ON-LINE APPENDIX

Materials and Methods

Smoker Score. The score includes the evaluation of 3 aspects of basilar artery dolichoectasia on axial T2 images:

$$\text{Diameter } (0 = <4.5 \text{ mm}, 1 = \geq 4.5 \text{ mm})$$

Laterality: (0 = midline throughout, 1 = medial to the lateral margin of clivus or dorsum sellae, 2 = lateral to lateral margin of clivus or dorsum sellae, 3 = at the cerebellopontine angle).

Height of bifurcation: (0 = at or below the dorsum sellae, 1 = within the suprasellar cistern [1 cut above the dorsum sellae], 2 = at the third ventricle floor [1 cut above suprasellar cistern], 3 = indenting and elevating the third ventricle floor [≥2 cuts above suprasellar cistern]).

The Smoker score ranges between 0 (normal) and 7 (marked dolichoectasia).

Curved Length and Linear Length Measurement. The step-by-step procedure to measure basilar artery length and tortuosity in the present study was the following:

1) All MRA native axial partitions were loaded into commercially available software (syngo MultiModality Workplace; Siemens).

2) The function Inspace Window was activated obtaining interactive 3D multiplanar reconstructions.

3) The "Vessel Analysis" menu was opened, and 2 anatomic basilar artery landmarks were identified on the basis of multiplanar and maximum-intensity-projection 3D reconstructions: 1) the confluence of the vertebral arteries (proximal/caudal basilar artery extremity), and 2) the bifurcation of the basilar artery into the posterior cerebral arteries (distal/rostral basilar artery extremity).

4) After setting the 2 above-mentioned landmarks with the function "Trace," the software automatically provided a curved line following the vessel path according to the different signal intensity of the basilar artery compared with the surrounding parenchymal structures and subarachnoid spaces. The exact correspondence between the line and the vessel course was accurately verified in all space dimensions.

5) Whenever the correspondence between the basilar artery and the curved line was suboptimal, the operator adjusted the course of the line manually, activating the function "Edit": This function shows several square dots along the curved line that can be manually positioned centrally in the vessel lumen until the curved line follows the vessel along its whole course (additional square dots can be placed if needed).

6) When the functions "Measure" and "Curve" are activated, the software provides the length in millimeters of the curved line running from the proximal and distal basilar artery extremities (curved length). After we recorded the measure, we deleted all the square dots except the proximal and distal extremes, obtaining a straight line joining the remaining 2 square dots. The software provided the corresponding measure in millimeters (linear length), which was also recorded. The tortuosity index was eventually calculated according to the following formula:

$$\text{Tortuosity Index} = (\text{Curved length}/\text{Linear length}) - 1.$$

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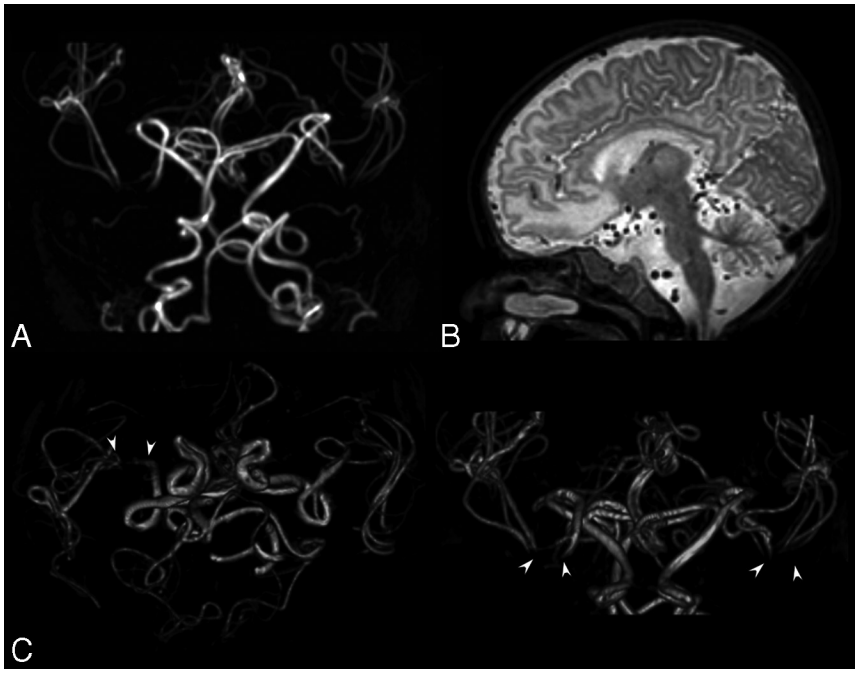
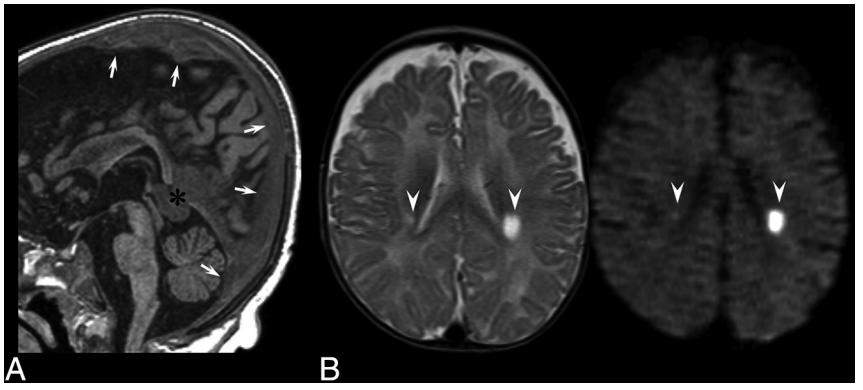
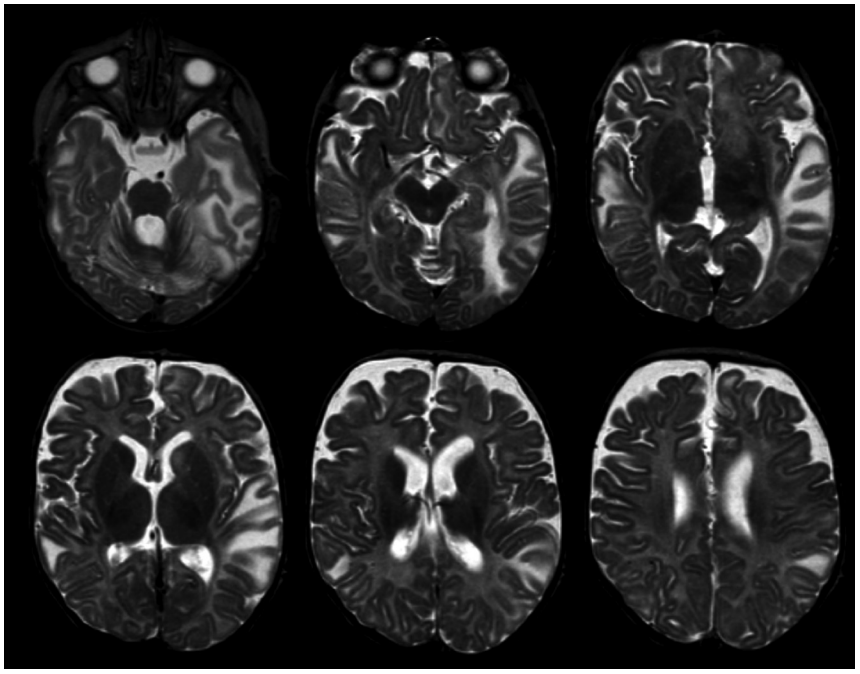


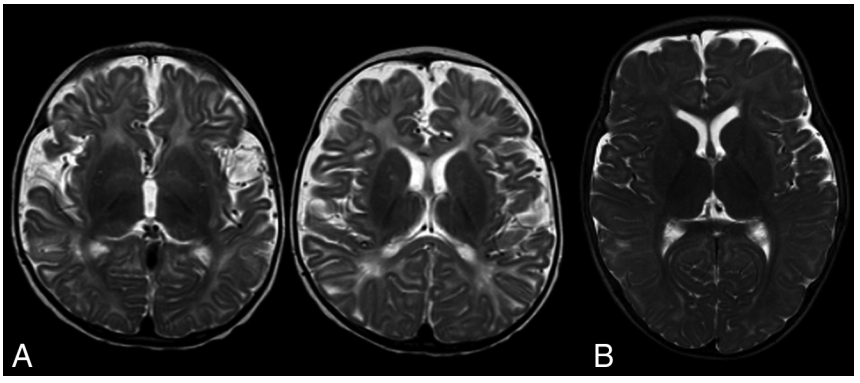
ON-LINE FIG 1. *A*, MR angiography (time-of-flight technique) of the extra-intracranial cerebroafferent arteries disclosing a typical increased vessel tortuosity in a 5-month-old boy affected by Menkes disease (patient 12). *B*, Parasagittal T2-weighted images in a 4-month-old boy. Note the numerous *black dots* corresponding to signal voids of the markedly tortuous intracranial arteries. *C*, 3D reconstruction (volume-rendering technique) of the intracranial arteries shown in *A*: craniocaudal view: the middle cerebral arteries seem to present distal stenosis (*arrowheads*) bilaterally; frontal view: "stenosis" cluster in the lower portion of the tortuous branches, thus revealing the artifactual nature of the lumen changes due to downward blood flow.



ON-LINE FIG 2. *A*, Midsagittal T1 image showing ectasia of the venous sinuses (*small white arrows*) in a 9-month-old boy (patient 4). The vein of Galen (*asterisk*) is also dilated. *B*, Axial T2 and diffusion-weighted images at the level of the centrum semiovale in an 8-month-old boy (patient 6) show an oval hyperintense lesion in the left hemisphere with decreased apparent diffusion coefficient values (not shown). A smaller mirror lesion in the contralateral hemisphere with identical signal features is also partially visible (*arrowheads*).



ON-LINE FIG 3. Axial T2 images in a 5-month-old boy (patient 10) showing bilateral but asymmetric tumefactive lesions involving the temporal lobes but also the parietal regions and the left frontal lobe (gyrus rectus and contiguous portion of the superior frontal gyrus). Note the left basal ganglia lesion, the cerebral (and cerebellar) atrophy, the global abnormal myelination for age, and the signs of increased vascular tortuosity (see the central image in the upper row disclosing the signal void of some arteries), which complete the neuroimaging involvement.



ON-LINE FIG 4. Axial T2-weighted images at the level of the basal ganglia. *A*, Image of a 9-month-old boy (patient 4) shows diffuse bilateral hyperintensity of the supratentorial white matter with sparing of the cortical spinal tract. Abnormal myelination in this child is probably due to the combination of delayed myelination and neurodegeneration. *B*, Image of a 7-month-old girl shows normal supratentorial myelination for comparison with *A*.

On-line Table: Main neuroradiologic findings from the literature review and in our sample

	Literature Review				Our Sample			
	First MRI		Follow-Up MRI		First MRI		Follow-Up MRI	
	62 Children with MD		23 Children with MD		26 Children with MD		8 Children with MD	
	No.	%	No.	%	No.	%	No.	%
Intracranial vessels								
Increased arterial tortuosity								
Yes	45	(73%)	14	(61%)	26	(100%)	8	(100%)
No	2	(3%)	0	(0%)	0		0	
NR	15	(24%)	9	(39%)				
Arterial stenosis and ectasia								
Yes	0		0		0		0	
No	0		0		17[a]	(100%)	8	(100%)
NR	62	(100%)	23	(100%)				
Ectasia of the venous sinuses								
Yes	1	(1%)	0		1	(4%)	1	(12%)
No	0		0		25	(96%)	7	(88%)
NR	61	(99%)	23	(100%)				
White matter involvement								
Tumefactive lesions								
Yes	21	(33%)	3	(13%)	7	(27%)	2	(25%)
No	3	(5%)	7	(30%)	19	(73%)	6	(75%)
NR	38	(61%)	13	(56%)				
Centrum semiovale lesions								
Yes	1	(1.6%)	1	(4%)	1	(4%)	0	
No	0		0		25	(96%)	8	(100%)
NR	61	(99%)	22	(96%)				
Nontumefactive lesions								
Yes	14	(23%)	3	(13%)	9	(35%)	3	(38%)
No	0		2	(9%)	17	(65%)	5	(62%)
NR	48	(77%)	18	(78%)				
Abnormal myelination								
Yes	20	(32%)	9	(39%)	19	(73%)	7	(88%)
No	0		0		7	(27%)	1	(12%)
NR	42	(67%)	14	(61%)				

Note:—NR indicates not reported/mentioned.

[a] Seventeen of 26 children with MD underwent MRA at the first examination; none presented with intracranial artery stenosis.