

Comment on: Diagnosis of Aicardi-Goutières Syndrome in Adults

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We read with great interest the manuscript by Videira and colleagues,¹ about the diagnosis of Aicardi-Goutières syndrome (AGS) in adults, and we would like to contribute with 2 more cases of an ongoing study in southern Brazil.

Two sisters with nonconsanguineous parents were evaluated at a tertiary center in Brazil. The first patient was a 20-year-old woman that presented with spastic paraplegia since the age of 3 and epilepsy with generalized tonic-clonic seizures controlled with carbamazepine. The mother reported that the patient had acquired a gait before she started showing motor symptoms. At the time of the evaluation, the patient walked independently, but was unable to run. She did not have cognitive impairment (scored 29/30 points on the Mini-Mental State Examination), neither did she have psychiatric symptoms or oculomotor changes. A computerized tomography scan showed linear and “spot-like” calcifications in the bilateral lentiform nucleus (Fig. 1). Magnetic resonance imaging showed mild diffuse cerebral atrophy and cavum septum pellucidum.

The second patient was her 30-year-old sister, whose clinical picture was more severe. This patient had an important neuro-

motor development delay and was never able to walk. At the time of examination, the patient was restricted to a wheelchair because of generalized dystonia and she had severe mental retardation and refractory epilepsy.

After an initial investigation, the patients underwent a total sequencing of exoma that revealed the presence of the homozygous variant c.529G>A, p.Ala177Thr in exon 7 of the *RNASEH2B* gene.

More than 30% of AGS patients have pathological variants of the *RNASEH2B* gene in the published case series. There are more than 20 pathological variants described for *RNASEH2B*, the most frequent being the replacement of amino acids c.529G>A (p.Ala177Thr) from exon 7,^{2,3} the same genotype found in the patient. The classic phenotype presents as a progressive encephalopathy and sometimes even death in the first years of life.²⁻⁵ The first patient presented began to show spasticity symptoms in the lower limbs at the age of 3, she did not have a clinically cognitive impairment, and she still walked without assistance at the age of 20. Few patients with pathological

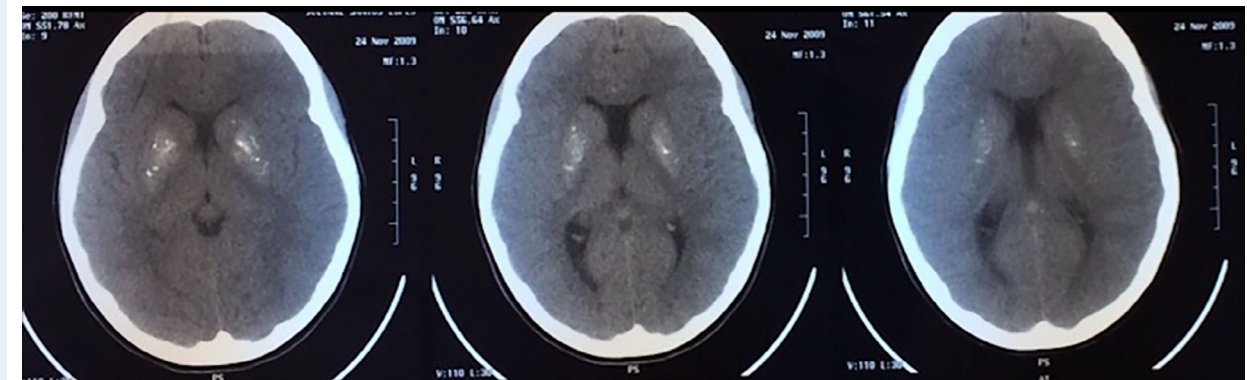


FIG. 1. Computed tomography scan showing spot-like calcifications.

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variants of the *RNASEH2B* gene and pure late-onset spastic paraplegia have been described in the literature. Crow and colleagues⁶ reported 2 sisters with pathological variants of the *RNASEH2B* gene and the onset of pure spastic paraplegia at 18 and 24 months of age who were still walking at 7 and 11 years of age and had no cognitive impairment. Travaglini and colleagues⁷ described a 4-year-old girl with the pathological variant c.529G>A (p.Ala177Thr) of the *RNASEH2B* gene and pure spastic paraplegia whose symptoms started at 12 months of age.

Calcifications located in the putamen, pale globe, and subcortical are the most common radiological findings in AGS as well as cerebral atrophy and an altered signal in the white matter. The leukoencephalopathy of patients with AGS may have a frontal fronto predominance or diffuse pattern. Rarely do patients with AGS have a normal neuroimaging exam.⁸ The patient in this study presented with a classic radiological pattern of calcification in the bilateral lentiform nucleus.

It was concluded that AGS that is related to pathological variants of the *RNASEH2B* gene should be included in the differential diagnosis of young people with autosomal-recessive pure spastic paraplegia from childhood onset without cognitive impairment, especially if there is calcification in the basal nuclei noted in the radiological exams.

Once again, we congratulate the authors on their efforts to report this condition, which is often underdiagnosed.

Author Roles

(1) Research Project: A. Conception, B. Organization, C. Execution; (2) Statistical Analysis: A. Design, B. Execution, C. Review and Critique; (3) Manuscript Preparation: A. Writing of the First Draft, B. Review and Critique.

E.P.: 1A, 1B, 1C, 2A, 2B, 2C, 3A, 3B

G.L.F.: 1A, 1B, 1C, 2A, 2B, 2C, 3A, 3B

S.R.: 1A, 1B, 1C, 2C, 3B

H.A.G.T.: 1A, 1B, 1C, 2C, 3A, 3B

Disclosures

Ethical Compliance Statement: The study was approved at the ethics committee by number: CAAE 06128812.0.0000.0096. Written informed consent for participating in this study was obtained from all patients. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

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