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Misdiagnosed Aicardi Goutières Syndrome Patient: A Case Report

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ABSTRACT

Aicardi Goutiere's syndrome is an autosomal recessive neurodegenerative disorder. Its clinical signs usually mimic TORCH-like clinical signs; which makes the differential diagnosis difficult. Here, we report a case with one homozygous pathogenic mutation c.529G>A p.Ala177Thr on RNASEH2B gene (NM_024570) that relates to Aicardi-Goutieres syndrome type 2 that had been misdiagnosed in about 5 years.

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Introduction

Aicardi Goutiere's syndrome (AGS) is an autosomal recessive neurodegenerative disorder. Its clinical signs usually include basal ganglia calcification encephalopathy, white matter abnormalities, congenital problems, high levels of interferon alpha, and TORCH-like clinical signs. The similarity between TORCH (Toxoplasmosis, Rubella, Cytomegalovirus, Herpes simplex virus) and AGS makes diagnosis difficult (1–4).

so the disease can be simply missed without a reasonable index of suspicion, especially in RNASEHB2 mutations. Late onset and absence of typical symptoms In RNASEHB2 variant make the diagnosis difficult (5). Although there is no cure for the disease, with proper diagnosis; we can prevent born of siblings with the same problem. we hereby report a case that had been misdiagnosed in about 5 years.

Case report

An 8 years old girl of consanguineous parents was presented with developmental delay. She did not have any birth complications. She could sit in 7 months and walk with help in 18 months. In 24 months, her parents noted that she has developmental delay and abnormal movements. Her axial brain CT (figure 1) revealed bilateral basal ganglion calcification but other parts

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(pons, midbrain, base skull, petromastoids region, internal auditory canals, cerebellopontine angles, cisternal spaces, posterior fossa, cerebellum, sella turcia, hypophysis, third and lateral ventricle, white and grey matter) were normal.

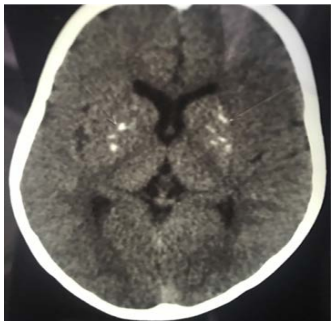

Figure 1. Brain CT scan at the age of 2 years shows the calcification of basal ganglia (specially globus pallidus and putamen), arrows present calcification area.

In 24 months her physical examination revealed exaggerated deep tendon reflexes, irritability, normal auditory brainstem response, mild dystonia, and head circumference of 46 centimeters; consequently, she was diagnosed and treated as a TORCH patient. When she was 3 years old, the intensity of the symptoms reduced. There was no similar problem in her family history. Findings of CT scan (calcification of only basal ganglia) and normal indexes of growth at birth (normal birth weight (3250 gr) and head circumference (35 cm)) indicated that she might be suffering from other diseases; so when she was 8 years old, we re-assessed her and ordered MRI.

basal ganglion calcification and white matter engagement (figure 2) along with history lead us to Aicardi Goutieres syndrome. her parents didn't let us perform lumbar puncture, so we directly referred her to genetic laboratory.

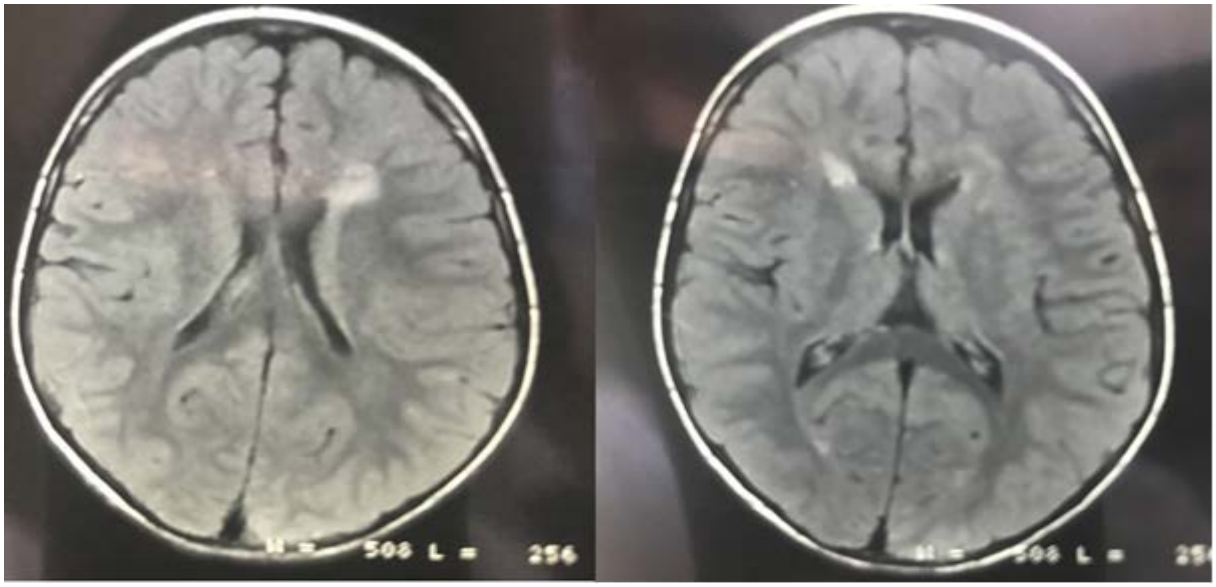

Figure 2: Brain MRI at 8 years old. In FLAIR sequences, it shows hyper signal intensity in white matter of right and left side

Based on history, medical geneticist described the disease and pattern of inheritance in the family (figure 3).

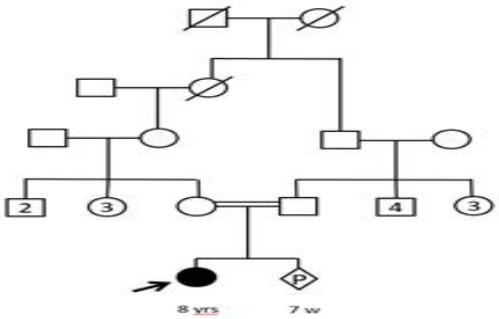

Figure 3. Pedigree of the AGS family. Circles: female, Square: male, P: pregnancy, arrow: patient, w: week, yrs: years

Molecular testing detected one homozygous pathogenic mutation c.529G>A p.Ala177Thr on RNASEH2B gene (NM_024570) which related to Aicardi-Goutieres syndrome type 2. Both parents were heterozygous for the variant. Since mother was pregnant (14 weeks), for prenatal diagnosis, chorionic villus sampling (CVS) was performed. After DNA extraction, the candidate variant was assessed through PCR and sequencing analysis. This variant had not been detected in the fetus which indicated that the fetus may not suffer from AGS (figure 4). Following the comprehensive genetic assessment, the patient received conservation therapy. After one year follow up, now she goes to school, and her visual and auditory functions are normal and she doesn't have any thrombocytopenia, however, dystonia is still positive.

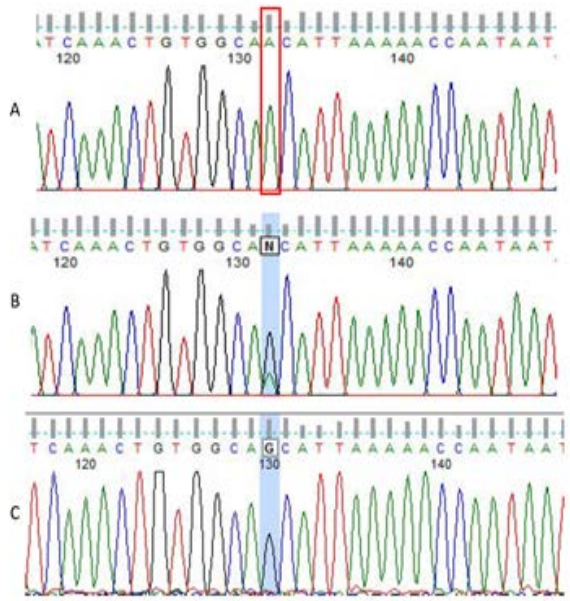

Figure 4. Sequence results of all family members. A: homozygote A/A in proband, B: heterozygote G/A in parents, C: homozygote G/G in fetus.

Discussion

Common discovered neurological signs in AGS cases include dystonic posturing, peripheral spasticity, truncal hypotonia, poor head control. One of the differences in RNASEH2B variant of AGS with other mutations (TREX1, RNASEH2C, or RNASEH2A) is the late onset of symptoms that appear after normal development growth at the age of 12 mo or beyond (5).

Our patient presented symptoms is in 24 months. Another difference of AGS variants is the severity of intellectual and physical functions, in which is totally absent in RNASEH2B cases. Unlike other variants, in RNASEH2B head circumference is normal. As a result, limited spectrum of signs in RNASEH2B cases is another challenge, besides TORCH mimicking in diagnosing patients (4,5). Radiologic finding includes calcifications in basal ganglia engagement of cerebellum, thalamus, dendate, cerebellar white matter, brainstem, striatum could be found in some cases respectively (6).

Conclusion

The similarities between AGS and TORCH makes the diagnosis of the patient very difficult and problematic. Therefore, Children with AGS syndrome usually remain unrecognized until the second child is born, So the importance of recognizing the disease is to prevent another child from being born with the same problem. Thus, it's important to consider the possibility of AGS in absence of clear evidence of infection, because the disease can be simply missed without a reasonable index of suspicion.

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Conflict of interest

There is no any kind of conflict of interest in this article.

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