Two Siblings with Myopathy and choreoathetosis and a Novel Variant of ATP8A2

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INTRODUCTION

ATP8A2 mutations are characterized by global developmental delay, severe hypotonia, hyperkinetic movement disorders and optic atrophy.

-ATP8A2 gene is highly expressed in the retina, brain, spinal cord, and testis; the highest levels have been reported in the cerebellum.

-ATP8A2 is critical for the developmental processes of the central nervous system, and alterations of this gene may lead to severe neurological phenotypes.

OBJECTIVE

To present a case report on 2 siblings presenting with myopathy and movement disorders.

METHOD

Baby T is a 2y old toddler referred for concerns of abnormal movements, hypotonia and global developmental delay. He is 6th born to first degree consanguineous couple. Mother reported an uneventful antenatal period, however she had had a previous bad obstetric history with history of anencephaly,hydrops and miscarriage in previous 3 respective pregnancies. BabyT was reported to have been born at 8months of gestation by LSCS due to transverse lie with average birth weight followed by uneventful postnatal period. By 2years of age, he was yet to achieve head control but had no feeding or breathing concerns. Family history was notable for an older sibling with similar history of global developmental delay, right eye squint with ptosis and choreoathetosis. On neurological examination he was noted to be alert, dolicocephalic head with myopathic facies, bilateral ptosis,ophthalmoplegia noted in left eye and bilateral optic atrophy, global hypotonia with absent DTRs, persistent choreo-athetoid movements in all extremities, occasional dystonia and scoliosis.

RESULT

Metabolic investigations , SMA testing, CPK were unremarkable. MRI brain showed mild cerebral atrophy and thin corpus callosum. WES done reported two homozygous variants of ATP8A2, NM_016529.5:c.810A>C p. (Leu270Phe) & NM_016529.5:c.856G>C p.(Val286Leu) in the patient and his older sibling.

CONCLUSION

-Patients with ATP8A2 genetic mutation have characteristic phenotypic of developmental delay, myopathy, severe hypotonia, choreoathetosis and optic atrophy.

-An awareness of this gamut of clinical manifestations can assist in clinical suspicion, targeted genetic testing and prognostication of this rare combination of myopathy with movement disorder

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