Perinatal Arterial Stroke due to Unilateral Cerebral Infarction: Case Report

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INTRODUCTION
Perinatal arterial stroke (PAS) is diagnosed primarily in term neonates and is responsible for at least 22 to 70% of congenital hemiplegic cerebral palsy in this population and probably some cases of spastic quadriplegic cerebral palsy. It is the second commonest cause of seizures in newborn of more than 32 week gestation and 12% of all neonatal seizures in full term infants are due to cerebral infarction.

CASE REPORT
A term baby girl was born by spontaneous vaginal delivery to a 25-year-old primi gravida mother at 41 ± 2 weeks. Parents are first cousins. Antenatal period was uneventful. Artificial rupture of membranes done 22 hours prior to delivery revealed a clear liquor and labor was augmented with pitocin. Some episodes of deep deceleration of the fetal heart rate were noted during the induction. Apgar scores were seven and nine at one and five minutes respectively. She was kept in the delivery room for routine observation. At five hours of age, she was noticed to be cyanosed but she improved with free flow O₂ and was admitted to the Special Care Unit (SCU) for close observation.

The first blood gas analysis done at six hours of age was normal. At 13 hours of age, she had clonic convulsions of the limbs which were treated with phenobarbitone injection. Two further episodes of clonic seizures at 18 hours and 23 hours were also treated with phenobarbitone and phenytoin and she was started on maintenance doses of both drugs. Vital signs including blood pressure were normal. She was lethargic and her anterior fontanelle was tense and bulging. Septic screening was negative. She was started on empirical antibiotics. Lumbar puncture failed. Cranial ultrasound examination on day two was normal. On repeat ultrasound on day five, compression of the left lateral ventricle with edema of the adjacent brain parenchyma was noted.

Her condition improved and anticonvulsants were gradually tapered and stopped by day eight and enteral feeds were started. On day nine, she had sudden deterioration with tachypnea and aspiration pneumonia was suspected on CXR. After a full septic screening including CSF examination, she was started on second line antibiotics. All cultures were sterile. On day 10, she developed severe metabolic acidosis and was transferred to intensive care unit for ventilation. She was noted to be hypertensive and was started on IV hydralazine. Echocardiogram on day 11 was normal.

Cranial ultrasound examination repeated on day 11, revealed an increase in the echogenecity of the left parieto-occipital region suggesting edema of the parenchyma with mass effect on the left frontal horn, effaced sulci and ill defined gyri. A suspicion of left middle cerebral artery infarction was raised (Fig. 1). Magnetic resonance imaging of the brain (MRI) and magnetic resonance
angiography (MRA) were done on day 14. MRI brain showed diffuse altered signal of the left cerebral hemisphere (sparring the thalamus and the medial surface) with diffusion restriction along the left middle cerebral artery territory (Fig. 2 and 3). MRA revealed narrowing of a long segment of the intracranial part of the left internal carotid artery with occlusion of the left middle cerebral artery (Fig. 4). Electroencephalogram (EEG) on day 29 showed a background activity of 3 - 4 HZ with asymmetry over the left hemisphere.

Protein S, Protein C and Antithrombin III levels were normal and maternal screening for Antiphospholipid syndrome was negative. Factor V Leiden mutation, Prothrombin 20210A mutation and MTHFR (methylene tetrahydrofolate reductase) mutation could not be done in Kuwait.

Her head circumference was below the 3rd centile for age. The deep tendon reflexes were brisk on the right side. She was sucking well by day 27. At discharge on day 41, she was alert and establishing good eye contact. Head circumference remained the same as at birth and except for brisk deep tendon reflexes on the right side no signs of hemiparesis were noted. At follow-up at three months of age, tone was increased on the right side. Head circumference was still below the 3rd centile on the chart. At five months of age, paucity of movements was noted on the right side. Psychosocial development was normal. At eight months, frank signs of a right hemiparesis could be noted and the head circumference had fallen well below the 3rd centile. She is on follow-up with the pediatric neurologist, and is on regular physiotherapy.

**DISCUSSION**

PAS occurs by definition between 28 weeks gestation and seven days of age although studies of PAS often include cerebro-vascular events occurring up to 28 days of life[4]. In the Canadian Pediatric stroke registry, a quarter of the children were term neonates[5]. Perinatal stroke has become increasingly recognized but the incidence is under estimated because of the variation in the presentation,
evaluation and diagnosis[3]. The incidence is reported as one in 4000 term births[4].

Factors contributing to the increased risk of stroke among neonates include complications that occur before, during and after delivery. Maternal conditions include prothrombotic disorders such as the presence of antiphospholipid antibodies (antiphospholipid syndrome), cocaine abuse, pre-eclampsia and placental conditions such as choioamnionitis and placental vasculopathy[5]. Foetal Parvovirus B19 infection can also predispose to stroke. During a traumatic delivery the infant may develop a cervical arterial dissection which may predispose to stroke especially in the context of thrombophilia.

Neonatal risk factors include cardiac disorders, blood disorders such as polycythemia, birth asphyxia (< 5%) and genetic thrombophilias such as factor V Leiden, Prothrombin 20210A mutation and MTHFR involved in homocysteine metabolism, elevated lipoprotein (a), Protein C deficiency and elevated factor VIII C[6]. Presence of factor V Leiden mutation may influence both the nature and combination of sites involved and lead to high risk of hemiplegia and when associated with high factor VIII C levels, it is associated with an 80% risk of poor neurological outcome[7]. But in a vast majority of infants as in this case, the cause is undetermined.

Newborns with PAS either present acutely with seizure or lethargy or may be clinically asymptomatic until several months of age when, pathologic handedness or seizures are first noted[8]. Seizures are the most common presenting feature as in this case and occur as early as 12 hours after birth and up to 10 days after delivery[9]. Seizures are usually focal and may occur in the absence of other signs of neonatal encephalopathy such as abnormalities of tone or feeding, or depressed level of alertness[9].

Focal neurological signs are rare, with hemiparesis present in less than 25% of the cases[8]. Many of the babies are well in the interictal period and are likely to remain undetected[9]. In one study, a male predominance of 1.5:1 was noted[10].

Diagnostic tests include computerised axial tomogram (CT), MRI, MRA and less commonly conventional angiogram. Cranial ultrasound has a limited role because of the peripheral location of most infarcts[11]. As noted in this case, cranial ultrasound by an experienced sonologist may reveal an echodense structure within the vascular territory after a phase of normal appearance[11].

MRI is more sensitive in detecting early or small infarcts. Diffusion weighted MRI is more sensitive than CT to detect early signs of the infarction. In this technique, as early as two days after the infarct, abnormal focal findings indicating cytotoxic edema can be seen before the above abnormality can be seen on regular MRI sequence. This diffusion restriction does not persist for more than one week. After five days, the diagnosis has to rest entirely on T2 weighted images[12].

Vascular imaging modalities such as MRA or conventional angiography can define the presence or absence of arterial stenosis or occlusion. In this case, MRA clearly demonstrated the narrowing of the intracranial segment of the left internal carotid artery and the occlusion of the left middle cerebral artery. Unilateral infarcts are more common on the left side and the anterior (carotid) circulation is five times more commonly involved than the posterior circulation[8].

Outcome of PAS is variable and depends on the severity, anatomic location and other factors not yet well characterized. In one third of newborns the outcome is normal. In two-thirds of survivors neurological deficits are detected after several years[8]. Infarct topography is a predictor of hemiparesis. It is more likely with concomitant MRI abnormalities in the basal ganglia, posterior limb of the internal capsule and the cerebral cortex[10].

In affected infants, upper limbs are affected more severely than the lower limbs with loss of independent finger movements. Seizures disorders are present in 15% of the children. Infants with acute presentation were more likely to develop epilepsy. Delayed presentation (> 28 days) was associated with increased risk for cerebral palsy[13]. Language delay, learning difficulties and behavioral disorders are more common in the acute group. Mortality is less than 10%. Recurrence risk for PAS is less than 5%,[8].

In the absence of a known pathophysiological mechanism, only supportive care is provided to the newborn[14]. Thrombolytic treatment is rarely if ever an option and anticoagulant therapy is controversial and rarely indicated given the relatively low recurrence risk. In the Canadian Pediatric stroke registry, less than 10% received anticoagulant therapy[8]. It should be considered when the etiology is clearly embolic in nature.

CONCLUSION

Recognition of PAS is important since early diagnosis and in selected cases specific therapy may improve the outcome. Seizures in the first three days of life combined with pathological EEG findings should lead to MRI regardless of a normal cranial ultrasound. There is much to be learned about the natural history of perinatal stroke and further evidence based strategies for prevention or treatment are needed to improve the outcome.
REFERENCES