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Case Report Open Access

Perinatal Arterial Ischemic Stroke: An Unusual Causal Mechanism

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Abstract

Perinatal Arterial Ischemic Stroke (AIS) is an important cause of neurological morbidity in infants. Some risk factors have been identified, but its pathogenesis remains unclear. We present a case of perinatal in which macroscopic examination of the placenta revealed the presence of a vasa praevia. We hypothesize that compression of the vasa praevia during labor could have determined the formation of thrombi, which were subsequently embolized into the fetal circulation causing perinatal AIS.

Background

Perinatal arterial ischemic stroke (AIS) is estimated to occur in 1/1600 to 1/5000 births [1]. Even if rare, it is an important cause of mortality and morbidity in neonates. A meta-analysis showed that 57% of infants who suffer perinatal AIS develop motor and/or cognitive deficits, and 3% die [2]. Risk factors proposed for perinatal AIS include maternal prothrombotic conditions and pre-eclampsia, chorioamnionitis, fetal distress, and placental disorders, such as thrombosis and placental chorioangiomas [1-4]. Although clinical and imaging findings of AIS are now well delineated, its causative mechanisms remain unclear. In the absence of documented pathogenic mechanisms, preventive strategies cannot be implemented. We report a case of perinatal AIS which we correlated to the presence of undiagnosed vasa praevia.

Case Report

A 41 year old nulliparous woman delivered a female newborn after spontaneous labor at 39.6 weeks gestation. Pregnancy was achieved by in vitro fertilization and intra-cytoplasmic sperm injection. An ultrasound scan at 20 weeks had revealed a low-lying placenta, which migrated to a normal insertion at follow-up scans. During labor the fetal heart rate tracing remained reassuring. The baby's Apgar scores were 9 and 10 at 1 and 5 minutes, respectively. Umbilical artery gas-analysis was normal, with a pH of 7.30; and birth weight was 3060 grams.

Five minutes after birth the newborn presented marked pallor, coldness and hypomobility of the right upper limb, with no right brachial pulse and normal axillary pulse. Color doppler ultrasound of the right arm documented absent flow in the humeral artery and increased resistance index in the right axillary artery. After 4 hours the arm spontaneously recovered normal temperature and motility and the color improved, with a complete clinical resolution of the ischemia within 16 hours of life. However at 11 hours of life the baby suffered an episode of generalized cyanosis and was admitted to the Neonatal Intensive Care Unit (NICU). No other clinical neurological signs were present and cerebral ultrasound was normal. At 24 hours of life clinical seizures were observed; an electroencephalogram (EEG) confirmed the presence of theta asymmetric activity in the central left hemisphere of possible vascular origin. The seizures were controlled with barbiturates and midazolam. Magnetic Resonance Imaging (MRI), with angiography and spectroscopy showed an ischemic lesion in the superficial territory of the left sylvian artery, normal patency of the arterial vessels, an increased flow in sylvian and posterior left arteries; the findings were interpreted as compensatory response to ischemia (Figure 1A-1C). These findings were confirmed by cerebral ultrasound with color Doppler performed on the same day, which showed a large area of hyperechoic parenchyma in the left hemisphere and signs of increased flow in the districts of the sylvian artery. No cardiac anatomic or functional abnormalities were found. Coagulation studies were in the normal range and disorders of the coagulation pathway were excluded. Thrombophilias were excluded both in the baby and in the mother.

Follow-up neuroimaging monitoring with ultrasound showed occurrence of hemorrhage in the previously identified ischemic area, with development of malacic areas over time. At color doppler ultrasound at 2 weeks of life, the flow in the subclavian, humeral, and ulnar arteries were normal.

The MRI performed at 2 months of life showed a large area of parenchymal malacia of the left cerebral hemisphere, affecting much of the frontal lobe in the territories of the superficial branches of the middle cerebral artery. In addition, the images showed the presence of: residual haemosiderin at the posterior margins, likely related

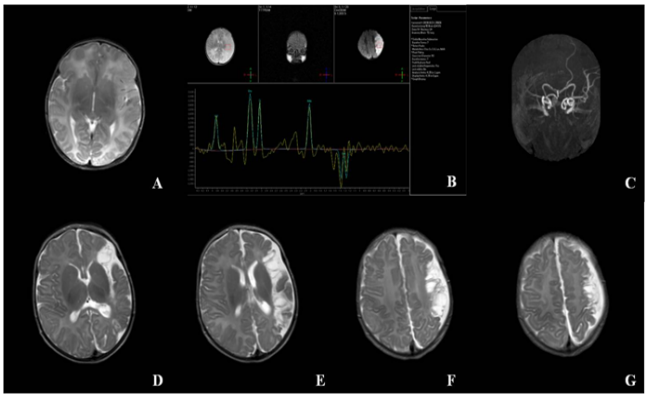

Figure 1: MRI performed at 24 hours of life (A-C) showing: ischemic lesion in the superficial territory of the left sylvian artery (A), reduced NAA/choline (Cho) ratios at spectroscopy (B), compensatory increase in the flow in sylvian and posterior left arteries.; MRI performed at 2 months of life (D-G) showing parenchymal atrophic evolution of the lesion.

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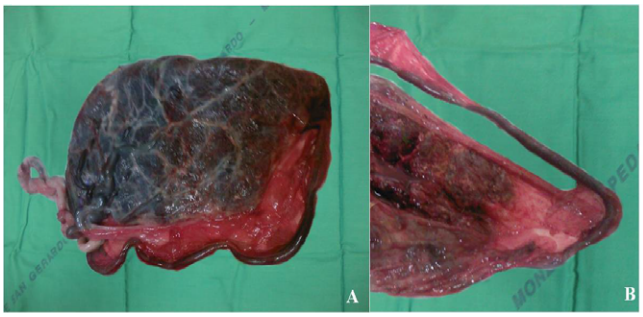

Figure 2: Macroscopic appearance of the placenta (A) with a detail of the vasa praevia (B).

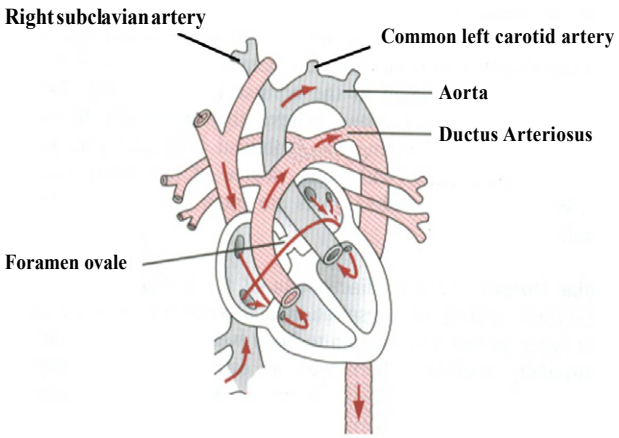

Figure 3: Schematic representation of emboli course through fetal vessels.

to previous focal haemorrhage; ex-vacuo enlargement of the left hemispheric liquoral structures; and slight asymmetry of the cerebral peduncles due to partial atrophy of the left. The rear portions of both internal capsules were also asymmetrical due to greater representation on the right. There were no focal lesions on the remaining areas (Figure 1D-1G).

At fifteen days of life, because of clinical signs of ischemic damage, the baby began **r**ehabilitative physiotherapy. Anticonvulsive therapy was stopped at 3 months. At 9 months the baby developed hemiparesis with right upper limb deficit.

Macroscopic placental examination at delivery revealed a marginal and velamentous cord insertion with a large venous collector running along the inferior pole of membranes, next to the point of their spontaneous rupture (Figure 2). Histological examination merely revealed fibrin depositions.

Conclusion

We report a case of AIS associated with vasa praevia. We hypothesize that the velamentous venous vessel running within the fetal membranes of the lower segment of the uterus without the protection of Warthon's jelly was temporary compressed by the descending fetal head at the time of labor. This mechanism could have determined stasis of blood flow, with formation of thrombi which were embolized through the umbilical vein and the ductus venosus, reaching the fetal right heart. As demonstrated by Miller et al. [5], emboli tend to reach the left atrium via the patent foramen ovale. Such emboli could have then travelled through the ascending aorta, lodging in the right subclavian artery, thus causing the transient humeral artery occlusion observed at birth. Other emboli, through the common left carotid artery, could have reached the cerebral circulation causing AIS in the region of the left middle cerebral artery (Figure 3). As shown by Miller [5], perinatal AIS is usually a consequence of thromboembolic events arising in either intracranial or extracranial vessels, the heart or the placenta. Thrombotic abnormalities are more often observed in the distribution of the middle cerebral artery then in the anterior and posterior cerebral arteries, and involve in most cases the left cerebral hemisphere [5]. This observation provides support to our pathogenetic hypothesis outlined above.

Factors contributing to an increased risk of perinatal AIS include complications that occur before, during, and after delivery. Atherosclerosis, one of the most important risk factors in adult AIS, has not been proven to be significant in the pathophysiology of either childhood or perinatal AIS [4]. Even if it has been recently demonstrated that maternal and fetal factors can be responsible for an early endothelial dysfunction and vascular damage [6,7], several studies have revealed that the neonatal brain is unique with a peculiar responsiveness to hypoxia–ischemia. Thus, causes of perinatal AIS differs from those seen in older children and may include maternal problems and other issues related to pregnancy and delivery [4-8]. Indeed, several conditions associated with perinatal AIS are determinants of vasculo-placenta pathology (e.g. diabetes, pre-eclampsia, chorioamnionitis, maternal or fetal hypercoagulability) [1]. Therefore, the main etiological hypothesis addresses the role of the materno-fetal vascular interface, i.e. the placenta and its vessels. Some Authors postulated that cord length, shape or insertion anomalies can induce a fetal thrombotic vasculopathy, most frequently in umbilical vein, which can extend to fetal organs [9,10]. Since 60% of the infants with AIS present early symptoms, as in our case, it is reasonable to suppose that labor is one of the moments at highest risk of placento-fetal emboli. In our case, the compression of the vasa praevia by the descending fetal head during labor could have been the determinant factor, or at least a co-factor, for the formation of vascular thrombi.

In a case-control study addressing the association between maternal and infant complications and the risk of perinatal AIS, Lee et al. [3] demonstrated that infertility is one of the independent risk factors of this event. Infertility was indeed present in our case and possibly conditioned the abnormal placental implantation. The anomalous course of the vasa praevia could have been suspected prenatally, since both *in vitro* fertilization and presence of low lying placenta in mid-gestation are known risk factors. Regrettably, no transvaginal sonographic exams were done in third trimester and the diagnosis was missed.

Our report shows that vasa praevia is an extremely dangerous obstetric complication, not only for the risk of rupture and for the consequent fetal hemorrhage, but also for the risk of thrombosis and ischemic accidents [3]. Attention to the placenta and cord insertion at prenatal ultrasonography may play an important role in the prevention of perinatal AIS.

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