A Retrospective Case Series of Indian Children With Homozygous RNASEH2B Mutations Presenting As 'Cerebral Palsy' Mimic

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INTRODUCTION

- Aicardi-Goutieres syndrome (AGS) is an inherited encephalopathy that affects newborn infants and usually results in severe neurodevelopmental morbidity.

Classic AGS

Spastic-dystonic syndrome presenting after age 1y

ADAR1-related bilateral striatal necrosis

'Non-syndromic' spastic paraparesis (*RNASEH2B, ADAR1, IFIH1*)

SAMHD1-related cerebrovasculopathy

Phenotypes associated with AGS1-7

A) Classic AGS with prenatal or infantile onset – Mimics congenital viral infections with irritability, with white matter disease and intracranial calcification on neuroimaging;

B) Disease presenting beyond the first year of

Life - neurological regression , variable combination of spasticity and dystonia, non-specific white matter changes and/or intracranial calcification.

C) Dystonia and neuroimaging characteristic of bilateral striatal necrosis, manifest in later childhood, due to ADAR1 mutations

D) Slowly progressive ('non-syndromic') spastic paraparesis confined to the lower limbs in mutations in ADAR1, IFIH1, and RNASEH2B.

E) Intracerebral, large vessel disease moyamoya and aneurysms with intracerebral haemorrhage and infarcts, representing SAMHD1-related disease.

METHODOLOGY

Case series of 6 patients from 5 different families.

Age 1 – 15 years. All were males.

A final diagnosis was achieved on genetic analysis using NGS.

All of the patients were homozygous for the mutation RNASEH2B c.529G>A.

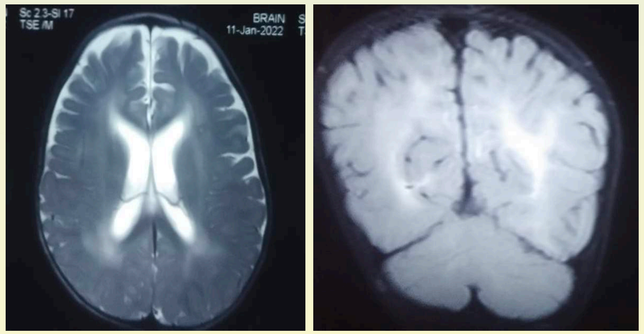
RESULTS

	CONSANGUINITY	CLINICAL PRESENTATION	BRAIN MRI	GENETIC STUDY
1	NO	Developmental delay, Exaggerated startle, truncal hypotonia, dystonia and mild spasticity of limbs.	T2 hypointensity in periventricular white matter and internal capsule	missense variation in RNASEH2B gene
2	NO	Developmental regression, spastic tetraplegia.	T2 hyperintensities in periventricular white matter	missense variation in RNASEH2B gene
3	NO	Developmental delay, febrile illness, central hypotonia and rigidity.	Subcortical white matter calcification and cerebral atrophy.	missense variation in RNASEH2B gene
4	YES	Developmental delay, Spasticity of 4 limbs	Diffuse white matter hyperintensities.	missense variation in RNASEH2B gene .
5	NO	Developmental regression, Spasticity in all 4 limbs.	B/L periventricular and peritrigonal white matter hyperintensities.	missense variation in RNASEH2B gene .
6	NO	Developmental delay, spasticity in all 4 limbs.	B/L T2 Hyperintensities in B/L frontal, peritrigonal and subcortical white matter	missense variation in RNASEH2B gene .

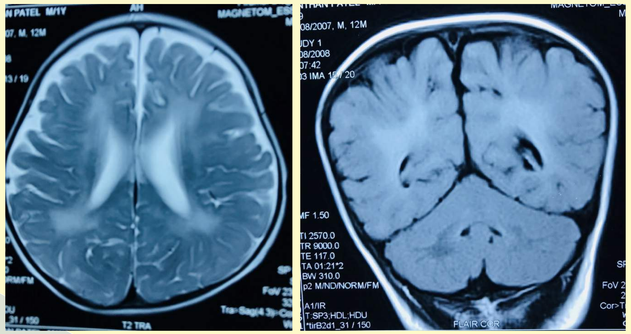
- All were autosomal recessive with missense variation in RNASEH2B gene

CONCLUSION

- A homozygous mutation c.529G>A in the RNASEH2B gene leads to a spastic cerebral palsy like presentation in children.
- This mutation should be tested for in children presenting in infancy with the MRI features.



Patient 1



Patient 2

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