

# Symptomatic Neonatal Arterial Ischemic Stroke With Prenatal and Postnatal Neuroimaging

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## Abstract

The authors report a girl born at term via planned cesarean delivery. Three days earlier, an antenatal magnetic resonance imaging study, showing no cerebral lesions in the fetus, was performed. Ten minutes after delivery, signs of progressive respiratory failure developed and the infant was transferred to the intensive care unit. On the next day, a computed tomography (CT) scan showed acute ischemic lesions in the areas of the left middle and posterior cerebral arteries. The exact mechanism of stroke remained unidentified. It is possible that emboli occluded the left middle cerebral artery and left posterior cerebral artery. At the age of 1 year and 4 months, the patient demonstrated a slight right-sided hemiparesis more pronounced in the hand. To our knowledge, there are no prior published case studies reporting a healthy fetal brain, which then undergoes an acute neonatal arterial infarction near or during birth following an elective cesarean delivery.

## Keywords

stroke, magnetic resonance imaging, neuroimaging, neonatal seizures, seizure

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Ischemic cerebral infarction can occur at any age, and the perinatal period is the second most common period for ischemic strokes.<sup>1</sup> The 2007 National Institute of Health Workshop defined neonatal arterial ischemic stroke as a subtype of perinatal ischemic strokes, which occurs between the 20th week of pregnancy and the 28th day of life.<sup>1</sup>

The exact timing and chronology for each type of perinatal stroke remain unclear, although data suggest that early neonatal arterial ischemic stroke is associated with late third trimester or labor.<sup>2</sup> As the injury is not immediately symptomatic, it is difficult to assess when the insult happened. Clues to the timing of the lesion come from magnetic resonance imaging (MRI), which provides an assessment of how old the injury is.<sup>3</sup>

Early neonatal arterial stroke manifests during the first 3 days postpartum.<sup>4</sup> Most commonly the babies evince impaired consciousness, breathing problems, and seizures. In cases of acute stroke, it is typical for the newborn to initially appear relatively healthy, reflected by high Apgar scores, and then deteriorate. Many of them do not immediately have lateralizing findings on examination, as hemiparesis emerges over time.<sup>5</sup>

The etiology of perinatal stroke is thought to be multifactorial. There have been studies associating neonatal stroke with intrapartum factors such as prolonged rupture of membranes, maternal fever, prolonged second stage of delivery, and tight nuchal cord.<sup>6</sup> In addition, both maternal- and infant-related prothrombotic conditions have been implicated.<sup>1</sup>

Another major group of risk factors are pathologies of the placenta. It has been observed that the placentas of neonates

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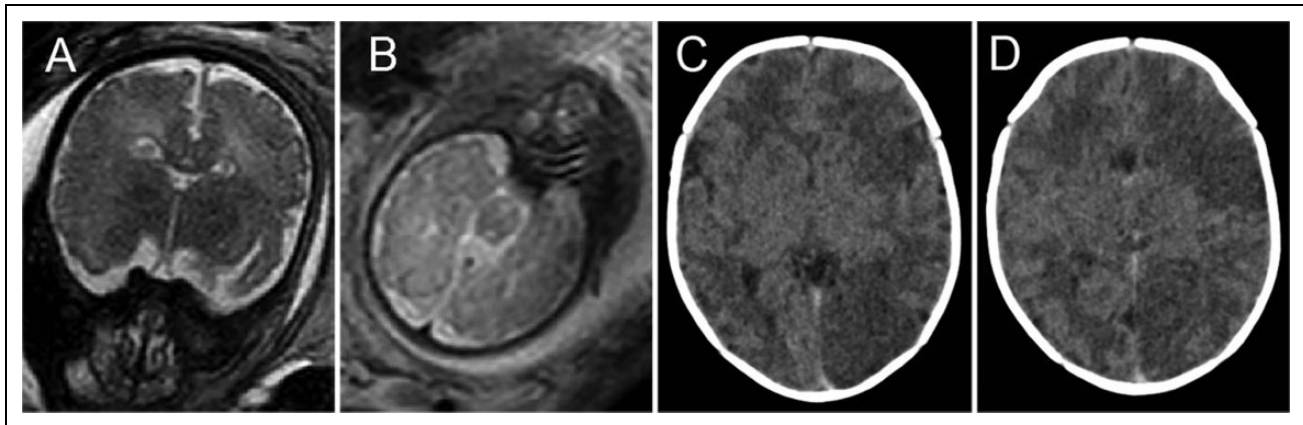
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**Figure 1.** A-B, Prenatal magnetic resonance imaging of the fetus, T2-weighted TSE sequences 3 days before birth showing no asymmetry in the fetal brain. C-D, Head computed tomography at the age of 29 hours showing hypoattenuations in the arterial supply areas of the left middle cerebral artery and the posterior cerebral artery, characteristic of irreversible ischemic damage; TSE: turbo spin echo.

with arterial ischemic stroke have signs of blood supply problems, which could exacerbate during delivery.<sup>7</sup> Unfortunately, the role of the placenta is relatively poorly exposed, because the placenta is often unavailable by the time the stroke is diagnosed.<sup>8</sup>

Antenatal MRI is used for evaluation of fetal or placental anomalies. It is indicated in situations where ultrasound findings are not specific enough or the interpretation thereof is hindered due to poor visibility and where the MRI might impact the management, counselling, or planning of delivery.<sup>9</sup>

## Case

A girl large for gestational age (3620 g, >90th percentile) was born at term (gestational age 37 weeks + 2 days) via a planned cesarean delivery due to marginal placenta previa. Three days earlier, an antenatal MRI scan was performed to study placenta placement and plan delivery. No lesions were detected in the fetal brain (Figure 1A, B). The mother had a history of a previous cesarean delivery and anemia during pregnancy. Additionally, during pregnancy, the mother was treated for anxiety and depression with sertraline.

Apgar scores were 8 at the first and fifth minute after an uneventful planned cesarean delivery. Amniotic fluid was clear, upon inspection the placenta was described as normal, with no further investigation considered necessary. Approximately 10 minutes after birth, signs of progressive respiratory failure developed and the infant needed supplemental oxygen. At the age of 1 hour, chest radiograph was indicative of wet lung, which was treated with bubble continuous positive airways pressure (CPAP). At the age of 3 hours, the infant had 2 short desaturation episodes, which led to the transfer of the infant into the intensive care unit. Four hours after delivery, generalized seizures manifested. These symptoms prompted further investigation.

Cerebral ultrasonography at the age of 6 hours did not reveal any significant pathology of the brain or abdomen except for mild differences in blood flow velocities of cerebral arteries. An emergency head CT scan was carried out on

the 29th hour of life. The scan revealed acute ischemic strokes in the areas supplied by the left middle cerebral artery and left posterior cerebral artery (Figure 1C, D). At the age of 3 days, the MRI confirmed arterial ischemic infarctions in the areas of the left middle cerebral artery and left posterior cerebral artery involving the cerebral cortex and basal ganglia (Figure 2A, B, D, E). Magnetic resonance angiography did not reveal any occlusions or stenoses of intra- or extracranial arteries or veins (Figure 2C, F).

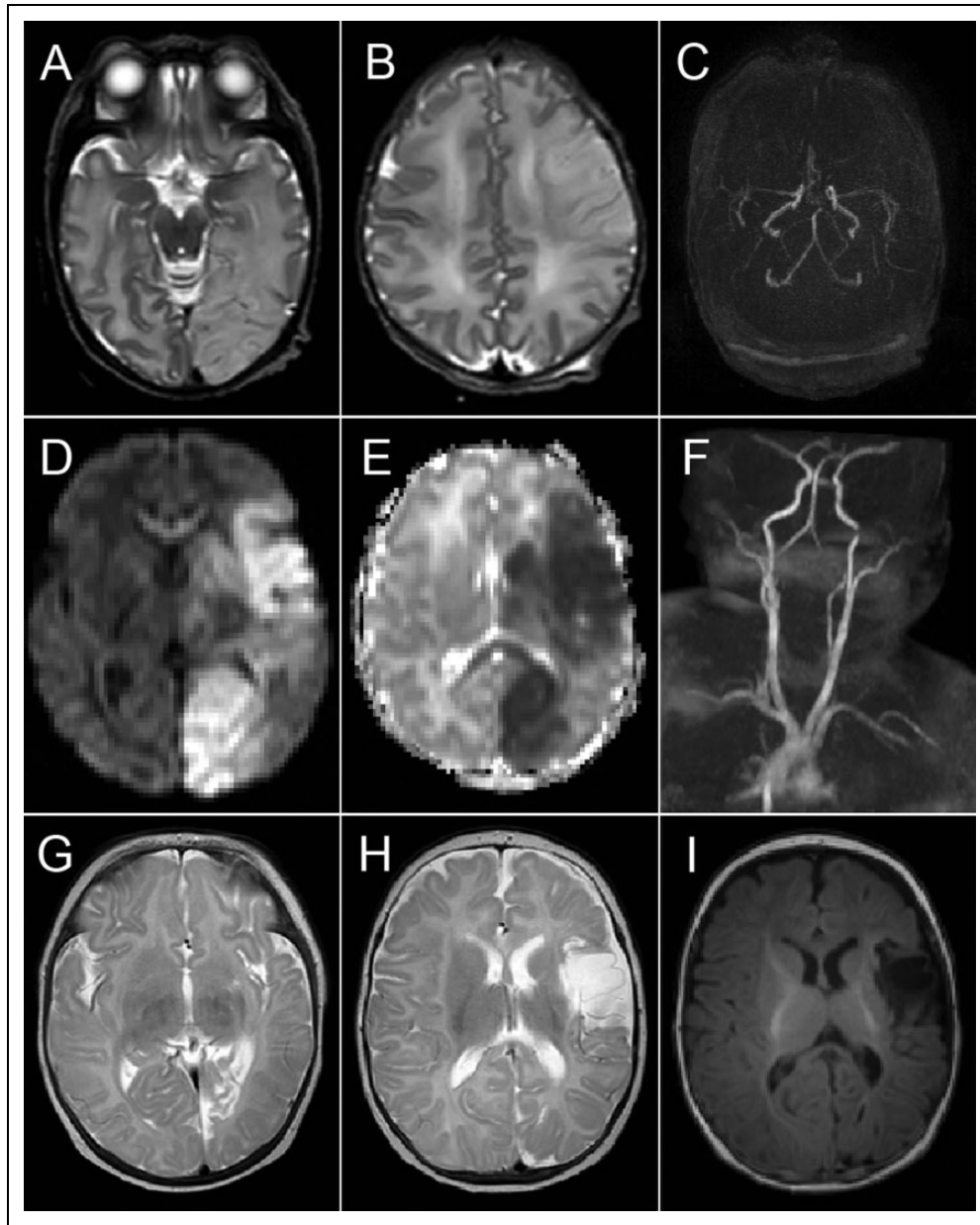
Extensive workup for thrombophilia markers performed on the child, the mother, and the father demonstrated no persistent aberrations. Electrocardiography and echocardiography on the third day of life did not reveal any significant cardiac pathologies apart from a patent foramen ovale with a diameter of 5 mm. The patient was treated using phenobarbital along with single doses of phenytoin, levetiracetam, and midazolam. The last clinically detectable seizure occurred on the third day of life.

At the age of 1 year and 4 months, the patient demonstrated a slight right-sided hemiparesis (hand more severely affected than leg). Magnetic resonance imaging at the age of 5 months demonstrated chronic lesions in the supply areas of the left middle cerebral artery and the posterior cerebral artery (Figure 2G, H, I). During the follow-up period, no additional seizures occurred.

## Discussion

Although the role of intrapartum factors in the pathogenesis of neonatal arterial ischemic stroke has been investigated in previous studies, there are no previously published case studies that report an antenatal MRI scan of a normal fetal brain, which then undergoes an acute neonatal arterial ischemic stroke near or during birth. The observation that the lesions occurred less than 3 days prior to delivery is suggestive of an important role of the intrapartum period.

Previously the association had been made by visualizing ischemic lesions in their acute stages on MRI, giving an approximate period for the injury after symptoms had arisen.<sup>10</sup>



**Figure 2.** At the age of 3 days: A-B, T2-weighted axial TSE sequence image of the brain showing hyperintensity in the cortical areas supplied by the left middle cerebral artery and the posterior cerebral artery, indicating edema; C-F, TOF angiography revealing no stenosis or thrombi; D-E, DWI and ADC map, respectively, showing diffusion restriction. At the age of 5 months: G-H, T2-weighted axial scan; I, FLAIR scan demonstrating chronic lesions from the left middle cerebral artery and posterior cerebral artery ischemic infarctions; ADC: apparent diffusion coefficient; DWI: diffusion weighted imaging; FLAIR: fluid attenuation inversion recovery; TOF: time of flight; TSE: turbo spin echo.

A previous study analyzed the timing of injury on a series of MRI scans carried out after the neonates developed symptoms.<sup>3</sup> Based on the dynamic appearance of cytotoxic edema on MRI, they concluded that the injury must have occurred near birth. Our case provides an additional fragment of data to support such a conclusion.

The trauma of surgery, such as a cesarean delivery, is a risk factor for thrombosis in the mother. The emergency cesarean delivery has previously been associated with neonatal stroke; however, the role of elective cesarean delivery in neonatal

stroke has not been studied.<sup>11</sup> Therefore, an increase in the risk of stroke due to surgery cannot be fully ruled out when planning delivery.

The exact mechanism of stroke remained unidentified. Among others, a causative factor could be emboli from the placenta, which would have had to pass through the patent foramen ovale and cause the occlusion of the left middle cerebral artery and the left posterior cerebral artery. Typical neonatal and presumed perinatal stroke lesions occur in the anterior circulation, and on the left side of the brain, most

commonly affecting the middle cerebral artery.<sup>12</sup> This could be caused by proximal emboli. The presence of several simultaneous lesions as well as a lack of pathological findings from magnetic resonance angiography of cerebral and neck arteries could further implicate embolism.<sup>8</sup>

Studies have associated various antenatal risk factors with both neonatal strokes and hypoxic ischemic encephalopathy. Fetal heart rate abnormalities, reduced fetal movement, meconium-stained amniotic fluid, low Apgar score, resuscitation at birth are well-recognized risk factors of hypoxic ischemic encephalopathy.<sup>13</sup> These risk factors are also seen more frequently in children who develop neonatal arterial ischemic stroke in comparison to healthy neonates. However, the profiles of risk factors seen in cases of either condition differ.<sup>6</sup> For example, it has been demonstrated that low umbilical cord pH and low Apgar scores, which are associated with hypoxic ischemic encephalopathy, are less frequent in neonatal arterial ischemic stroke.<sup>14</sup> In contrast, maternal fever and premature rupture of membranes are significantly more common in neonatal arterial ischemic stroke cases.<sup>6</sup>

Furthermore, the lesion morphology and clinical findings of hypoxic ischemic encephalopathy, which is caused by birth asphyxia, differ distinctly from those of neonatal stroke.<sup>11</sup> Although the morphology, and thus the direct causes of injury appear to be different, it is possible that a subclinical level of fetal distress could either be a final trigger or be the consequence of neonatal arterial stroke.<sup>6</sup>

The lesions reported in our case are similar to the injuries caused by emboli, which are thought to originate from the placenta, bypass the lung circulation via the patent foramen ovale, and then pass into cerebral vessels. Such emboli could be caused by the same disease responsible for fetal distress or be dislodged from the placenta by the fetal stress response to asphyxia.<sup>8</sup>

## Summary

The authors report a case of a neonatal arterial ischemic stroke that occurred in the immediate perinatal period, possibly due to emboli from the placenta during a planned, otherwise uneventful cesarean delivery. Three days before birth, antenatal magnetic resonance imaging demonstrated a healthy brain. No clear etiological factor was discovered. The placenta was not available for pathological analysis.

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## Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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## Ethical Approval

The study was approved by the Research Ethics Committee of the University of Tartu (223/T-10) and informed consent was obtained from the parents and the child for participation in the study.

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