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A Rare Case of Autosomal Recessive Spastic Ataxia of Charlevoix - Saguenay

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Abstract: ***Background: Autosomal recessive spastic ataxia of Charlevoix - Saguenay (ARSACS or SACS) is an early onset neurodegenerative disease with high prevalence (carrier frequency 1/22) in the Charlevoix - Saguenay - Lac - Saint - Jean (CSLSJ) region of Quebec. It is caused by mutations in SACS gene on chromosome 13 which encodes the protein Sacsin. It is characterized by triad of spasticity, cerebellar symptoms and sensory and motor polyneuropathy. Clinical Case: A 29 years old unmarried female born out of non - consanguineous marriage presented to the hospital with a history of difficulty in maintaining balance while walking since 17 years, dysarthria and stiffness in lower limb. She had no significant drug history or other medical illness. There was history of intentional tremors in father since 3 years. Her mother died at the age of 40 due to some neurological issue with unknown cause. On neurological examination, there was all four limbs spasticity, deep tendon reflexes were exaggerated, with bilateral extensor plantar response. Examination also revealed dysmetria, dysdiadochokinesia and abnormal knee - heel - shin test on left side. The patient was swaying from side to side with open eyes and her feet positioned opposite each other. Romberg's test was negative. There were no significant findings on systemic examination. Fundus and retinal examination were normal. Her routine blood works were within normal limits. On MRI brain imaging, there were areas of edema involving the bulky pons and striped Hypointensities with mild cerebral and moderate cerebellar atrophic changes. Nerve conduction study indicated axonal demyelinating polyneuropathy, involving sensory nerves more than motor nerves, and affecting lower limbs more than upper limbs. Conclusion: The diagnosis of Autosomal Recessive Spastic Ataxia of Charlevoix - Saguenay was established based on clinical manifestations, radiological imaging and nerve conduction studies. Index of suspicion should be higher for early diagnosis in young patients with gait ataxia and spasticity with cerebellar atrophy in the brain imaging. treatment in this patient was focused on symptomatic relief and supportive care including physical and occupational therapy.***

Keywords: ARSACS (Autosomal Recessive Spastic Ataxia of Charlevoix - Saguenay), neurodegenerative, dysmetria, dysdiadockokinesia, striped hypointesities, cerebellar atrophy, axonal demyelinating polyneuropathy

Case Presentation

1. Introduction

Autosomal recessive spastic ataxia of Charlevoix - Saguenay (ARSACS or SACS) was described as a French - Canadian founder effect in 1978. ARSACS is an early onset neurodegenerative disease with high prevalence (carrier frequency 1/22) in the Charlevoix - Saguenay - Lac - Saint - Jean (CSLSJ) region of Quebec. It was Initially thought to be prevalent only in Canada but it is now being increasingly reported from the rest of the world. It is caused by mutations in the SACS gene on chromosome 13 which encodes the protein Sacsin. It is characterized by triad of spasticity, cerebellar symptoms and sensory and motor polyneuropathy.

2. Case Presentation

A twenty- nine year old unmarried female presented to the hospital with a history of difficulty in maintaining balance while walking since seventeen years which was gradual in onset, progressive in nature which had worsened since the last two years. She also complained of dysarthria and stiffness in the lower limb. Dysarthria was gradual in onset and very slow in progression, was in the form of scanning speech and was not associated with hoarseness of voice. Stiffness in the leg was also gradual in onset and slow in progression with no diurnal variation. It was not associated with inability to walk. There was a history of tremulousness of movement of the upper limb which was intentional in nature and relieved on rest. There was no history of confusion, trauma, dizziness, vertigo, nausea, vomiting, headache, weight loss, fever, breathlessness or chest pain. She was taking a mixed diet with preserved appetite, normal sleep, normal bowel and bladder habits. She was born out of a non - consanguineous marriage and had no significant history of other medical illnesses. She had no significant drug history. There was a history of intentional tremors in her father since 3 years. Her mother had died at the age of 40 due to some neurological issue for which there was no documentation available.

On general examination, the patient was conscious, oriented to time, place and person. Patient was well built and well nourished with a BMI of 21 Kg/m 2. Her Heart rate was eighty - eight beats per minute in the right radial artery in supine position with normal force, volume, tension and with no radio - radial or radio - femoral delay. Pulse was normal in all four limbs. Blood pressure was 108/70 mm Hg in the right brachial artery. Respiratory rate was twenty per minute. SpO2 was 99% on room air. Patient was afebrile. On examination there

was no pallor, icterus, clubbing, cyanosis, lymphadenopathy or edema. There was no skin pigmentation or swelling.

3. Neurological Examination

Patient was fully conscious, oriented to time, place and person. Patient was right handed. Patient was uneducated. Dysarthria was present in the form of scanning speech with separation of syllables, normal repetition and comprehension. There was no history of hoarseness of voice. Patient had intact short term and long term memory. There was no history of hallucination or delusion.

There was no anosmia/parosmia, visual field disturbances, diplopia, normal direct and consensual light reflex, normal color vision, normal extraocular movement and no ptosis. Muscles of mastication and facial expressions were normal on examination. Patient had normal taste sensations, normal hearing with Rinne`s and Weber test and no hyperacusis, tinnitus or dizziness and vertigo. Gag reflex was intact on both sides of the palate and pharynx. Patient had no difficulty in shrugging of shoulders and turning the neck against resistance. Patient had no difficulty in speaking labials like b, p or pronouncing ta, da or aah.

Patient was well built and well nourished with a BMI of 21 kg/m 2. Patient's all four extremities were of normal girth, both proximally and distally. Tone of all four extremities were increased with velocity dependent hypertonia, with predominant involvement of upper limb flexor compartment, suggesting spasticity. Power of all four extremities, at all the joints was normal. Examination of coordination revealed dysmetria during finger - nose - finger test, dysdiadochokinesia on left side and abnormal knee - heel - shin test on left side. The patient was swaying from side to side with open eyes and her feet positioned opposite each other. Romberg's test was negative. Patient was unable to do tandem walking. There was tremulousness of movement of the upper limb which was intentional in nature and relieved on rest. There were no chorio - athetoid movements or tics. Reflexes of all four extremities were exaggerated, there were bilateral extensor plantar responses. Left sided ill - sustained clonus was also present. Fine touch, pressure, crude touch, pain, temperature, vibration, proprioception, stereognosis, two point discrimination, graphaesthesia and examination for neglect were normal.

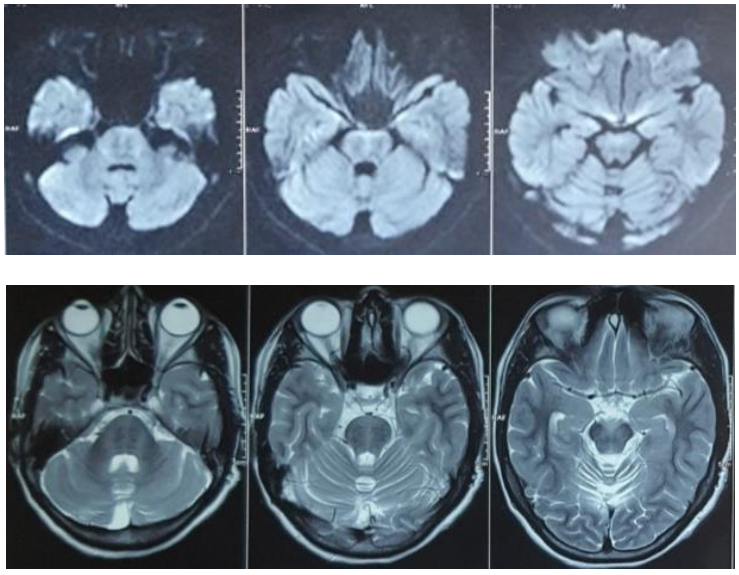
There were no significant findings on systemic examination of respiratory, cardiovascular or gastrointestinal systems. Fundus and retinal examination were normal. There was no telangiectasias or tendon xanthomas on head to toe general examination.

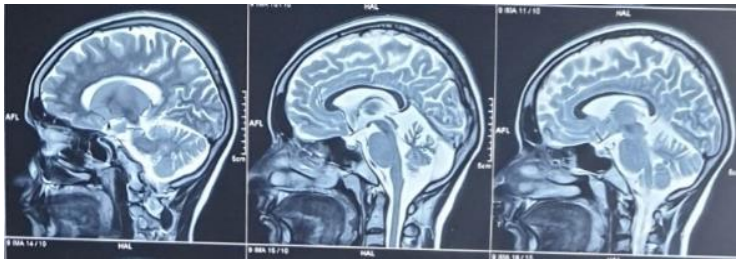
4. Investigations

Hemoglobin - 11.6 mg/dL	Serum Urea - 15 mg/dl
WBC - 5670 / microL	Serum Creatinine - 0.6 mg/dl
RBC - 5080000/ microL	Serum Sodium - 139 mEq/L
Hct - 40.8 %	Serum Potassium - 4.6 mEq/L
MCV - 80.3 fL	Serum Total Billirubin - 0.4 mg/dL
APC - 306000/microL	Serum SGPT - 24 IU/mL
Serum Vitamin E – 9.2 mg/L	Serum TSH - 2.3 microIU/mL
Serum B12 - 460 pg/mL	Random Blood Sugar – 104 mg/dL

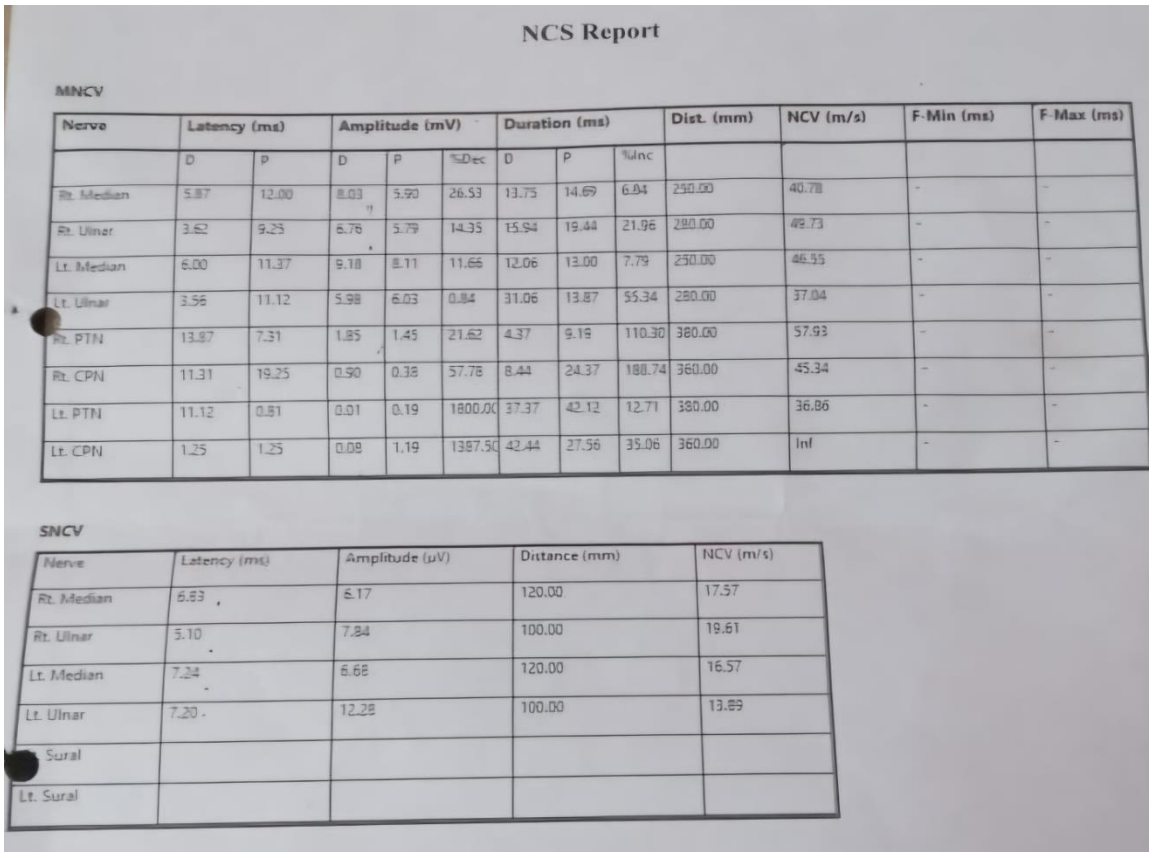
5. Radiological Findings

On MRI brain imaging, there were areas of edema involving the bulky pons and striped hypointensities consistent with the findings of Autosomal Recessive Spastic Ataxia of Charlevoic - Sanguenay Syndrome. Also it showed mild cerebral and moderate cerebellar atrophic changes with no evidence of acute infarcty or hemorrhage or space occupying lesion.





Nerve conduction study indicated axonal demyelinating polyneuropathy, involving sensory nerves more than motor nerves, and affecting lower limbs more than upper limbs.



NCS Report

MNCV

Nerve	Latency (ms)		Amplitude (mV)			Duration (ms)			Dist. (mm)	NCV (m/s)	F-Min (ms)	F-Max (ms)
	D	P	D	P	%Dec	D	P	%Inc				
Rt. Median	5.87	12.00	8.03	5.90	26.53	13.75	14.69	6.84	250.00	40.78	-	-
Rt. Ulnar	3.62	9.25	6.76	5.79	14.35	15.94	19.44	21.96	200.00	49.73	-	-
Lt. Median	6.00	11.37	9.18	8.11	11.66	12.06	13.00	7.79	250.00	46.55	-	-
Lt. Ulnar	3.56	11.12	5.98	6.03	0.84	31.06	13.87	55.34	280.00	37.04	-	-
Rt. PTN	13.87	7.31	1.85	1.45	21.62	4.37	9.19	110.30	380.00	57.93	-	-
Rt. CPN	11.31	19.25	0.90	0.38	57.78	8.44	24.37	188.74	360.00	45.34	-	-
Lt. PTN	11.12	0.81	0.01	0.19	1800.00	37.37	42.12	12.71	380.00	36.86	-	-
Lt. CPN	1.25	1.25	0.09	1.19	1387.50	42.44	27.56	35.06	360.00	Inf	-	-

SNCV

Nerve	Latency (ms)	Amplitude (μV)	Distance (mm)	NCV (m/s)
Rt. Median	6.83	6.17	120.00	17.57
Rt. Ulnar	5.10	7.84	100.00	19.61
Lt. Median	7.24	6.68	120.00	16.57
Lt. Ulnar	7.20	12.28	100.00	13.89
Sural				
Lt. Sural				

Differential Diagnosis -
Given the progressive nature of symptoms and neurological findings, the differential diagnosis would include other hereditary ataxias such as Friedreich`s ataxia and spinocerebellar ataxia, as well as metabolic disorders like Refsum disease and vitamin E deficiency.

Diagnosis -
The diagnosis of Autosomal Recessive Spastic Ataxia of Charlevoix - Saguenay syndrome was established based on clinical manifestations, radiological imaging and nerve conduction studies and excluding other possible above mentioned pathologies. Genetic sequencing was not carried out due to economic constraints of the patient.

Treatment -
Treatment in this patient was focussed on symptomatic relief and supportive care including physical and occupational therapy. Pharmacological treatment included baclofen to manage spasticity and improve quality of life.

Ethical considerations -
Patient's informed consent was obtained for the clinical information, details of investigations and radiological findings to be reported in the journal.

References

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