Brain computed tomography still plays a critical role in the diagnosis of Aicardi-Goutières syndrome

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OBJECTIVES

Aicardi-Goutières syndrome (AGS) is a rare genetic neurological disorder with different clinical manifestations, heterogeneous genetic varieties and leukodystrophic imaging features. Magnetic resonance imaging (MRI) is mostly found normal therefore,calcification in brain computed tomography (CT) is still very valuable for diagnosis (1). The aim of this study is to review the clinical, radiological and molecular diagnostic findings with AGS presenting in childhood.

METHODS

We reviewed the clinical records and brain MRI/CT images of 16 patients whom had a molecular diagnosis of AGS. Two patients with IFIH1 (12.5%) considered as epileptic encephalopathy spectrum.

RESULTS

Fourteen individuals with AGS admitted in the first year of life. Patients presented with developmental delay (87.5%), spasticity (87.5%), speech delay (62.5%), truncal hypotonia (75%) and seizures (56.2%). Brain MRI showed white matter abnormalities (62.5%), and cerebral atrophy (50%). MRI images included leukodystrophic findings but did not show a specific diagnosis. Brain CT was performed in 12 patients, and 11 of them showed small, punctate, multifocal calcifications in the lentiform nuclei, deep cerebral and cerebellar white matter (91.6%). Calcification suggestive image was observed in only five patients with brain MRI. Homozygous mutations were identified in TREX1 (25%), RNASEH2B (25%), RNASEH2A (6.3%), RNASEH2C (6.3%), SAMHD1 (6.3%). Heterozygous mutations in 3 patients with TREX1(18.8%), In follow-up improvement in myelination was observed in the control MRIs of four patients.

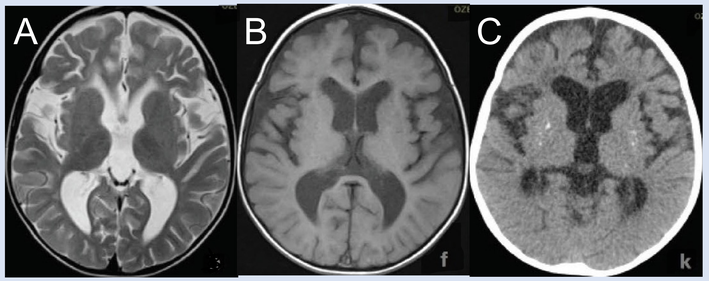

Fig 1. T2 and T1 axial images (A, B) of the patient with RNASEH2A mutation show ventriculomegaly, mild cerebral atrophy, no signs of calcification, Brain CT shows bilateral calcifications in the thalamus and putamen (C).

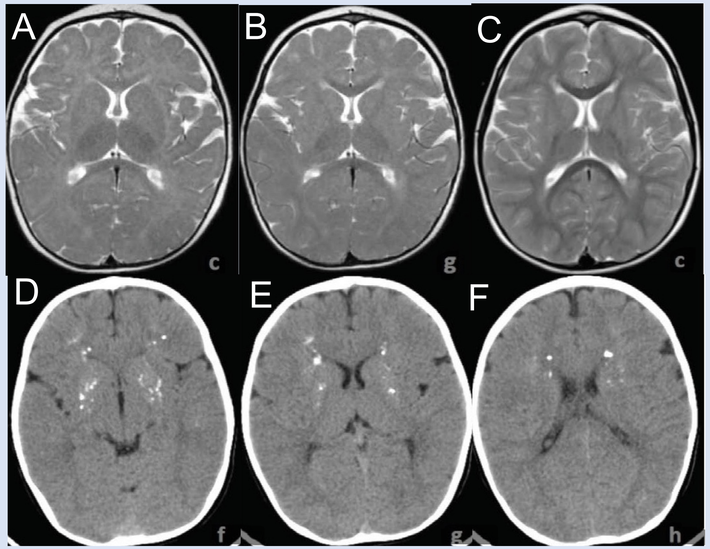

Fig 2. MR imaging of the patient who was found to have a homozygous mutation in the TREX1 gene. T2 axial image at 8 months shows hypomyelination (A), T2 axial image at 20 months shows increased myelination, (B),no calcification (C). Brain CT imagines at the age of 4 show calcifications in bilateral basal ganglia and white matter (D,E,F).

CONCLUSIONS

AGS is a genetic immune-mediated disorder caused by mutations in one of 7 genes (TREX1, RNASEH2B, RNASEH2C, RNASEH2A, SAMHD1, ADAR1 and IFIH1) identified to date. Brain calcification, leukoencephalopathy, and cerebral atrophy are the classic hallmarks of the disease and have suggested the diagnosis of AGS in the majority of cases. However, the disease is likely underdiagnosed, in part because of a lack of recognition by clinicians, but also possibly due to clinical and radiologic variability. The detection of calcification remains an important clue. MRI could detect calcification especially when gross and numerous and also when gradient echo (GRE) or susceptibility weighted imaging (SWI) sequences are added.CT scan should be performed when the clinical and MRI data are consistent with a diagnosis of AGS and the MRI does not reveal calcium deposits (1). We aimed to raise awareness about AGS and to show the importance of brain CT. CT is not preferred because it is an old technique and risk of radiation especially in children. In these cases, the age at diagnosis is delayed due to nonspecific clinical and MRI findings. CT is instructive where brain MR findings are not diagnostic.

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