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MR angiography findings in infants with neonatal arterial ischemic stroke in the middle cerebral artery territory: A prospective study using circle of Willis MR angiography

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ABSTRACT

Aim: Neonatal arterial ischemic stroke (NAIS) results from a focal disruption of the blood flow in a cerebral artery by a not well understood mechanism. Our objective is to describe the acute MRangiography (MRA) findings in infants with an NAIS in the middle cerebral artery (MCA) territory and correlate them with early parenchymal infarcts and motor outcome.
Methods: Among one hundred prospectively followed neonates with NAIS, we studied thirty-seven patients with an MCA infarct explored with circle of Willis MRA. MCA flow characteristics were documented, along with infarct location/extent and motor outcome at age 7 years.
Results: Twenty-three (62%) of the children showed arterial changes, all ipsilateral to the NAIS, with occlusion in six, thrombus-type flow defect in nine, and unilateral increased flow in enlarged insular arteries in the remaining eight. There was a statistically significant correlation between parenchymal and arterial MR findings ($p = 0.0002$). A normal MRA had a negative predictive value of 100% (95% CI: 76.8-100) in ruling out a main branch infarct. Patients with abnormal MRA tended to be at increased risk for cerebral palsy (OR = 3.1). Occlusion was associated with a worse outcome ($p = 0.04$).
Interpretation: MRangiography shows arterial abnormalities suggesting that embolism is a frequent cause of NAIS.

1. Introduction

The neonatal period is the most common time for paediatric arterial ischemic stroke (AIS); the prevalence is 13/100,000 live births [1,2]. Neonatal AIS (NAIS) is a widely-recognized cause of neurologic morbidity in children [1–4]. Large stroke size [5] and corticospinal tract injury [6–9] are both valuable predictors of poor motor outcome. The causal mechanisms of NAIS are poorly understood [2–4,10]. While AIS is deemed more common than venous infarctions [11,12], the exact cause of arterial lesions in the acute stage remains unclear. Better knowledge of arterial abnormalities in AIS may help in identifying possible mechanisms. MR imaging – the imaging modality of choice of neonatal brain injury – allows non-invasive study of the brain vasculature, via MRangiography (MRA). The primary aim of this longitudinal study was to analyze the early MRA patterns in a cohort of newborns with NAIS, focusing on the middle cerebral artery (MCA), whose territory is most com-

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monly affected. The second aim was to correlate those patterns with both early parenchymal infarcts and motor outcome at age 7 years, in order to indirectly assess the functional consequences of flow disruption on the brain parenchyma.

2. Methods

2.1. Patients

This study was part of the longitudinal AVCnn (*Accident Vasculaire Cérébral du nouveau-né*, [neonatal stroke]) study (EudraCT 2010-A00329-30; Clinical trial NCT02511249). That study included 100 patients with NAIS recruited consecutively from 2003 to 2006 at thirty-nine hospitals throughout France [13]. Both the initial enrolment and age 7 follow-up were approved by the regional ethics committee in September 2003 and May 2010, respectively. Informed consent was obtained from each participant.

Enrolled children were full-term neonates who experienced a neurologic event, mostly clonic/tonic seizures, during the first 28 days of life. No infant suffered from an embolic cardiopathy or a severe infection such as meningitis. All patients had neuroimaging studies (CT, MRI or both), reviewed jointly by two experienced paediatric radiologists to confirm a cerebral infarct in an arterial territory. Eighty-six MRIs were performed on various 1.5-T MRI scanners. All of the children had T1- and T2-weighted imaging in at least the axial plane, along with diffusion-weighted imaging (DWI) when MRI was performed before day 10 after the onset of clinical signs. The acute stage of stroke was confirmed using diffusion-weighted data for exams performed within the first 10 days after symptoms. Because DWI could be normalized in exams performed after this time interval, T1 and T2 patterns were correlated with CT performed at the acute stage to confirm the absence of early atrophic parenchymal changes. Though no serial MRIs were recommended in the MR protocol, one patient studied at day 1 of life had a follow-up MRI six days later. Because the MCA territory is the most frequently-affected arterial territory in NAIS and anatomical variations are rarer on the MCA than on the anterior or posterior cerebral arteries, we focused on the 73 patients with unilateral MCA ischemia.

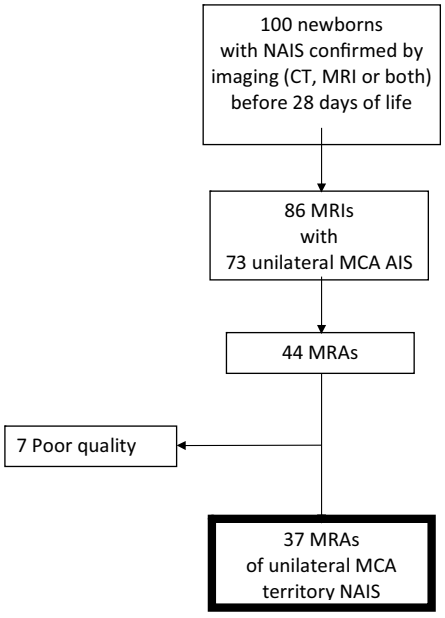
2.2. MRA

Among these 73 patients with unilateral MCA on MRI, 44 had a circle of Willis MRA. The recommended imaging protocol for circle of Willis MRA was as follows: 3D Time-of-Flight (TOF) sequence with TR 22/TE = 6.9 ms, thickness 1.2/Gap = 0.7 mm, matrix 131 × 384, angle 12-20, FOV = 160, 1 acquisition, without contrast. Source images, maximum intensity projections (MIPs) and 3D reconstructed images were used to analyse the data. Seven of the 44 MRAs performed were excluded due to motion artefacts.

Hence our final population consisted of 37 full-terme neonates with unilateral MCA AIS explored by MRI before day 28 with a good quality MRA (Fig. 1). Thirty of them were imaged in the first ten days (81%), and the others between day 12 and day 26.

2.3. Control subjects

For controls we selected eight neonates that had been scanned due to neonatal seizures within the first ten days of life between 2003 and 2006, and whose MRIs had been considered normal. Two of those neonates had moderate hypoxic-ischemic encephalopathy and the others had isolated seizures. The MRIs with MRA were performed according to the same protocol as that used for the babies with NAIS included in the present study. Those MRAs were reviewed to ensure that the MRA abnormalities seen in an NAIS setting are not also seen in neonates with no neonatal ischemic lesion, particularly NAIS.



NAIS: neonatal arterial ischemic stroke
MCA: middle cerebral artery
MRA: magnetic resonance angiography

Fig. 1. Study population.

2.4. Vascular distribution of parenchymal lesions

The MCA infarct territories were divided using a previously-published scheme [11,14]. Cortical branch infarcts (cortical infarct of superior and/or inferior MCA division) involved peripheric white matter and cortex within the frontal, parietal, temporal and occipital lobes. Lenticulostriate branch infarcts (deep infarcts of the basal ganglia) involved the basal ganglia. The main branch infarcts (mixed infarcts affecting both the basal ganglia and the cortical MCA territory) involved the cortical branch territory with additional lesions within the basal ganglia and the internal capsule.

2.5. Arterial analysis

Both distal internal carotid arteries, the horizontal segment and proximal insular branches of both MCAs, the basilar artery and the initial segments of both anterior and posterior cerebral arteries were checked for visibility. An abrupt cut-off of the flow was considered an occlusion (Fig. 2a). A round filling defect in an artery was considered a thrombus-type flow defect (Fig. 3a). Increased flow in the cortical insular branches was defined as the observation of larger and longer insular arteries (all) compared with the contralateral side (Fig. 4a).

2.6. Clinical follow-up

Children were followed with routine visits at ages 1, 2 and 3.5 years, and families were offered an assessment with standardized neurological examination at age 7 years. This last clinical evaluation was performed by a paediatric neurologist or a paediatric physical and rehabilitation medicine practitioner. The definition given by the Surveillance for Cerebral Palsy in Europe [15] was used to assess motor sequelae: (1) permanent abnormal tone or decreased strength, associated with (2) a patent functional deficit, as a conse-