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Clinical Insights into ARSACS: A Case Report

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Introduction

Autosomal recessive spastic ataxia of Charlevoix Saguenay (ARSACS) is a rare neurodegenerative disorder characterized by the triad of cerebellar ataxia, progressive spasticity, and sensorimotor neuropathy. While cases have emerged worldwide, there has been only one reported case in Korea. Here, we present a case diagnosed with ARSACS through the identification of mutations within the SACS gene using next-generation sequencing (NGS).

Case report

An 8-year-old male with no notable obstetric history presented at our hospital with gait disturbance. He is of Korean-Egyptian descent (with a Korean mother and an Egyptian father) and has a family history of learning disabilities in his uncle during childhood. There was a slight gross motor development delay, with independent walking possible at 17 months. Neurological examination revealed both ankle spasticity, Modified Ashworth Scale grade 1. In cerebellar function testing, he exhibited mild intentional tremor, ataxic features and displayed difficulty with tandem gait. He showed immature and slow handwriting with poor general pencil control.

Brain MRI (Fig. 1.) and laboratory tests were performed, all of which yielded unremarkable results. NGS was conducted to exclude other forms of ataxia, revealing a compound heterozygous mutation in the SACS gene, c.3328dup (p.Ile1110AsnfsTer2) and c.1394G>T (p.Ser465Ile), a key finding in ARSACS diagnosis. Regarding comorbidity assessment, fundoscopy, optical coherence tomography(OCT) indicated increased thickness of the retinal nerve fiber layer (Fig. 2.) and electrophysiology study presented demyelinating mixed sensorimotor polyneuropathy, consistent with ARSACS. The patient exhibited an ataxic gait pattern in gait analysis and scored 43 on the Pediatric Balance Scale. Manual muscle testing revealed no gross muscle weakness in the extremities. Speech and language assessments revealed a slight high-pitched tone and a slow speech rate. The Wechsler Intelligence Scale showed a Full-Scale Intelligence Quotient of 78, indicating borderline intellectual functioning.

We will provide physical therapy, occupational therapy, speech therapy, and dietary supplementation to alleviate symptoms and enhance the patient's quality of life.

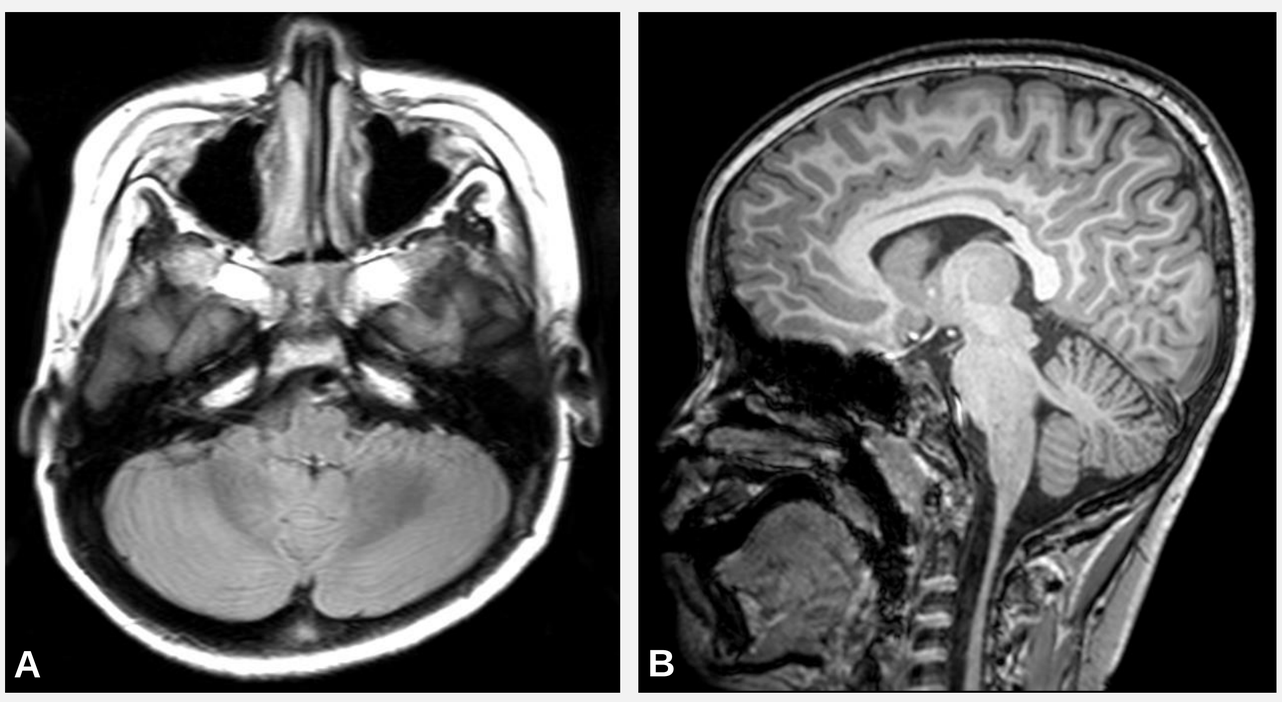

Fig. 1. (A) Axial FLAIR[1)], (B) Mid sagittal T1-weighted MR images

Abbreviation : 1) fluid-attenuated inversion recovery images

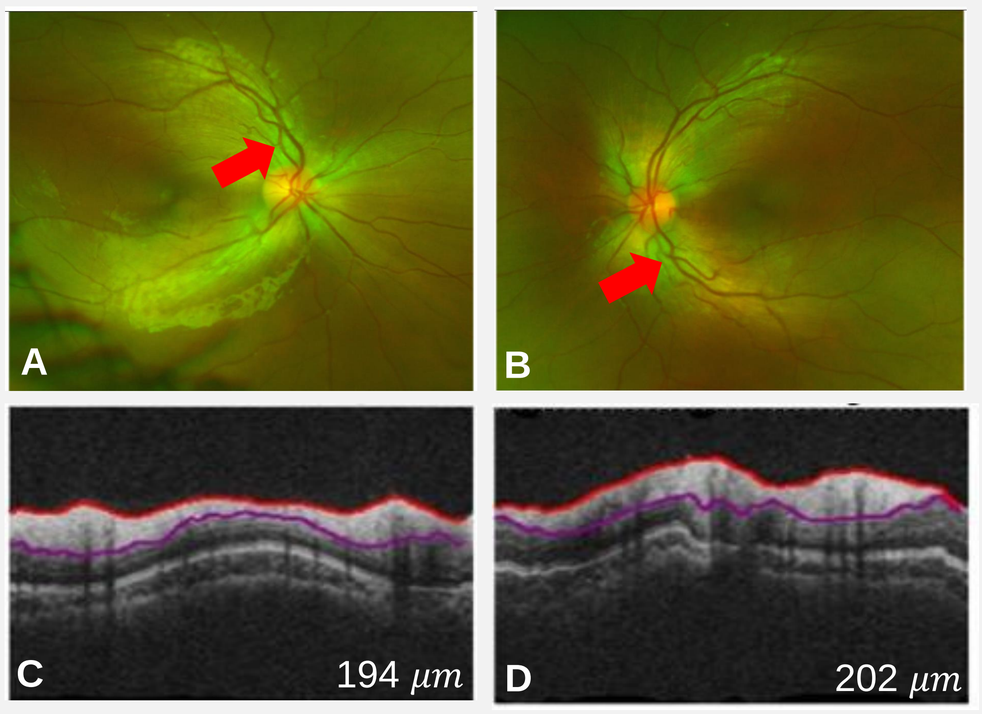

Fig. 2. Fundoscopy and OCT show increased retinal nerve fiber thickness. Rt eye (A), (C) and Lt eye (B), (D)

Table 1. Nerve conduction study results were suggestive of demyelinating mixed sensori-motor polyneuropathy

Sensory nerve	Stimulation Site	Recording Site	Latency (ms)	Amplitude (μV)	Vel (m/s)
Lt Median	Wrist	3rd finger	NR[1)]	-	-
Rt Ulnar	Wrist	5th finger	NR	-	-
Lt Sup Peron[2)]	Ankle	Lateral ankle	NR	-	-
Rt Sural	Calf	Posterior ankle	NR	-	-
Motor nerve	**Stimulation Site**	**Recording Site**	**Latency (ms)**	**Amplitude (mV)**	**Vel (m/s)**
Lt. Median	Wrist	APB[3)]	6.2	6.1	-
	Elbow		11.6	5.5	**30**
Rt. Ulnar	Wrist	ADM[4)]	4.1	5.7	-
	Elbow		8.5	5.4	**36**
Lt. Peroneal	Ankle	EDB[5)]	6.3	2.2	**-**
	Fibular Head		15.2	2.1	**26**
Rt. Tibial	Ankle	AHB[6)]	5.3	7.9	**-**
	Knee		15.1	6.5	**33**

Abbreviations: 1) No response, 2) Superior peroneal nerve, 3) Abductor pollicis brevis, 4) Abductor digiti minimi, 5) Extensor digitorum brevis, 6) Abductor hallucis brevis

Conclusion

Next-Generation Sequencing (NGS) advancements have greatly improved rare disease diagnosis, especially in pediatric rehabilitation. In this case, NGS enabled distinct diagnoses, comprehensive testing for associated conditions, facilitating the effective individualized rehabilitation programs. It is believed that improvements in the cost and accessibility of genetic testing would aid in early diagnosis and treatment planning for rare diseases.