

Autosomal Recessive Spastic Ataxia of Charlevoix-Saguenay: A Report of MR Imaging in 5 Patients

CASE REPORT

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SUMMARY: We present findings on MR imaging in 5 patients with autosomal recessive spastic ataxia of Charlevoix-Saguenay (ARSACS). In the literature, early atrophy of the superior vermis as well as progressive atrophy of the cerebellar hemispheres and cervical cord was described. We found linear hypointensity on T2 and T2 fluid-attenuated inversion recovery–weighted images in the pons in all of our 5 patients.

Autosomal recessive spastic ataxia of Charlevoix-Saguenay (ARSACS) was first described in 1978 as a recessive form of spastic ataxia found in Quebec, Canada. To this day, there are more than 300 affected people in the Charlevoix-Saguenay-Lac-St-Jean region, where the carrier frequency is estimated to be 1 in 22 with an equal male-to-female ratio.¹ The ARSACS syndrome has shown a consistent pattern of clinical symptoms and electrophysiologic and morphologic findings that have led to the identification of the responsible gene localized on chromosome 13q.² Since then, several cases have been described in other countries with new mutations and some variations in clinical signs and evolution.³ On imaging studies, such as CT or MR imaging, early atrophy of the superior vermis is the predominant finding, followed by progressive atrophy of the cerebellar hemispheres and the spinal cord. The atrophy of the superior vermis is common in both hereditary and acquired cerebellar ataxias but occurs more precociously in ARSACS, which suggests that it might be a congenital feature.^{1,3} In this report, MR imaging in our 5 patients demonstrated linear hypointensity on T2- and T2 fluid-attenuated inversion recovery (FLAIR)-weighted images in the pons that, so far, has not been described previously. These changes could help diagnose ARSACS earlier in preschool children, in whom the disease is often mistaken for cerebral palsy.

Case Reports

Case 1. A 9-year-old girl first presented with slight ataxia, increased deep tendon reflexes and clonus in the lower limbs on physical examination at 3 years old. The history revealed a normal pregnancy and delivery in the mother. The father originated from the Charlevoix region. The patient also had a 6-year-old sister who showed similar manifestations. Imaging demonstrated discrete atrophy of the superior vermis (Fig 1) and linear hypointensity on proton density and T2-weighted images in the pons, not seen on T1-weighted images. Genetic diagnosis of ARSACS was confirmed.

Case 2. A 9-year-old girl presented with early difficulty with gait and a tendency to fall. The history also revealed a normal pregnancy and delivery in the mother, without a family history of neurodegen-

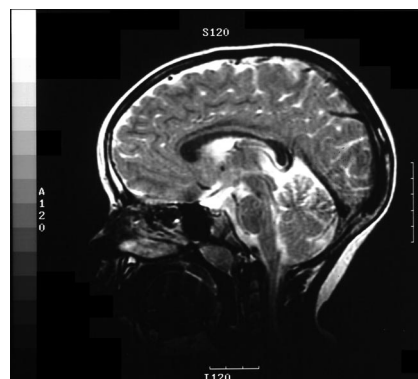


Fig 1. Midsagittal T2-weighted MR image demonstrates slight atrophy of the superior vermis.

erative disease. Both parents were from an area close to the Saguenay region. When she was 8 years old, the physical examination of the girl revealed a slight dysarthria, dysmetria on a finger-to-nose test, slowing of fast repetitive movements, and increased tricipital reflex. When she was 9 years old, increased deep tendon reflexes in the lower limbs were present, and she also experienced saccadic ocular movements during voluntary pursuit. Electromyography (EMG) demonstrated an axonal neuropathy, predominantly sensory. Imaging studies showed linear hypointensity on T2- and T2 FLAIR-weighted images in the pons (Fig 2 and 3). Genetic diagnosis of ARSACS was confirmed.

Case 3. A 17-year-old girl reported spasticity, ataxia, reduced fine motoricity, and abnormal plantar response since she was 5 years old. The family history was negative except for a cousin with a form of dystrophy. Neither of the parents were from the Charlevoix-Saguenay region. EMG showed signs of both sensory and motor demyelinating polyneuropathy. Imaging studies demonstrated linear hypointensity on T2- and T2 FLAIR-weighted images in the pons (Fig 4, 5 and 6). Genetic diagnosis of ARSACS was confirmed.

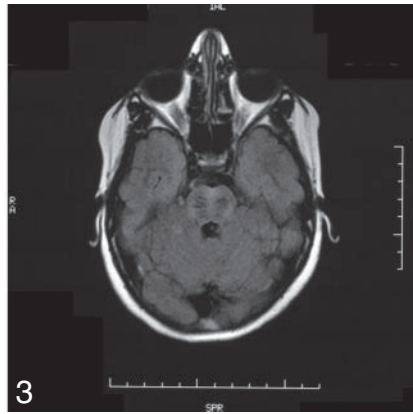
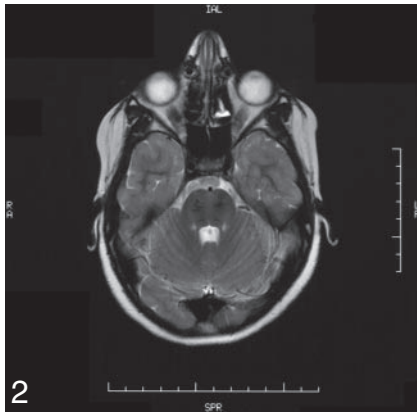
Case 4. An 8-year-old girl had early signs of ataxic gait. Again, the history did not show any complications during pregnancy or delivery in the mother. The father had a slow gait and delayed language development. The rest of the family history was negative. Both parents came from the Charlevoix region. When she was 6 years old, physical examination of the girl showed the presence of an ataxic syndrome with slightly increased deep tendon reflexes and clonus in the lower limbs. There were no myelinated retinal nerve fibers on funduscopy. EMG did not show any abnormalities in nerve conduction. The results of a muscle biopsy showed moderate atrophy of the muscle fibers without necrosis or regeneration. These findings were not specific.

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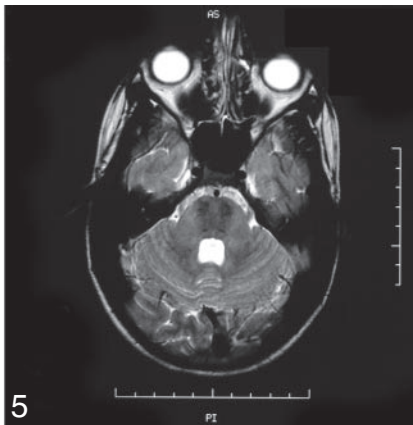
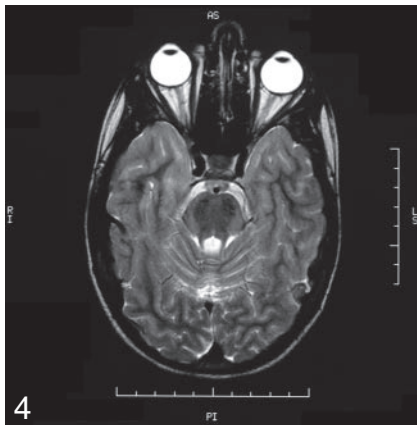
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Figs 2 and 3. Axial T2- and T2 FLAIR-weighted MR images of the same patient show linear hypointensity in the pons.



Figs 4 and 5. Axial T2-weighted MR consecutive images demonstrate linear hypointensity in the pons.

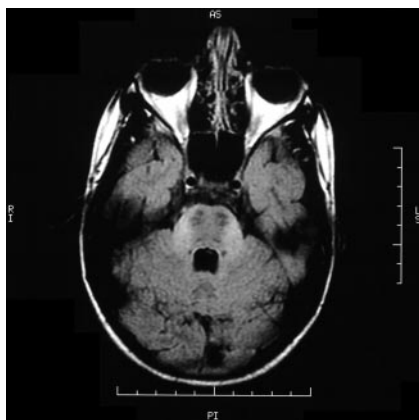


Fig 6. Axial T2-FLAIR-weighted MR image shows linear hypointensity in the pons.

Linear hypointensity on T2-weighted images was seen in the pons. Genetic diagnosis of ARSACS was confirmed.

Case 5. A 52-year-old woman presented with early difficulty in gait, mostly spastic. The diagnosis was made when she was 15 years old. EMG demonstrated signs compatible with ARSACS. Electroencephalogram was normal. Imaging studies showed atrophy of the superior vermis and cerebellar hemispheres on CT and MR imaging and linear hypointensity on proton density and T2-weighted images in the pons on MR imaging.

Discussion

From a clinical standpoint, ARSACS shows pyramidal tract and cerebellar progressive signs and, later, in the third decade of life, manifestations of polyneuropathy. Also, early nonpro-

gressive ocular manifestations are most typical of the disease, which include saccadic alteration of ocular pursuit and prominent myelinated fibers radiating from the optic disc and embedding the retinal blood vessels at funduscopy, possibly indicative of an early abnormal process in myelination.² In most patients, EMG reveals severe denervation in the distal muscles by the end of the third decade.¹ More specifically, nerve conduction studies demonstrate signs of early demyelination and progressive axonal neuropathy; the latter is confirmed by nerve biopsy.¹ Electroencephalographic abnormalities occur in more than 60% of patients and are nonspecific. Generalized epilepsy is present in 7% of patients, beginning in their late teens.¹

Until now, imaging findings described in relationship to ARSACS are not specific and include early and progressive atrophy of the superior cerebellar vermis on CT or MR imaging. The inferior vermis remains thicker throughout the disease, but there is a progressive cerebellar cortical atrophy. Furthermore, there is ubiquitous cerebral atrophy in later life. Nevertheless, the cerebral white matter does not reveal abnormal signals, even in more advanced disease. The cervical spinal cord is flattened and markedly atrophied.^{1,2,4}

All of the 5 patients described in our study had complementary investigation by MR imaging, which demonstrated also bilateral, symmetrical linear hypointensity on proton density (not pictured), T2- and T2 FLAIR weighted images in the pons, though more noticeable in the latter. However, it should be noted that proton density and T2 FLAIR-weighted images were not made for all 5 patients in this report. No correlation could be found on T1-weighted images. The cere-

bral white matter did not show abnormal signals. The hypointensity on T2-weighted images was visualized close to the anatomic location of the corticospinal tracts in the pons. However, the hypointensity was elongated and comma shaped (as opposed to round shaped), with a more posterior extension. These features suggest a perpendicular orientation to the corticospinal tracts and an involvement of the pontocerebellar fibers or pontine nuclei, or both, in the disease, which gives the appearance of a moth-eaten bun. That these abnormalities in signal intensity are mostly seen on each side of the midline and the pontocerebellar fibers are crossing the midline could most likely support the involvement of the pontine nuclei, which are not on the midline. Also, from a clinical standpoint, the pontine nuclei have an important role in ocular pursuit and formation of saccades, and these major abnormalities are seen very early in patients with ARSACS.

There is no autopsy material available from pediatric cases of ARSACS. The pathologic findings of the cerebellar and pons in a young man was published in 1991.⁴ In the cerebellar hemispheres, only focal rarefaction of the Purkinje cells could be suspected. The dentate nucleus and inferior olives were within normal limits. Corticospinal tracts were small in the pons, but the pontine nuclei seemed normal.⁴ Pathologic findings showed demyelination along the corticospinal tracts in the medulla and spinal cord.⁴ A storage disease was also proposed later because of swollen thalamic and cerebellar cortical neurons.¹ Most of these cells had dense, lipofuscin-like granules within their lysosomes. The activity of 18 lysosomal enzymes was studied and found to be within normal limits. Identification of the chemical nature of this storage material is still unknown.¹ Low T2 signal intensity in the basal ganglia was described in 4 patients affected with autosomal dominant cerebellar ataxia.⁵ The apparent loss of signal intensity in the deep gray matter of middle-aged patients may represent a patho-

logic process because the patients had clinical extrapyramidal manifestations. Histologic examination revealed increased iron positivity in the basal ganglia and thalami compared with control specimens.⁵ Iron deposition may account for a low signal intensity on T2-weighted images. Another fact supporting the assumption that the pontine nuclei could be involved in the disease is that abnormal material is usually accumulating in the cell bodies.

Conclusion

A prospective study could be done, with complementary MR imaging including sequences such as gradient echo and diffusion-weighted imaging to evaluate the hypothesis of abnormal deposition of substances. Also, a complementary diffusion tensor imaging sequence and T2- and T2 FLAIR-weighted images in the coronal and sagittal planes would be useful to determine a more precise anatomic location of the hypointensity. The prospective study could also help to analyze the specificity of the linear hypointensity on T2- and T2 FLAIR-weighted images in the pons compared with other types of recessive ataxia. Finally, the evaluation of these signals across different age groups in the ARSACS population and involving more cases with adults would allow us to determine their evolution in the course of the disease.

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