Stable Leukoencephalopathy in a Patient With ACTA2–associated Multi-system Smooth Muscle Disorder

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A 14-year-old girl with recently diagnosed ACTA2 multi-system smooth muscle dysfunction syndrome (de novo R179H (G536A) ACTA2 variant) was referred for headaches. MRI revealed extensive increased T2 signal in the periventricular white matter (Figure 1), consistent with a stable leukoencephalopathy. CT angiogram revealed fusiform aneurysms of the petrous and cavernous internal carotid arteries bilaterally, (Figure 2A), and short M1 segment of the middle cerebral arteries (MCA) (Figure 2B). ACTA2 (OMIM#613834) is an autosomal dominant condition due to variants affecting the vascular smooth muscle alpha-actin gene. Characteristic features of ACTA2 and those present in our patient are outlined in Table 1[1,2].
References


Figure Legends

Figure 1:

MRI axial T2-FLAIR images demonstrate extensive T2 hyperintensity throughout the white matter of both cerebral hemispheres (arrowheads), which spares the subcortical U-fibers. The white matter volume is preserved. These findings were unchanged from previous imaging.
Figure 2A:

CT angiogram showing a single axial image at the skull base. Both internal carotid arteries are enlarged with fusiform aneurysms (arrows), right larger than left. Within the right ICA is also a large clot (asterisk).

Figure 2B

3-dimentional shaded surface display of the CT angiogram data demonstrating the narrow M1 segments bilaterally (arrows) in addition to findings described in Figure 2A.
Table 1

<table>
<thead>
<tr>
<th>Features characteristic of ACTA2 associated multi-system smooth muscle disorder</th>
<th>Features present in our patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Periventricular white matter lesions</td>
<td>Extensive periventricular and subcortical white matter abnormality (leukoencephalopathy)</td>
</tr>
<tr>
<td>Fusiform dilatation of internal carotid arteries</td>
<td>Fusiform aneurysms of the petrous and cavernous internal carotid arteries bilaterally, and right vertebral artery at C1.</td>
</tr>
<tr>
<td>Stenosis of M1 and A1 segments of middle cerebral and anterior cerebral arteries</td>
<td>Narrow M1 segment of middle cerebral arteries bilaterally. Hypoplasia of P1 segment of right posterior cerebral artery.</td>
</tr>
<tr>
<td>Moya-moya disease</td>
<td>Not present</td>
</tr>
<tr>
<td>Thoracic ascending aortic aneurysm and dissection</td>
<td>Dilatation of the ascending and descending aorta</td>
</tr>
<tr>
<td>Persistent ductus arteriosus</td>
<td>Large patent ductus arteriosus (PDA) and atrial septal defect (ASD) repaired in infancy</td>
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<tr>
<td>Pulmonary hypertension-associated vascular changes</td>
<td>Pulmonary hypertension prior to PDA and ASD surgery</td>
</tr>
<tr>
<td>Premature coronary artery disease</td>
<td>Not present</td>
</tr>
<tr>
<td>Premature ischemic stroke</td>
<td>Not present</td>
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<tr>
<td>Congenital mydriasis</td>
<td>Present</td>
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<tr>
<td>Intestinal malrotation</td>
<td>Not present</td>
</tr>
<tr>
<td>Hypoperistalsis of the bowel</td>
<td>Present only after repair of aortic aneurysm</td>
</tr>
<tr>
<td>Hypotonic bladder</td>
<td>Present only after repair of aortic aneurysm</td>
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<tr>
<td>Livedo reticularis</td>
<td>Not present</td>
</tr>
<tr>
<td>Variable learning difficulties</td>
<td>Learning difficulties</td>
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</table>
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