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Original research article

Circle of Willis abnormalities in children with neurofibromatosis type 1

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ABSTRACT

Background and purpose: The aim of the study was to assess anatomical variants and abnormalities in cerebral arteries on magnetic resonance angiography in 67 children with neurofibromatosis type 1 (NF1).

Materials and methods: The study included 67 children aged 9 months to 18 years (mean 6.6 years). Control group comprised 90 children aged 2–18 years (mean: 11.8 years). All patients were examined at 1.5 T scanner.

Results: We found cerebral arteriopathy (moyamoya disease) in one child (1.5%) in the study group. No aneurysms were found. Twenty-nine NF1 children (43.3%) had arterial anatomical variants. In 13 of them, more than one variant was diagnosed (44.8% of group with variants, 19.4% of study group). In control group, 19 children (21.1%) had variants, including four children with more than one variant (21% of group with variants, 4.4% of control group). Arterial variants were more common in NF1 patients compared with control group ($p = 0.026$, binomial test for two proportions). Percentage of multiple variants was higher in study group than in control group, but this difference was not significant. Variants were more frequent on left side than on the right one (significant difference in control group; $p = 0.022$, McNemara test). In study group, the number of left-sided anomalies (25) was similar to that of right-sided ones (22). There was no correlation between gender and variants, unidentified bright objects and variants or between optic gliomas and variants.

Conclusions: Occurrence of arterial variants in NF1 patients was twofold higher than in control group. Multiple variants were more frequent in the study group although the difference did not reach statistical significance. Features of cerebral arteriopathy were found in one child with NF1.

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1. Introduction

Neurofibromatosis type 1 (NF1) is an autosomal dominant genetic condition caused by a mutation in, or a deletion of, the *NF1* gene located within the long arm of chromosome 17. More than 250 mutations have been identified in affected individuals. The gene product – neurofibromin – serves as a tumor suppressor. The estimated incidence of NF1 is 1:3000 [1].

Clinical diagnosis of NF1 is established in the presence of at least 2 of 7 criteria: (1) six or more *café-au-lait* spots or hyperpigmented macules greater than or equal to 5 mm in diameter in children younger than 10 years and to 15 mm in adults, (2) axillary or inguinal freckles, (3) two or more typical neurofibromas or one plexiform neurofibroma, (4) optic nerve glioma, (5) two or more iris hamartomas (Lisch nodules), (6) sphenoid dysplasia or typical long-bone abnormalities such as pseudarthrosis, (7) first-degree relative with NF1 [2].

Renal artery stenosis secondary to fibromuscular dysplasia and other vascular lesions, also in the central nervous system (CNS), such as vascular ectasias, stenoses, moyamoya disease, and aneurysms, are reported more frequently in patients with NF1 than in general population [3,4]. Rarely, coronary artery aneurysms are identified in symptomatic or even asymptomatic individuals with NF1 [5].

Available literature contains mainly case reports concerning CNS vasculopathy. To our knowledge, there are only three papers based on the bigger material [6–8]. The purpose of this study is to assess the presence of anatomical variants and vascular abnormalities in cerebral arteries in children with NF1 on magnetic resonance angiography (MRA) in a group of 67 children with NF1.

2. Materials and methods

The material consisted of 67 children with NF1 diagnosed according to the above mentioned National Institute of Health Criteria Consensus Conference, aged between 9 months and 18 years (mean age 6.6 years). There were 35 boys and 32 girls in this group.

The control group consisted of 90 children aged 2–18 years, mean age 11.8 years (53 girls, 37 boys). The children included in the control group had no signs of CNS injury and were referred to magnetic resonance imaging (MRI) only because of headache.

All the children were examined at a 1.5 T scanner (GE Signa HDxt) with a 16-channel head coil. The protocol included the following sequences: SE/T1-weighted images (T1WI) in axial plane; FSPGR/3D/T1WI, sagittal; FSE/T2WI, axial, coronal; FLAIR/axial; GRE/T2*WI, axial; DWI. Children with NF1 underwent orbital magnetic resonance imaging (MRI) as well with IDEAL/T1WI, axial and FSE/T2WI + fatsat, coronal. The gadolinium-based contrast medium was administered, if necessary, in patients with NF1 in a standard dose of 0.1 mmol/kg. Magnetic resonance angiography was performed in 3D/TOF/SPGR sequence without contrast medium administration. The sequence parameters were as follows: repetition time TR = 25 ms, echo time TE = 3 ms, number of acquisitions NEX = 1, matrix MX = 384 × 224, field of view FOV = 22 × 16.5 cm, slice thickness/interslice gap ST = 1.4/−0.7 mm.

All the examinations were a part of routine clinical work-up of the patients – NF1 patients were included in the study when MRI was requested by the referring oncologist. Magnetic resonance angiography was additionally included to the routine protocol of brain MRI in children with NF1 for the purpose of this study. It made the whole examination 7 min longer. Magnetic resonance angiography was ordered by the referring neurologists as an addition to brain imaging in children included in the control group.

The institutional Bioethics Committee approval for this study was obtained. The one-sided binomial test for two proportions, McNemara two-sided significance test and Pearson correlation were used for statistical analysis of the data.

3. Results

Cerebral arteriopathy was defined as any abnormality of the intracranial arterial system that could not be considered as normal variant [7]. In the study group, one child (1.5% with 95% confidence interval [0.07%, 9.13%]) showed the signs of cerebral arteriopathy and was diagnosed as moyamoya disease (Fig. 1). We found no aneurysms in the study group and control group.

Twenty-nine children with NF1 (43.3%), 16 boys and 13 girls, turned to have arterial anatomical variants of the circle of

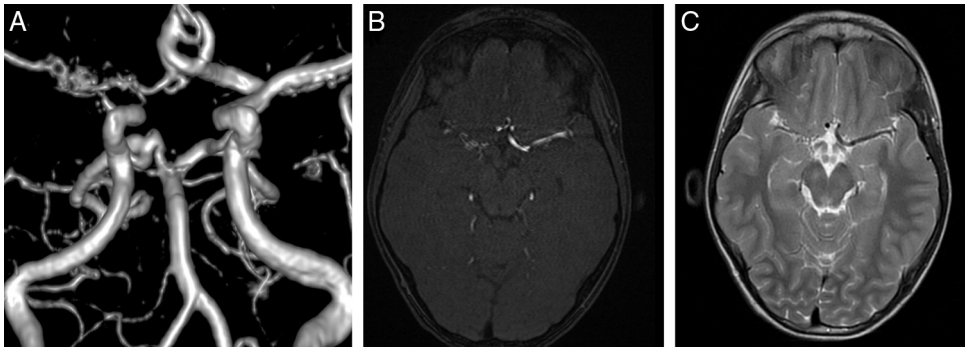

Fig. 1 – A 10-year-old boy with NF1 and stenosis/occlusion at the terminal portion of the right internal carotid artery resulting in the abnormal vascular network in the vicinity of the middle cerebral artery and anterior cerebral artery (A1). (A) MRA, VR reconstruction. (B) MRA, raw data. (C) FSE/T2WI/ax.