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Original article

Diffusion restriction in the corticospinal tracts and the corpus callosum in neonates after cerebral insult

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Abstract

Background: In neonatal brains diffusion restriction, which is not limited to the region of insult, but is also found in distant locations from it seems to be a frequent finding, called pre-Wallerian degeneration.

Objectives: The purpose of this study was to describe these findings and to estimate the frequency of their occurrence with an attempt to determine their clinical significance.

Methods: 125 brain MRI examinations of neonates with confirmed brain damage performed or consulted in our Institute were retrospectively reviewed, focusing on the presence of restricted diffusion in corticospinal tracts (CST) and corpus callosum (CC). Apparent diffusion coefficients (ADC) were measured in callosal splenium and compared to normal neonatal brains.

Results: Restricted diffusion was found in 21 newborns (16.8%): in 4 in CST (3.2%), in 5 in CC (4.0%), in 12 in both (9.6%). Mean ADC value in CC was 0.638, standard deviation (SD): 0.211 $\mu m^2/s$ and in the control group 0.995, SD: 0.162 $\mu m^2/s$ ($p = 0{,}001$).

Conclusions: Neonatal brain MRI should be searched for DWI abnormalities which are not rare and require careful studying of ADC maps. Diffusion restriction in the corpus callosum and/or corticospinal tracts below the region of insult should not be mistaken for acute ischemia as it most likely reflects early phase of secondary neuronal degeneration called pre-Wallerian degeneration. This finding helps in prognostication and guides the management of the affected neonates.

Keywords: Neonates; Brain insult; Magnetic resonance imaging (MRI); Diffusion restriction; Pre-Wallerian degeneration (pWD)

1. Introduction

The development of magnetic resonance imaging (MRI) brought diffusion-weighted imaging (DWI) into the clinical practice. In this sequence water diffusion is measured *in vivo* in body tissues which helps in many clinical situations, e.g. acute ischemia. Technical progress of MRI-associated hardware brought MR-compatible incubators into the clinical practice.

Abbreviations: MRI, magnetic resonance imaging; DWI, diffusion-weighted imaging; ADC, apparent diffusion coefficient; pWD, pre-Wallerian degeneration; HI, hypoxia-ischemia; CC, corpus callosum; CST, corticospinal tracts; CNS, central nervous system; GW, gestational weeks

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This resulted in increased availability of these examinations to the youngest patients – neonates [1]. Restricted diffusion of water can be seen in many lesions [2], in neonatal brain it is found most commonly in hypoxic-ischemic injury but also in stroke, abscess, encephalitis. Diffusion restriction has also been described in the early phase of secondary neuronal degeneration – Wallerian degeneration – and was called pre-Wallerian degeneration (pWD). Reports on MRI findings of pWD are very sparse – searching for "pre-Wallerian degeneration, MRI" in PubMed one finds only 5 papers including our first report [3–7]. In our material of the tertiary referral neonatal center we noticed relatively high frequency of diffusion restriction in neonatal brains, which is not limited to the region of insult, but also found in distant locations from it. The purpose of this study was to describe these findings and to estimate the frequency of their occurrence with an attempt to determine their clinical significance.

2. Materials and methods

2.1. Patients

We retrospectively reviewed last 200 neonatal brain MRI examinations performed or consulted in our Institute which had confirmed brain damage. Institutional Bioethics Committee approval was not required due to the retrospective nature of the study. In each case written informed consent for clinical MRI was obtained from the parents/legal guardians. The inclusion criteria were as follows: (1) MRI performed in the neonatal period, (2) DWI sequence available, (3) abnormal brain MRI with hypoxic/ischemic (HI), ischemic, hemorrhagic or inflammatory lesion. The babies with suspected pathology that was not confirmed on MRI, with congenital abnormalities, minor non-parenchymal bleeding and venous sinus thrombosis without the consequences to the brain tissue were excluded from the study.

Finally the study comprised 125 newborns (60 females, 65 males). The following hemispheric lesions were found: intraparenchymal hemorrhage in 58 neonates (46.4%), hypoxic-ischemic lesions – 37 (29.6%), co-existing HI or ischemia and intraparenchymal bleeding – 17 (13.6%), stroke – 12 (9.6%), brain abscesses – 1 (0.8%).

2.2. MR imaging

All patients underwent MRI in 1.5T scanners. Most examinations ($n = 109$) were performed in our Institute always according to the same protocol which included echo-planar DWI sequence obtained with the following parameters: repetition time (TR) = 5200 ms, echo time (TE) = 100 ms, field of view (FOV) = 18 × 18 cm, acquisition matrix (MX) = 128 × 128, slice thickness/interslice gap = 3.0/0.3 mm, *b*-values of 0 and 1000 s/mm2, number of acquisitions (NEX) = 2. ADC map was generated in each case. The other sequences were as follows: coronal, sagittal and axial FSE/T2-weighted images (T2WI), axial SE/T1WI, axial SWI sequence, and axial FLAIR sequence with the following parameters:

- T1WI (TR = 400 ms, TE = 11 ms, FOV = 18 × 13,5 cm; MX = 256 × 192, slice thickness/interslice gap 3.0/0.3 mm, NEX = 2),
- T2WI (TR = 4000 ms, TE = 98.8 ms, FOV = 18 × 18 cm, MX = 288 × 288, slice thickness/interslice gap = 3.0/0.3 mm, NEX = 1.50),
- SWI (TR = 6000 ms, TE = 40 ms, FOV = 18 × 18 cm, MX = 256 × 512, slice thickness/interslice gap = 3.0/0.3 mm, NEX = 4),
- FLAIR (TR = 8000 ms, TE = 141 ms, TI = 2000, FOV = 18 × 18 cm, MX = 320 × 192, slice thickness/interslice gap = 3.0/0.3 mm, NEX = 1).

Additional sequences relevant to each case were performed, if necessary.

Sixteen examinations performed at other sites were consulted in our center, in these varying imaging techniques were used.

MRI analysis was carried out on the Advantage Workstation 4.4 (GE Healthcare) which provided software to calculate the apparent diffusion coefficient (ADC) maps.

2.3. Qualitative image analysis

Assessment of the quality of MRI data sets was performed on the basis of visual inspection and it was found satisfactory in all the analyzed cases. Images were assessed in agreement by two radiologists (MBF, 24 years of experience with MRI, 19 years of experience with neonatal MRI, and one of the remaining authors) in each case and final decisions were reached by consensus. The observers assessed the presence of DWI hyperintensities in the corpus callosum (CC) and corticospinal tracts (CST). Diffusion was considered restricted only when hypointensity had been found on ADC maps in the regions corresponding to DWI hyperintensities which was determined on the basis of qualitative visual assessment.

2.4. Quantitative image analysis

Since the lesions in CST were too tiny in neonatal brains to reliably measure ADC values, we only performed their quantitative analysis in the CC. The oval regions of interest (ROIs) were placed in the callosal splenium in 9 neonates from the study group and in 11