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Research papers

# Vessel shape alterations of the vertebrobasilar arteries in Mucopolysaccharidosis type IVa (Morquio A) patients

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ABSTRACT

*Purpose:* Main symptom of mucopolysaccharidosis type IVa (MPS IVa) is progressive systemic skeletal dysplasia. This is routinely monitored by cerebral and spinal MRI. The vascular system is generally not in the primary focus of interest. In our population of MPS IVa patients we observed vessel shape alterations of the vertebrobasilar arteries, which has not been described before.

*Material and methods:* MRI-datasets of 26 patients with MPS IVa acquired between 2008 and 2015 were eligible for retrospective analysis of the vertebrobasilar arteries. The vessel length and angle of the basilar artery (BA) and both vertebral arteries (VA) were analyzed. A deflection angle between 90° and 130° in the vessel course was defined as tortuosity, less than 90° as kinking. The results were compared to a matched control group of 23 patients not suffering from MPS.

*Results:* The deflection angle [°] of the VA and BA was significantly decreased in the majority (85%) of MPS IVa patients compared to the control group: BA 132 ± 24 vs. 177 ± 6, BA/VA transition 113 ± 21 vs. 152 ± 13, right VA 108 ± 23 vs. 156 ± 13, left VA 110 ± 22 vs. 157 ± 14 (all $p < 0.005$). Likewise, vessels of MPS IVa patients were significantly longer compared to the control group: BA 27 ± 4 vs. 21 ± 2, right VA 20 ± 6 vs. 10 ± 1, left VA 18 ± 5 vs. 11 ± 2 (all $p < 0.005$).

*Conclusion:* MPS IVa is associated with significantly increased tortuosity of vertebrobasilar arteries. Therefore the vascular system of MPS IVa patients should be monitored on routinely basis, as vessel shape alterations had been associated with dissections, leading to a higher risk of cerebrovascular events.

## 1. Introduction

Mucopolysaccharidosis type IVa (MPS type IVa, Morquio A syndrome) was first described in 1929 by Luis Morquio in Uruguay [1] and by James Frederick Brailsford in England [2]. It is an autosomal recessive inherited lysosomal storage disorder, caused by a mutation in the *GALNS* gene [3], which causes a deficiency of N-acetylgalactosamine-6-sulfate sulfatase (GALNS). The clinical occurrence of MPS IVa is variable and covers a wide range from mild to severe symptoms [3–5]. GALNS deficiency results in an excessive accumulation of glycosaminoglycans (GAGs) including keratan sulphate (KS) and chondroitin-6-sulfate (C6S) in lysosomes [6–10], causing skeletal dysplasia.

Skeletal dysplasia is the main leading clinical symptom, causing short stature, odontoid hypoplasia and atlanto-axial joint instability, which can lead to spinal cord compression, preferentially of the cranio-cervical junction and/or cervical spine [11–17].

However, MPS IVa patients do not suffer from mental retardation. Moreover, the clinical course is progressive with the majority of patients not reaching their thirties with the most common cause of mortality being respiratory and cardiac failure [4,18].

MRI findings of skeletal affections are reported frequently in the literature [11,12,16]. Cerebral and spinal MRI of patients with MPS IVa is routinely performed in our institute mainly to monitor skeletal dysplasia at the cranio-cervical junction. With the field of view on cranio-spinal MRI also depicting the vertebrobasilar arteries, elongation and increased tortuosity was noted as a secondary finding. The goal of this study was to analyze the morphology of the vertebrobasilar arteries in our patients with MPS IVa.

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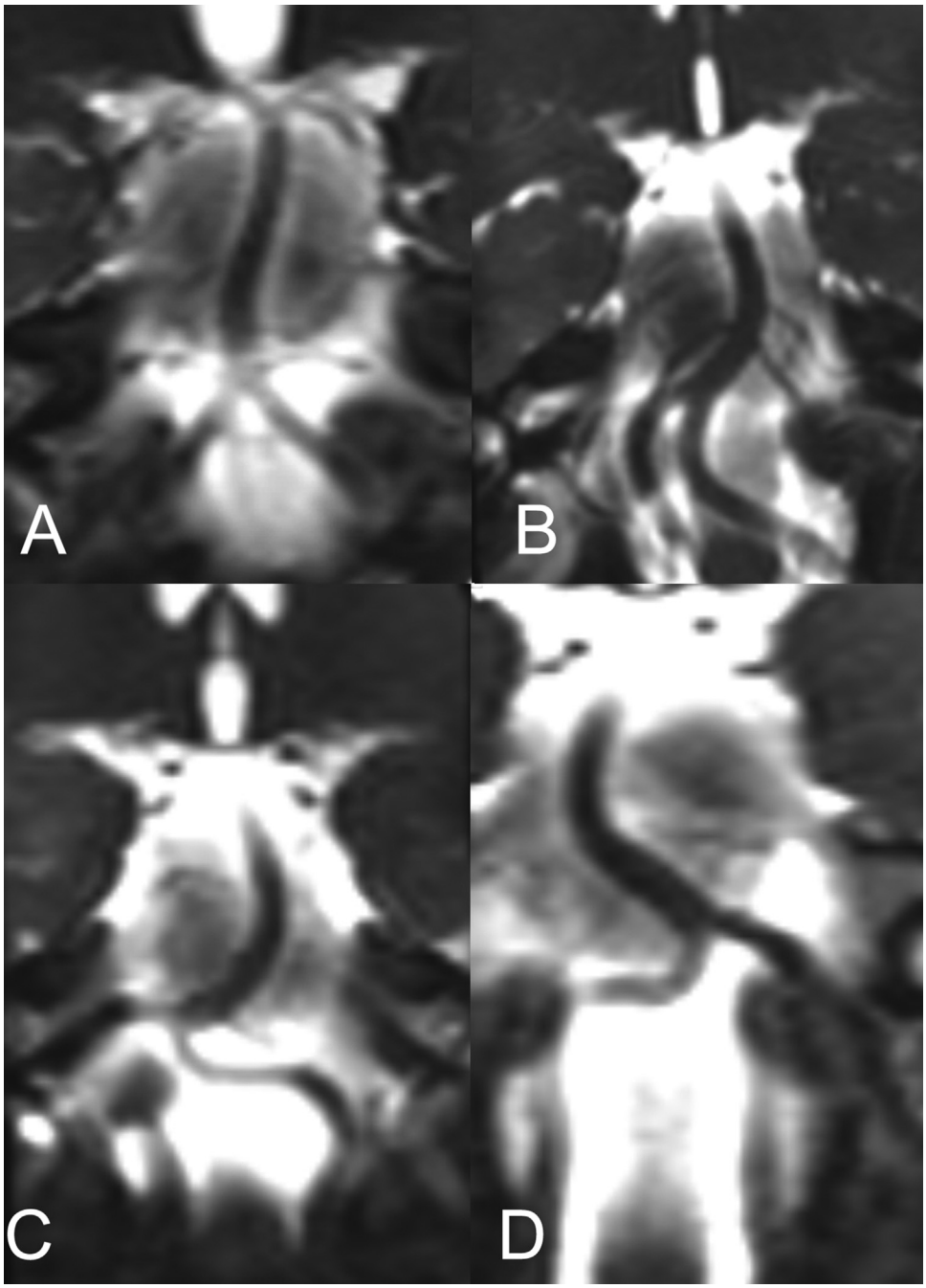


**Fig 1.** Coronal view MRI of the vertebrobasilar arteries in four patients suffering from MPS IVa A) normal course of the BA and VAs, B) tortuosity of both VAs in the V4 segment, "C"-shaped BA, C) kinking in the left vertebrobasilar transition, kinking in the left V4 segment, tortuosity in the left V4 segment, "C"-shaped BA, D) kinking in the right V4 segment, "C"-shaped BA.

## 2. Material and methods

### 2.1. Patient population

Between 2008 and 2015, 43 cranio-cervical MR examinations (1.5 T Magnetom Espree, Siemens AG, Munich, Germany) were performed in 26 patients (8 females, 18 males; age: 19 ± 12 years (mean ± 1 SD), range 5–48 years) suffering from MPS IVa. All patients were of small stature (mean ( ± 1SD) body height 117.5 ± 18 cm). The latest acquired MRI was chosen for each patient, making 26 MR examinations eligible for statistical analysis.

MR images of 23 patients (12 female, 11 male; mean age ± 1 SD: 18.8 ± 15.57, range 1–47 years) not suffering from MPS acquired between 2015 and 2016 served as controls. These examinations had been carried out to investigate hearing loss or to exclude acoustic neuroma.

Intracranial MRI included sagittal 3D constructive-interference-in-steady-state- (CISS-) sequence (slice thickness 1 mm) and time of flight angiography for one patient. VA and BA were analyzed in their entire course. The VA is commonly divided into 4 segments (V1 to V4), with V1 originating from the subclavian arteries, V2 representing the intraforaminal section, V3 being the atlantic/extradural section (C2-level to the dura) and V4 being the most distal section between the dural leaf and the confluence, where both VAs unite to form the basilar artery [10].

Vessel shape alterations along the course of the VA and BA were measured:

- at the extra-intradural transition (V3/V4-segment)
- in the course of the V4-segment
- at the confluence of the VA (focusing on the VA with the steeper angle to the BA)