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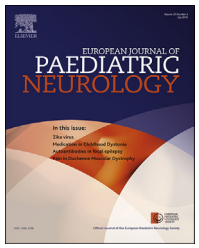

Original article

Perinatal arterial ischemic stroke related to carotid artery occlusion

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ABSTRACT

Background: The aetiology of perinatal arterial ischemic stroke remains speculative. It is however widely accepted that the aetiology is multifactorial, involving various maternal, placental, foetal and neonatal risk factors. A resulting thromboembolic process is hypothesized and the placenta identified as the most plausible source. An arteriopathy, as observed in a significant proportion of childhood ischemic stroke, is thought to be rare.
Methods: We report here five cases of perinatal stroke that differ from the vast majority by documented carotid occlusion, and add eleven other similar cases from the literature.
Results: In the majority, an intraluminal thrombus of placental origin is the most probable hypothesis, while in the remaining ones, one can reasonably presume a direct vessel wall injury related to a traumatic delivery, yet generally unproven by imaging.
Conclusion: We hypothesize that most of these cases share similar pathophysiology with the more common perinatal arterial ischemic stroke but differ by a persistent identified thrombus in the carotid artery at the time of first imaging, leading to a more severe and extended ischemic damage responsible for an adverse neurological outcome.

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1. Introduction

Perinatal arterial ischemic stroke (PAIS) encompasses a variety of conditions where a focal area of cerebral tissue is damaged as a result of blood flow disruption in a cerebral artery, which occurs between 20 weeks of foetal life and 28 days of life. Recent studies suggest an incidence of 1 per 2300 to 1 per 4000 live births, rendering PAIS the most frequent form of ischemic stroke in children.[1,2] When manifestations are delayed, usually with motor asymmetry developing after a few months of life, the label *arterial presumed perinatal ischemic stroke* (APPIS) is used whereas the term *neonatal arterial ischemic stroke* (NAIS) is applied when stroke clinically manifests within 28 days after birth, often in the first days of life with unilateral recurrent seizures.[3,4] Despite growing literature, the mechanisms underlying the entire group of PAIS remain poorly understood, hindering the implementation of appropriate therapeutic and preventive strategies apart from rare circumstances.[5] The primary hypothesis is a thromboembolic phenomenon arising from the placenta and, in accordance with the foetal circulation, passing through the patent foramen ovale into the aorta and cerebral circulation.[6,7] This placento-embolic mechanism has been supported by the known hypercoagulable state encountered during pregnancy, notably in the peripartum, compounded with a variety of synergistic prothrombotic factors of maternal and foetal origin.[6] Another proposed mechanism for stroke occurring acutely after birth is a direct vessel injury during the birth process itself or an intrinsic arteriopathy by analogy with childhood ischemic stroke.[3,8–10] Yet, intraluminal thrombi in cerebral arteries, evidence for vessel wall injuries or arteriopathy, are seldom documented in neonates on angiographic sequences. In fact, in the vast majority of NAIS, cerebral vessels are patent and exhibit normal anatomy at the time of first acute imaging provided that cervical vessels imaging is often bypassed.[4] This article reports five distinctive cases of PAIS that differ from the vast majority by an identified carotid occlusion upon MR angiographic sequences that might provide aetiological clues. In addition, the related literature is reviewed. Due to the fact that the precise timing of the carotid occlusion and subsequent stroke is not known, we have voluntarily kept the abbreviation PAIS rather than NAIS that implicitly favours a peripartum event.

2. Methods

Fives cases were collected from various tertiary centres in Switzerland (two) and France (three) and are reported herein. Among the three French cases, two are enrolled in the AVC nn cohort but detailed clinical data were not reported in previous publications.[8] We subsequently reviewed in the medical literature cohort studies on NAIS and relevant case reports and series, published in English or in French, using the following keywords: neonatal, perinatal, arterial ischemic stroke, occlusion, carotid artery and placenta abnormality, and thereafter through cross-referencing. Cases were included in the review only when the following information was provided: 1) clinical manifestations; 2) imaging evidence of a carotid artery occlusion; 3) associated stroke; and 4) elements of the antepartum and peripartum history. Data regarding potential risk factors and outcome were carefully reviewed but were not mandatory for inclusion. Only the most relevant images are provided in this paper but others are available on request.

3. Case presentations

3.1. *Case report 1*

A one-day-old male infant was referred to the neonatology ward following convulsions and respiratory distress. He was born at 37 weeks following a normal pregnancy by caesarean section due to a reduction in foetal movements and a pathological cardiotocographic tracing. His 34-year-old mother had a history of one elective abortion but otherwise had no medical history. Apgar scores were 5–7–8 and arterial pH at the umbilical cord was 7.13. Birthweight was 2650 g and head circumference 32 cm (10–25th centile). Signs of respiratory distress started soon after birth, requiring intubation and mechanical ventilation. Laboratory findings were unremarkable apart from a thrombopenia at 74 G/L and a hypoglycaemia at 1.9 mmol/L. Left-sided hypotonia became manifest a few hours after birth, with clonic movements of the left lower limb. The Magnetic Resonance Imaging (MRI) on day 3 enabled the identification of a right hemispheric extensive ischemic stroke on T2-weighted images and diffusion-weighted imaging (DWI) (Fig. 1a and b). Absent internal carotid flow was noted on axial T1-sequences (Fig. 1c) and on MR angiographic (MRA) sequences (Fig. 1d). Coagulation studies were normal. The infant was not given any antithrombotic therapy and neonatal convulsions subsided spontaneously without use of antiepileptic drugs. MRI at 3 months revealed diffuse cortical and subcortical atrophy of the right hemisphere (Fig. 2a). The right internal carotid artery had not recanalized (Fig. 2b). Neurological examination at two years was characterised by left-sided unilateral cerebral palsy and global development delay. He has developed focal epilepsy, currently well controlled on monotherapy.

3.2. *Case report 2*

A female infant born at 38 weeks with a birthweight of 2500 g (5th–10th centile) presented with severe perinatal asphyxia. After an uneventful pregnancy, the mother suddenly developed vaginal bleeding, epigastric pain and reduction in perceived foetal movements. Foetal heart rate recordings showed marked bradycardia and poor variability, leading to an urgent caesarean section. The Apgar scores was 4 at 3 min. Arterial cord pH was not available. Due to meconium fluid aspiration and altered alertness, the infant was immediately intubated and transferred to a neonatal intensive care unit. Lactate serum levels rose to 19.6 mmol/L after 6 h. A transcranial ultrasound performed at day of life (DOL) 2 showed an area of focal hyperechogenicity, suggestive of a brain infarction, later confirmed within the superficial areas of the right middle cerebral artery, sparing the deep grey matter and the right posterior cerebral artery by cerebral computed tomography (CT) at day 5. MRI at day 9 confirmed the above findings