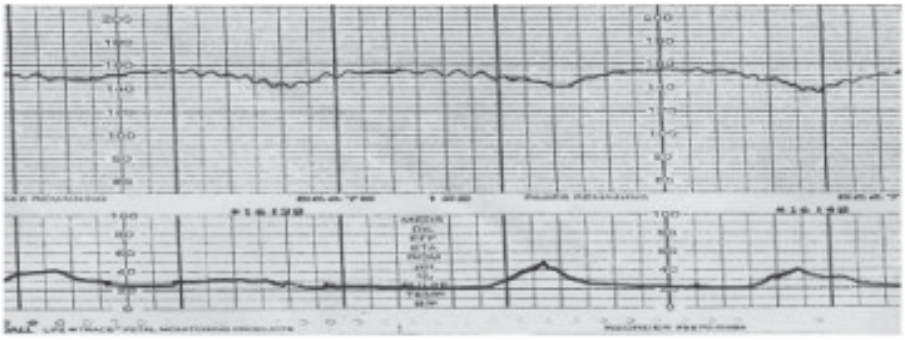

Fig. 5. CTG showing sinusoidal pattern.

the CTG. The obstetrician decided to observe and she progressed rapidly in labour. The cervical os was full 2 hours later (0740 am) and a baby girl, weighing 2985 g, was delivered vaginally at 0758 am. The baby had Apgar of 5 at 1 minute and 6 at 5 minutes and was intubated for poor respiratory effort. The arterial umbilical pH was 7.23 with base excess of -1.1.

The baby developed seizures on day 1 of life and was treated with phenobarbitone. She remained areflexic with hypertonic upper limbs and flaccid lower limbs. Computed tomography (CT) scan on day 2 showed no acute intracranial haemorrhages with mild cerebral oedema. Infective and metabolic screen was normal. Placenta histology was normal.

The couple was counselled on the grave prognosis of the baby, but they subsequently decided to bring the baby home against medical advice. The baby was weaned off the ventilator and brought home on day 20. The baby subsequently died on day 33 of life due to pneumonia. The parents declined postmortem examination of the baby.

Case 3

A 34-year-old woman, with 3 full-term uncomplicated deliveries, was followed-up antenatally at the polyclinic. Screening scan was normal. She was booked at 31 weeks' gestation and had a growth scan which showed growth parameters at the 50th percentile. She was admitted at 38 weeks' gestation with complaint of decreased fetal movement over the previous few days. The admission CTG showed a baseline heart rate of 140 to 150 bpm with no accelerations, markedly decreased variability and contractions every 1 in 3 minutes (Fig. 4). Examination showed the cervical os to be 3 cm dilated; amniotomy was performed and clear liquor was noted. Subsequently, the CTG showed a sinusoidal pattern with recurrent shallow late decelerations (Fig. 5).

An emergency caesarean section was performed for non-reassuring fetal status. A baby boy was delivered weighing 3098 g. The Apgar scores were 1 and 4 at 1 minute and 5 minutes, respectively. The arterial umbilical cord blood gas was pH 6.88 and base excess -20.3.

The baby was intubated for bradycardia and noted to be pale and hydropic. The haemoglobin was 3.9g/dL with a mean cell volume of 118 fl. A Blauke-Kleihauer test showed a feto-maternal haemorrhage of 170 mL. The baby was hypotensive and required inotropic support. He developed neonatal seizures on day 1 and required intravenous phenobarbitone administration. Cranial ultrasonography showed grade 2 intraventricular haemorrhage on day 7. He was weaned off the ventilator on day 15 and was discharged from the intensive care unit on day 22. At 3 months' follow-up, the baby was noted to have normal neurodevelopment and assessment. However, the prognosis for neurodevelopmental outcome remained guarded in view of severe neonatal encephalopathy and the baby is currently on follow-up with the paediatrician.

Discussion

In 75% to 90% of cases of cerebral palsy, a single identifiable cause cannot be elucidated.[6,7] It is a common belief among patients, attorneys and even obstetricians that cerebral palsy is caused by intrapartum asphyxia, despite data indicating that most children diagnosed with cerebral palsy did not have birth asphyxia.

A large prospective United States National Collaborative Perinatal Project involved 56,000 births from 1959 to 1966.[6] It showed that among the 189 children with cerebral palsy, 40 (21%) had at least 1 marker suggestive of birth asphyxia; only 17 of these 40 (9% of all cases) lacked major congenital malformation or other intrinsic factors that might have contributed to an unfavourable outcome.

Asphyxial-induced cerebral palsy is one of the rarest forms of cerebral palsy with a reported incidence of 1 in 10,000 births.[7] In a matched case-control study involving 183 children with spastic cerebral palsy, it was estimated that in only 8% of all children with spastic cerebral palsy had intrapartum asphyxia as the possible cause of their brain damage.[7]

The incidence of neonatal encephalopathy associated with perinatal hypoxia in term infants has remained essentially unchanged in many countries for the last 40 years.[8] The incidence of moderate/severe encephalopathy in first week of life is reported to be 3.8 per 1000 full-term live births.[9] Approximately 80% of infants with moderate encephalopathy will be neurologically normal. Of those infants studied with severe newborn encephalopathy, all either died or had long-term neurological sequelae.[10] In a matched case-control study involving 89 cases of neonatal encephalopathy, only 15% of the cases and no controls suggested significant intrapartum hypoxia.[9] However, a large proportion of these cases had a significant antepartum history, so that the intrapartum period alone was implicated as the likely cause of neonatal encephalopathy in only 6% of the cases. In a recent study involving 164 term infants with moderate/severe newborn encephalopathy, 113 (69%) had only antepartum risk factors; 39 (24%) had antepartum and intrapartum factors; 8 (5%) had only intrapartum factors; and 4 (2%) had no recognised antepartum or intrapartum factors.[11]

Signs of intrapartum fetal distress may be the first signs of pre-existing neurological abnormality and events occurring in the antepartum period are important causes of neurological abnormality in the newborn infants.[12] A complicated antenatal history is more likely among cases of cerebral palsy than controls (OR 1.8; 95% CI 1.2-2.8) and among cases of death than controls (OR 2.8; 95% CI 1.3-5.8).[13] Significant antepartum risk factors for newborn encephalopathy include unemployed status (OR 3.6; 95% CI 1.1-11.8), family history of seizures (OR 2.6; 95% CI 1.3-4.9), severe pre-eclampsia (OR 6.3; 95% CI 2.3-17.6), maternal thyroid disease (OR 9.7; 95% CI 2.0-47.9), moderate/severe bleeding (OR 3.6; 95% CI 1.3-9.9), viral illness (OR 3.0; 95% CI 1.5-5.8), intrauterine growth restriction (OR 38.2; 95% CI 9.4-154.8), post-maturity (OR 13.2; 95% CI 5.0-34.8) and having abnormal placenta (OR 2.1; 95% CI 1.2-3.7).[14]

There are 2 postulated mechanisms of injuries. Firstly, it is suggested that prenatal factors associated with chronic hypoxia in the fetus may result in damage to the developing brain. A second mechanism is that the vulnerability of the fetus to the normal stress of labour may already be altered by prenatal factors, leading to intrapartum hypoxic damage under conditions which a normal fetus could resist.

In our first 2 case reports, no antepartum or intrapartum risk factors were identified as possible causes for severe newborn encephalopathy. There were no identifiable sentinel hypoxic events in the peripartum period. Although the CTG was suspicious in the 2 cases, the cord blood gas for both cases ruled out metabolic acidosis (pH >7.0 and base excess <12 mmol/L) and thus did not support an acute intrapartum hypoxic event. As described, 2% of newborn encephalopathy had no identifiable antepartum or intrapartum risk factors.[11]

Case 3 illustrated an antecedent antepartum event of feto-maternal haemorrhage. Hence, signs of intrapartum fetal distress may be the first signs of pre-existing neurological abnormality, and events occurring in the antepartum period are important causes of neurological abnormality in the newborn infants.

The degree of metabolic acidosis is measured by the umbilical artery pH and base deficit. Metabolic acidosis occurs as the tissue oxygen deficit increases in duration, reflecting hypoxia, to accumulation of fixed acids.[15] In a review of 129 term births associated with umbilical arterial pH <7.00, the incidence of encephalopathy was 31%.[16] Neonatal seizures occurred in 9% of infants with umbilical arterial pH between 6.90 and 6.99 while 80% with pH between 6.61 and 6.70.[16] Marked acute changes in the arterial carbon dioxide tension and acid-base status occur in the immediate post-natal period in infants delivered in the presence of pathologic fetal acidemia, in whom the risk for hypoxic-ischaemic cerebral injury is high. There could be significant differences between the umbilical arterial and initial postnatal pH and arterial blood gases even within the first hour of life.[17] The acid-base status may normalise by the second hour of postnatal life. Therefore, umbilical arterial blood gases may be more accurate than postnatal acid-base status in reflecting fetal acidemia.

Intrapartum uterine contractions can potentially compromise the oxygenation status of the fetus. In a study of uterine and umbilical artery flow resistance during the oxytocin challenge test, it was shown that umbilical artery flow resistance increased significantly during contractions.[18] This was associated with fetal heart rate decelerations. In term infants, intrauterine hypoxia/birth asphyxia has been reported to be associated with an increased risk of cerebral palsy (adjusted OR 18.1; 95% CI 1.8-186).[19]

Within the period that many of us have practised obstetrics

and gynecology, many non-specific markers have been used to represent intrapartum asphyxia or birth asphyxia. These markers include meconium-stained amniotic fluid, abnormalities in the electronic fetal monitoring and poor Apgar scores at birth. Given the lack of equivalence of any of these criteria, in addition to their lack of specificity, the potential for diagnostic misclassification is substantial.[20] A contemporary survey of the views of healthcare professionals shows that the risk of cerebral palsy was over-estimated by a factor of 10 compared with published figures.[21] As discussed, only 8% of all children with spastic cerebral palsy had intrapartum asphyxia as the possible cause of their brain damage.[7]

What does this mean for the practising obstetrician? There is a need for all of us to use precise terminology when assigning the cause of cerebral palsy. In deliveries with significant respiratory depression, we recommend that umbilical arterial cord blood gas be analysed and documented. Similarly, histopathologic examination of the placenta and placental membranes and umbilical cord may reveal clues as to the cause of the newborn's condition.[22] The causes of newborn encephalopathy and cerebral palsy are heterogeneous and many of the causal pathways probably start in the antepartum period. As the mechanism of these insults remains unclear in many such cases, prevention is not always possible.

Conclusion

Prevention of neonatal encephalopathy was not possible in these 3 case reports. We recommend that umbilical cord blood gases at delivery be clearly documented in such cases to reduce unnecessary obstetrics litigation due to inappropriate assignment of intrapartum asphyxia as the significant contributing factor to the poor neonatal outcome. Clinicians must have a high index of suspicion of antecedent causes and perform the necessary investigations to elucidate the aetiology of the neonatal encephalopathy.

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