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Congenial ischemic stroke related to COL4A1-related disease: A case report

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Introduction

- ✓ *COL4A1*-related disorders are diseases that cause small-vessel brain disease of varying severity, including diffuse periventricular leukoencephalopathy, lacunar infarcts, microhemorrhage, dilated perivascular spaces, and deep intracerebral hemorrhage, and are variably associated with eye defects and systemic findings such as kidney involvement, muscle cramps, cerebral aneurysms, Raynaud phenomenon, cardiac arrhythmia, and hemolytic anemia.
- ✓ It is caused by pathogenic variant in the *ASXL3* gene. Since the first report in 2013, about 30 cases have been reported up to date.
- ✓ These disorders are inherited in an autosomal dominant manner.
- ✓ This case report is about a child diagnosed with a *COL4A1*-related disorder.

Case report

- ✓ A 3-month-old boy was referred to the department of rehabilitation medicine with a suspicion of torticollis. The child was born at 39 weeks with a weight of 3040g through normal spontaneous vaginal delivery, and the perinatal history was non-specific.
- ✓ At the time of the visit, the child had right tilting torticollis and left-sided flattening of the posterior head with positional plagiocephaly (plagiocephaly index 12mm), with no other significant findings on physical examination except for a asymmetric right reaction.
- ✓ Physical therapy for torticollis was initiated, and the follow-up a month later showed improvement.
- ✓ At 12 months of age, the child was revisited with concerns of delayed gross and fine motor development identified during routine pediatric screening.
- ✓ Physical examination revealed left hand dominance, a tendency of fisting in the right hand, suspected increased right DTR activity, and increased muscle tone in the right upper and lower limbs. The GMFM-88 scores showed total dimension of 25% (lying & rolling 76.5%, sitting 35%, standing 2.56%, walking, running & jumping 2.78%), indicating delayed gross motor development compared to peers.
- ✓ A brain MRI was performed, revealing cystic encephalomalacia and lateral ventricle dilation, presumed to be caused by ischemia in the Lt. MCA territory, and moderate to severe stenosis of left middle cerebral artery (Figure 1).
- ✓ Microangiopathy NGS panel testing for congenital ischemia and vessel stenosis identified a *COL4A1* c.2589G>T variant, inherited from his mother. The family history revealed that the child's maternal grandfather had a history of stroke (Figure 2).
- ✓ This variant was classified as a likely pathogenic variant according to the ACMG's sequence variant interpretation guidelines. The child is currently undergoing rehabilitation treatment for congenital ischemic stroke.

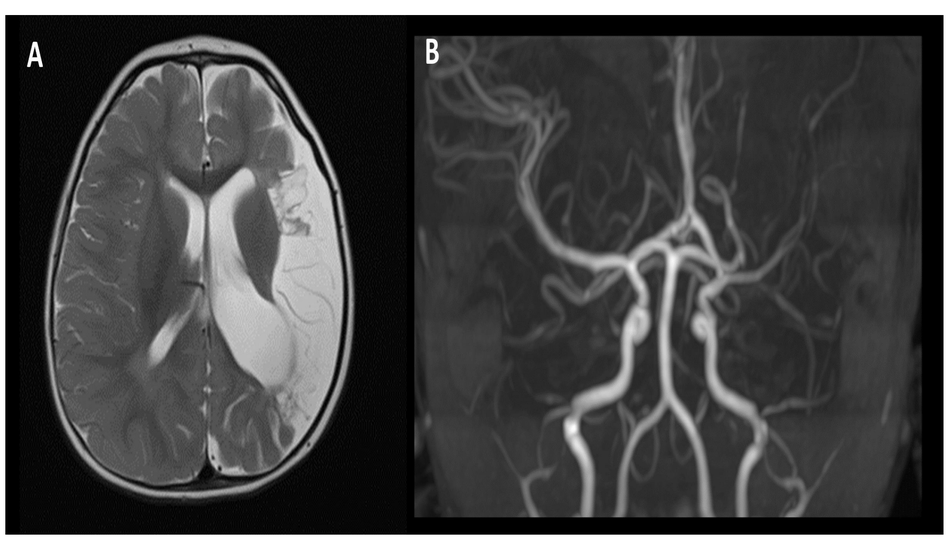

Figure. 1. The child underwent Brain MRI and MRA at 12 months. (A) T2-weighted images showed cystic encephalomalacia in the Lt. MCA territory and dilated lateral ventricle. (B) MRA revealed moderate to severe stenosis of Lt. MCA.

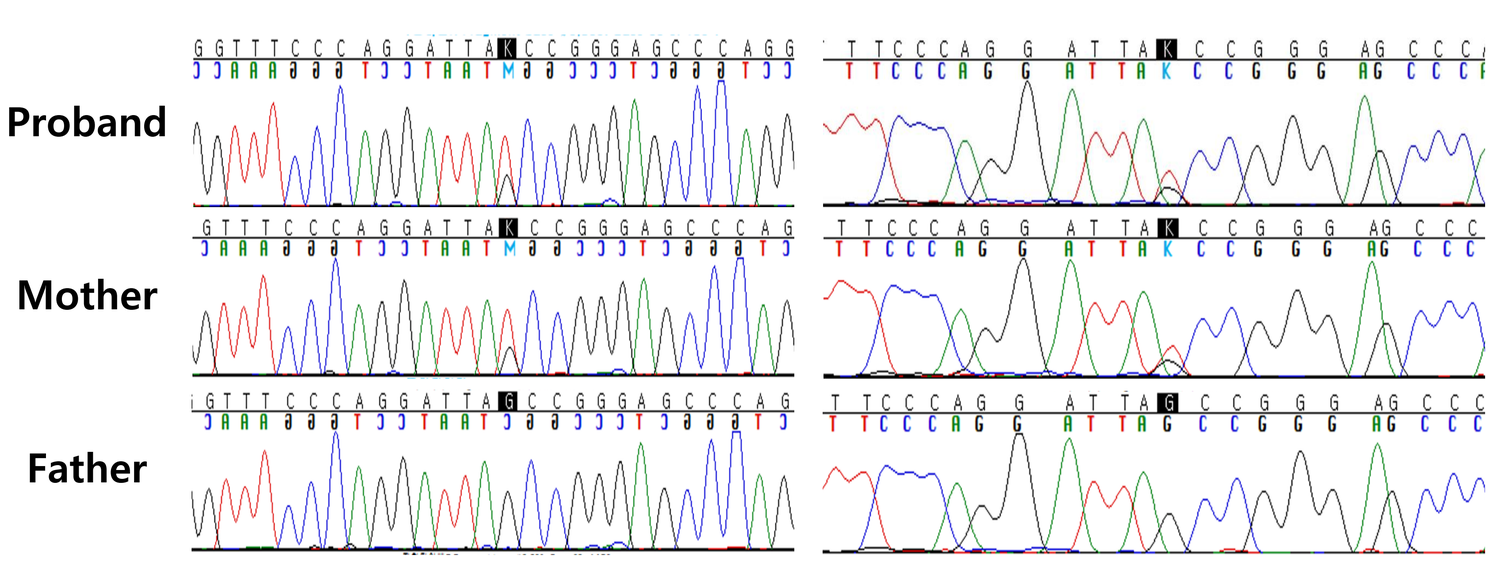

Figure. 2. Microangiopathy NGS panel testing for congenital ischemia.

Conclusion

- ✓ With the advancement of genetic technology, genetic diagnosis for congenital disorders such as congenital anomalies has become very important for understanding the disease, establishing treatment plans, and predicting prognosis in affected children.
- ✓ This case report, diagnosing *COL4A1* related disease in a child diagnosed with congenital ischemic stroke, highlights the importance of genetic diagnosis for congenital stroke or infant or child onset stroke.