Autosomal recessive spastic ataxia of Charlevoix–Saguenay: Two case reports

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INTRODUCTION

•Autosomal recessive spastic ataxia of Charlevoix–Saguenay (ARSACS) is a rare neurodegenerative disorder caused by biallelic mutations in the SACS gene. [1]
•It is classically characterized by the triad of ataxia, pyramidal involvement and axonal-demyelinating sensorimotor neuropathy. [1]
• Although more prevalent and initially noted in the Charlevoix-Saguenay-Lac-Saint-Jean (CSLSJ) region of Quebec, cases have now been reported from all over the world.
•Disease onset of classic ARSACS is often during the toddler period, presenting as delayed walking due to ataxia. However, it can present later in life.
•Other features such as speech & oculomotor disturbances, neuropathy, and pyramidal signs are also evident.
•MRI findings of cerebellar atrophy along with linear T2 hypointensities over pons are characteristic.
•We present 2 cases of ARSACS.

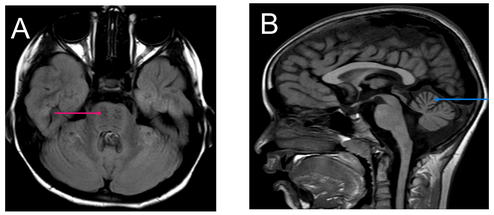
CASES

• **HISTORY -** First was a 7-years-old girl born of a non-consanguineous marriage, presented with mild motor delay, unclear speech, and imbalance in walking since early childhood. The second was a 9-years-old boy born of 3rd-degree consanguineous marriage, who was recently diagnosed with leukemia & was admitted for the same. History revealed a motor delay with difficulty in walking & performing fine motor activities .

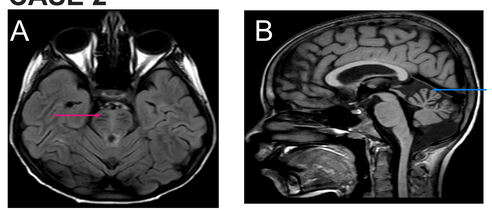
•**EXAMINATION** - Both had positive cerebellar signs. The girl also had lower limb spasticity, absent reflexes & bilateral pes cavus. Tone and reflexes were normal in the boy. Fundus examination was normal in both.

•**NEUROIMAGING-**

- CASE 1



- CASE 2



- MRI brain of both the children revealed linear FLAIR-T2-(Axial) hypointensities in the pons (A, red arrow), with mild atrophy of the superior vermis & cerebellar hemispheres (T1 sagittal images. B, blue arrows).

• **NERVE CONDUCTION STUDIES** - CASE 1: sensory-motor demyelinating neuropathy in the girl child,

•CASE 2: Normal

•**GENETICS** (WES) –

- CASE 1: compound heterozygous autosomal recessive mutations in the SACS gene. (novel variant)

- CASE 2: autosomal recessive homozygous mutations (novel) in the SACS gene.

• **TREATMENT & FOLLOW – UP**

- Physical therapy was initiated for both patients.
- No progression was noted on one-year follow-up.

DISCUSSION

• ARSACS is an important differential for any child with toddler age onset ataxia.
• Close clinical differentials include Friedreich's ataxia, Ataxia telangiectasia, Hereditary spastic paraplegia, Abetalipoproteinemia, Autosomal recessive ataxia with vitamin E deficiency, Disorders with hypomyelination like Pelizaeus Merzbacher disease and early onset spinocerebellar ataxias.
• As consistent with the literature [1], both of our patients had ataxia, MRI findings of T2 linear pontine hypointensities, and cerebellar atrophy.
•However, although neuropathy and spasticity are frequently associated with ARSACS [1](97% and 75% respectively), our 2nd case did not have both of these features.
• Cases without neuropathy and without spasticity have been individually reported in the literature [2], but the absence of both these features in the same patient has not been reported yet. It is possible that in our case, one of these features may manifest in the future (on follow-up).
•Also, although thickened retinal hypermyelinated fibers appearing as yellow streaks radiating from the edges of the fundus are commonly seen in ARSACS[3], both cases had a normal fundus exam.
•Importantly, the genetic study of our second case revealed a novel mutation, variant 'c.12218_12219del'on the exon 10 of the SACS gene.
• Although the presence of T-ALL in case 2 could be co-incidental, it should be noted for future reference. As of today, no association of ARSACS with leukemia has been reported.

CONCLUSION

•ARSACS is a rare childhood-onset neurodegenerative disorder characterized by a triad of ataxia, spasticity & neuropathy due to mutations in the SACS gene. However, few cases may present only with ataxia, especially early in the course.
•Linear T2 - hypointensities over pons are characteristic of it, which help in clinching the diagnosis in an ataxic child.
•Currently, only supportive care can be given to these children.
• Genetic counseling should be offered to the parents.

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