

Autosomal recessive spastic ataxia of Charlevoix-Saguenay

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ABSTRACT

Autosomal recessive spastic ataxia of Charlevoix-Saguenay (ARSACS) is an extremely rare disease in countries other than Canada. We presented the clinical data and magnetic resonance imaging (MRI) findings of four patients diagnosed with ARSACS in our clinic. In the literature, early atrophy of the superior vermis, progressive atrophy of the cerebellar hemisphere and cervical cord, and linear hypointensity in the pons on T2-weighted images were described. According to the literature, we have described the same typical MRI findings of ARSACS.

Keywords: Ataxia, autosomal recessive spastic ataxia of Charlevoix-Saguenay, genetics, magnetic resonance imaging, neuroradiology.

Autosomal recessive spastic ataxia of Charlevoix-Saguenay (ARSACS) is a rare neurodegenerative disease caused by homozygous mutations in the SACS gene, characterized by spastic ataxia and other neurologic findings.^[1] The ARSACS presents three main findings beginning in infancy: progressive cerebellar ataxia, lower limb pyramidal signs, and peripheral neuropathy.^[2] It is related to progressive degeneration of the spinal cord and cerebellum.^[3] Typical T2-hypointensities in the pons on magnetic resonance imaging (MRI) with the classical triad (progressive cerebellar ataxia, lower limb pyramidal signs, and peripheral neuropathy) distinguishes the ARSACS from unexplained ataxias.^[4] Other

clinical manifestations seen in the ARSACS are dysphagia, dysarthria, amyotrophy, nystagmus, pes cavus, urinary tract problems, scoliosis, hearing loss, recurrent seizures, and intellectual disability.^[5] The ARSACS first presents with gait disturbance at the age of 12 to 18 months, and patients are usually unable to walk at the age of 40 years.^[2] Knowing the genetic and the molecular causes of the ARSACS paves the way for the development of disease-specific treatments in the future.^[1] Therefore, it is important to diagnose ARSACS early and to differentiate it from other unexplained ataxias. Here, we describe the clinical and radiological features of four patients with the ARSACS and highlight the necessary findings for early diagnosis.

Received: July 14, 2021 **Accepted:** July 16, 2021 **Published online:** September 07, 2021

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Cite this article as:

Mammadov T, Aslan B, Gündoğmuş CA, Sever Hİ, İnan Gürçan N, Ekinci G. Autosomal recessive spastic ataxia of Charlevoix-Saguenay. D J Med Sci 2021;7(2):168-172.

CASE REPORT

Case 1- The first symptoms of a 32-year-old male patient started at the age of six to seven years as imbalance, difficulty in walking, and weakness in the lower extremities. From the age of 25, the patient's complaints increased, and the patient became unable to walk without support. There were complaints of urinary incontinence from the age of 10 to 11. The other symptoms were dysarthria, tremor in the upper limbs, bilateral arthrodesis of finger, and pes cavus deformity. The patient's cognitive function and ophthalmologic evaluation were normal. Electroneuromyography findings were found compatible with sensorimotor polyneuropathy, demyelination, and axonal degeneration with prominent involvement in the lower extremity. The patient's parents are relatives. No similar disease was observed in the family. The patient's genetic analysis is compatible with the homozygous variant of the SACS gene mutation. T2-weighted MRI showed linear hypointensity in the pons and atrophy in the cerebellar hemispheres and superior vermis.

Case 2- Spasticity and ataxia were the first clinical signs of a 24-year-old male patient, which started at the age of 18 months. Later, progressive walking difficulty, nystagmus, and

urinary system problems developed. Examination revealed bilateral pes cavus deformity, Achilles tendon contracture, and increased deep tendon reflexes. Cognitive functions and hearing were normal. Electroneuromyography demonstrated diffuse sensorimotor polyneuropathy, more prominent in the lower extremities. The patient's history revealed a normal gestation and delivery, and the parents are in a consanguineous marriage. The patient was followed up in another center until the age of 19 years with a diagnosis of hereditary polyneuropathy. The genetic test was compatible with the homozygous variant of the SACS gene. T2-weighted MRI showed linear hypointensity in the pons and atrophy in the cerebellar hemispheres and superior vermis.

Case 3- An 18-year-old female patient was admitted to our clinic with difficulty in walking. The patient started walking late and had progressive walking difficulties from the age of three years. Cognitive functions were preserved, and there was no balance disorder. At the first admission to our hospital, there was contracture in the lower extremity joints. The patient was born normal as one of the twins, and the parents are relatives. T2-weighted MRI showed linear hypointensity in the pons

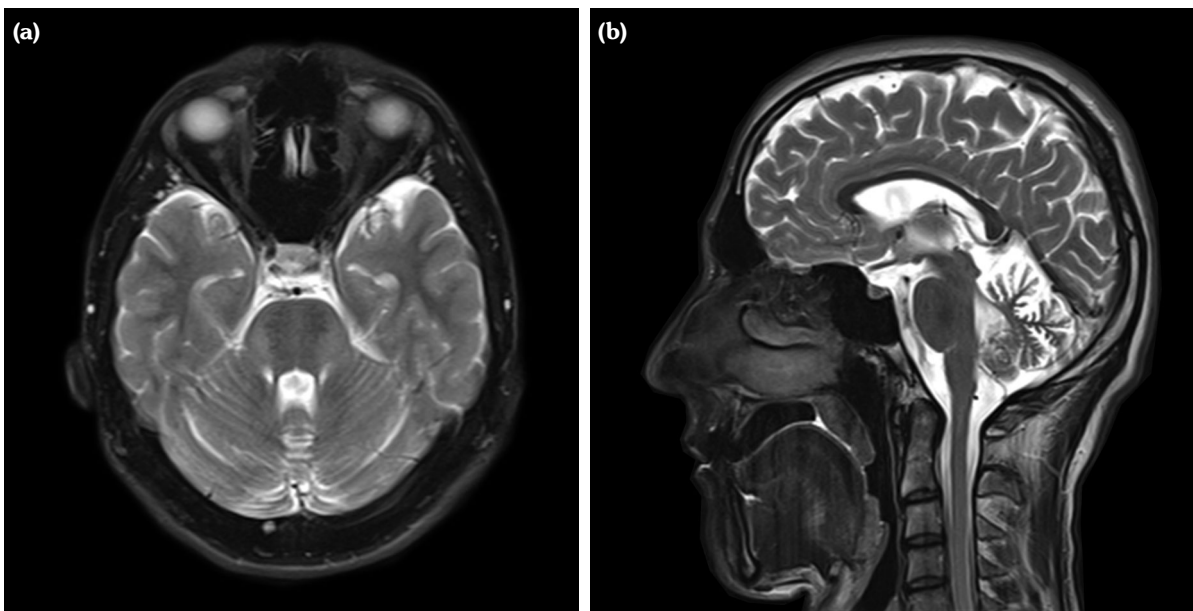


Figure 1. Patient 1. (a) Axial T2-weighted magnetic resonance imaging shows linear hypointensity in the pons (tigroid pattern). (b) Sagittal T2-weighted image shows the bulky pons, cerebellar and superior vermis atrophy.

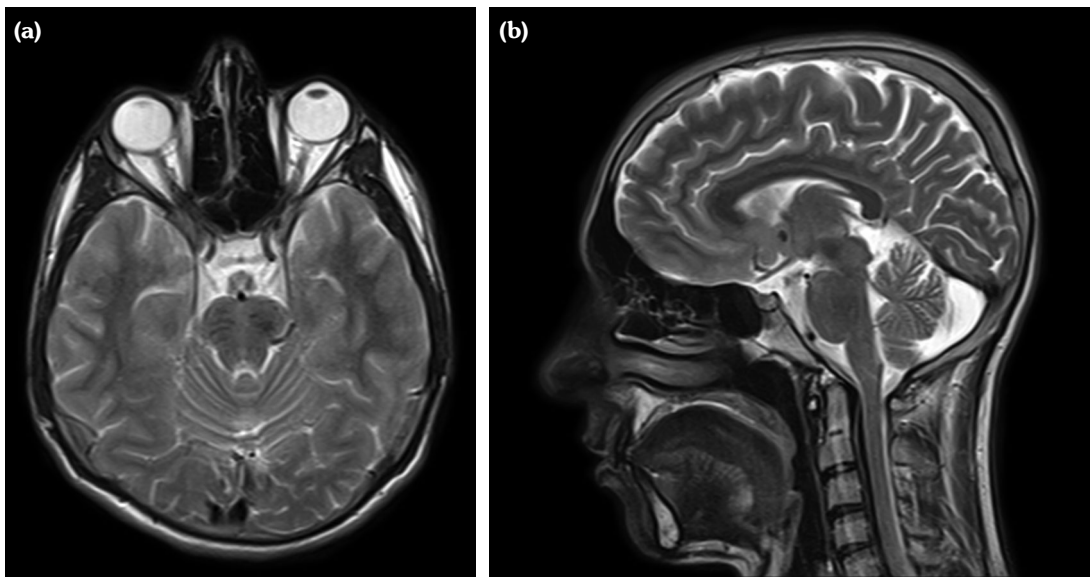


Figure 2. Patient 2. **(a)** Axial T2-weighted magnetic resonance imaging shows linear hypointensity in the pons (tigroid pattern). **(b)** Sagittal T2-weighted image shows the bulky pons, cerebellar and superior vermian atrophy.

and atrophy in the cerebellar hemispheres and superior vermis.

Case 4- A 23-year-old male patient was admitted to our clinic with difficulty in walking. The patient had a history of delayed speech and delayed walking. Electroneuromyography

revealed sensorial polyneuropathy findings in the lower extremities. The patient had pes cavus deformity and scoliosis. The patient's cognitive functions were normal, and the patient had no nystagmus. The patient's parents are relatives. The genetic diagnosis of ARSACS was confirmed.

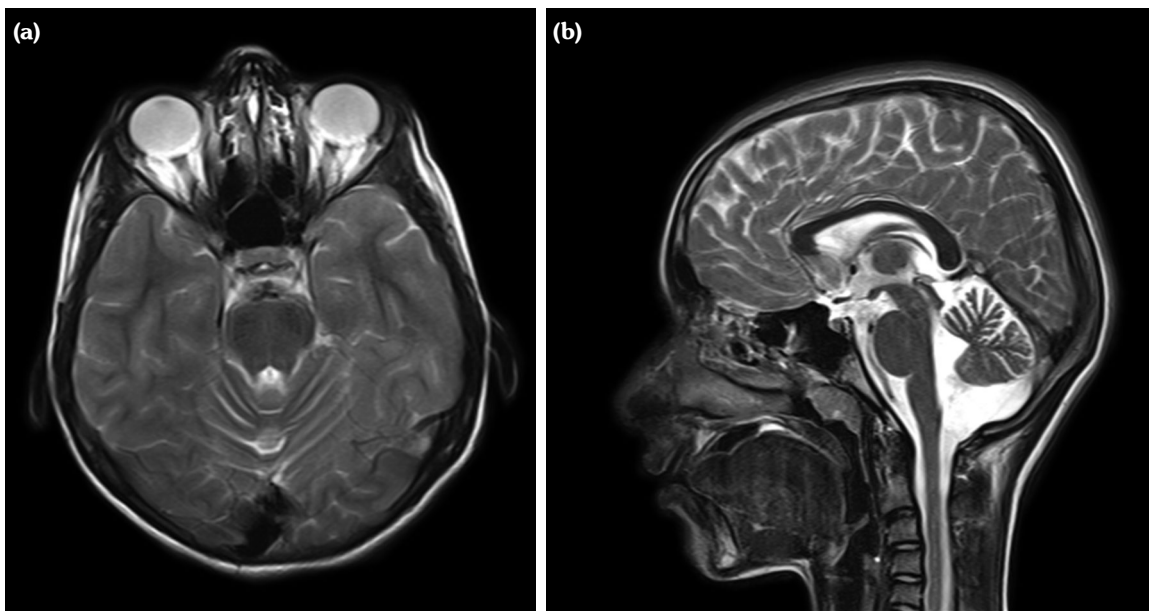


Figure 3. Patient 3. **(a)** Axial T2-weighted magnetic resonance imaging shows linear hypointensity in the pons (tigroid pattern). **(b)** Sagittal T2-weighted image shows the bulky pons, cerebellar and superior vermian atrophy.

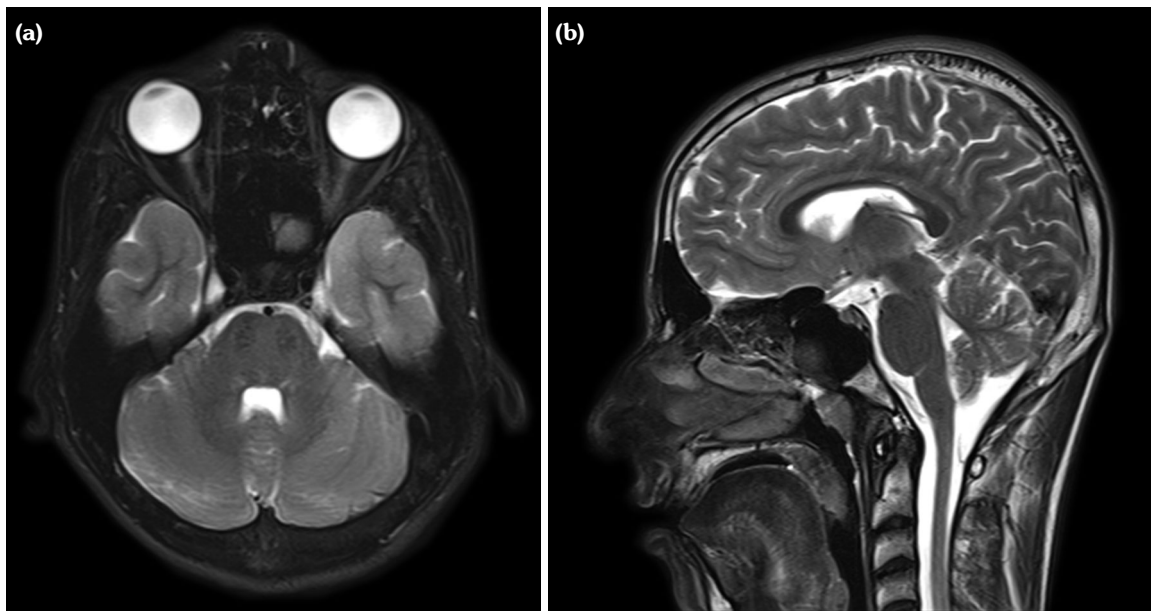


Figure 4. Patient 4. **(a)** Axial T2-weighted magnetic resonance image shows linear hypointensity in the pons (tigroid pattern). **(b)** Sagittal T2-weighted image shows the bulky pons, cerebellar and superior vermician atrophy.

T2-weighted MRI showed linear hypointensity in the pons and atrophy in the cerebellar hemispheres and superior vermis.

DISCUSSION

The ARSACS is an inherited neurodegenerative disorder characterized by early-onset spastic ataxia, dysarthria, finger and foot deformities, distal muscle wasting, mixed sensorimotor neuropathy, hearing loss, nystagmus, and retinal hypermyelination.^[6] In recent years, the elucidation of the molecular basis of the disease has allowed the emergence of specific treatment methods. Early diagnosis is important to prevent the clinical manifestations of the disease before it progresses. Therefore, radiological imaging methods are of great importance in making the diagnosis. Magnetic resonance imaging of the patient with ARSACS shows disease-specific changes such as superior vermician atrophy, linear hypointensity in T2, and flair sequences in the pons (tigroid pattern). In addition, atrophy in the cerebellar hemispheres, bulky pons sign, thinning of the posterior part of the corpus callosum, and superior spinal cord atrophy are other rare findings. Although genetic analysis is necessary for the definitive

diagnosis of the disease, MRI provides an important opportunity to lead the genetic analysis. In our case series involving four patients, superior vermician atrophy, bulky pons sign, linear hypointensity in the pons (tigroid pattern), and thinning of the posterior part of the corpus callosum were found on MRI. The MRI findings of the first patient, who was older, were more pronounced. In all cases, the parents are relatives. Considering the studies and case series conducted in other countries, the age of the cases at the time of diagnosis is significantly higher than in Canada.^[1,4] This delays the proper treatment of patients and reduces the chance of treatment success.

In conclusion, the prevalence of ARSACS in the world may be greater than previously suspected, and knowing the MRI findings can increase the detection of the disease.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

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