Aicardi Goutières syndrome: unlocking the puzzle of early encephalopathy

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Background :

Aicardi Goutières syndrome is a rare genetic disorder that presents in neonates and infants. It is associated with TREX1 gene mutation. Autoimmunity has been found recently as part of the pathophysiology of the disease.

Aim:

To expand the differential diagnosis of early encephalopathy in pediatric population and explore possible treatable entities.

Materials and methods :

Detailed clinical history, family history, and MRI (magnetic resonance imaging), EEG were done. Whole exome sequencing was also done in view of a positive family history.

Results :

a 4 year old male born out of a non-consanguineous marriage and normal birth history presented with global developmental delay and failure to thrive. The mother also noticed dystonic posturing of the limbs with spasticity. The patient was also having stimulus-sensitive myoclonus. On examination, microcephaly was present. With increased tone and dystonic posturing of limbs on walking. Deep tendon reflexes were exaggerated, and babinski sign was positive. MRI brain was s/o white matter changes. The patient's younger brother has also been having similar complaints at the age of 10 months.

Conclusion:

Neurological symptoms- seizures, dystonia, myoclonus, poor neck holding, irritability, spasticity.

Systemic manifestations -erythema, glaucoma, hypothyroidism, pulmonary hypertension, cardiomyopathy, autoimmune hepatitis, myopathy and arthropathy.

Recent advances in possible treatment options like JAK inhibitors. It has role in suppressing interferon activation.

Gene & Transcript	Location	Variant	Zygosity/ Inheritance	OMIM Phenotype	Clinical Significance
TREX1 (+) NM_033629.6	Exon 2	c.58dupG (p.Glu20Glyfs*82)	Compound Heterozygous /Autosomal Recessive	Aicardi-Goutieres syndrome	Pathogenic (PVS1, PM2,, PP5)
TREX1 (+) NM_033629.6	Exon 2	c.393C>G (p.Phe131Leu)			Uncertain significance (PM2)