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Visual Diagnosis

Chronic Encephalopathy, Startle, and Intracranial Calcification: Think Beyond Intrauterine Infections

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This five-year-old boy presented with developmental delay, excessive startle, and motor regression. He had experienced repeated episodes of fever and prolonged lethargy following routine vaccination between ages six weeks and 15 months. The periods of lethargy lasted for two to three months, followed by slow and incomplete recovery. The perinatal period was uneventful, and his family history was unremarkable. Examination showed normal head circumference and optic fundi as well as the presence of nasal twang, upper limb dystonia, lower limb spasticity, brisk muscle stretch reflexes, bilateral ankle contractures, and Babinski signs. The systemic examination was unremarkable. Neuroimaging showed intracranial calcifications and leukoencephalopathy (Fig 1A-C). Next-generation sequencing detected a homozygous missense mutation p.Ala177Thr in the *RNASEH2B* gene on chromosome 13; his parents could not be tested.

Aicardi-Goutieres syndrome (AGS) is an early-onset, progressive encephalopathy that is associated with significant cognitive and neuromotor impairment.[1] Early presentations in infants can mimic congenital intrauterine infections and may be accompanied by hepatosplenomegaly, elevated liver enzymes, thrombocytopenia, and abnormal neurological examination. Presentations in later life characteristically include subacute onset of prolonged encephalopathy, intermittent sterile pyrexias, neuroregression, feeding problems, extreme irritability, or lethargy. The hallmark cerebrospinal fluid features are lymphocytosis and raised interferon-alfa levels. The typical neuroimaging features include cerebral calcification, white matter abnormalities, and cerebral atrophy. Mutations of the gene encoding subunit B of ribonuclease H2 (AGS type 2) cause characteristic subacute encephalopathy and intracranial calcifications, with spastic paraparesis, preserved cognition, and lower mortality rate.[2] The differential diagnoses

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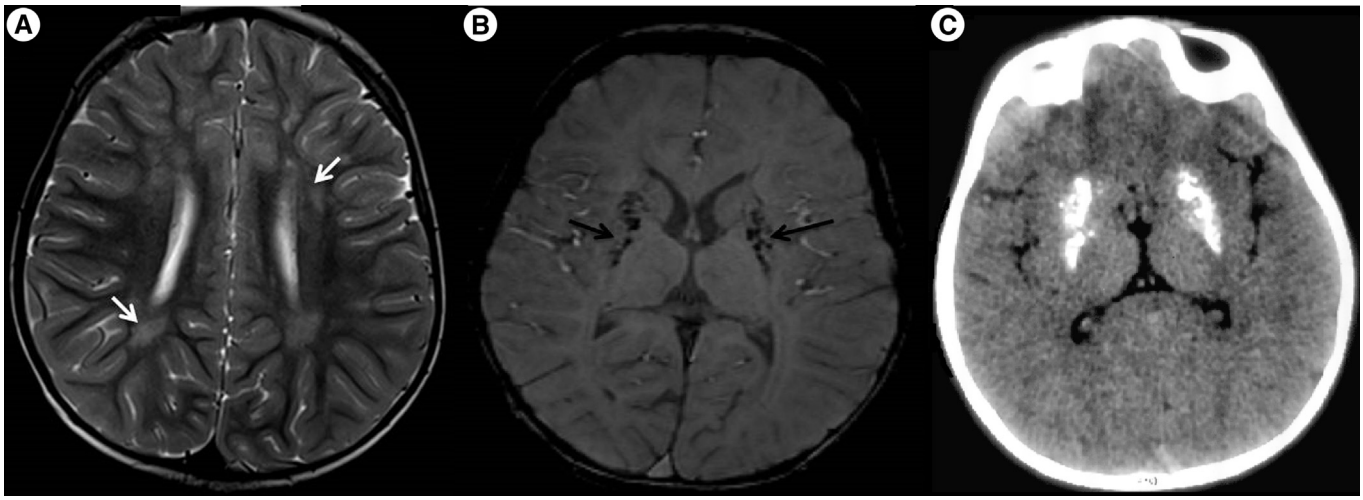

FIGURE 1. Magnetic resonance imaging of the brain. (A) Axial T2-weighted sequence demonstrating multiple periventricular (white arrows) hyperintensities. (B) Axial susceptibility-weighted sequence image revealed multiple bilateral basal ganglia calcifications (black arrows). (C) Noncontrast computed tomography showed bilateral basal ganglia calcifications.

include congenital infections, mitochondrial cytopathies, and Cockayne syndrome.[1]

In conclusion, AGS should be considered in the differential diagnosis of children with developmental delay or episodic neuroregression and intracranial calcifications. Prompt diagnosis prevents unnecessary investigations and helps with prenatal counseling.

References

1. Crow YJ, Chase DS, Lowenstein Schmidt J, et al. Characterization of human disease phenotypes associated with mutations in TREX1, RNASEH2A, RNASEH2B, RNASEH2C, SAMHD1, ADAR, and IFIH1. Am J Med Genet A. 2015;167A:296–312.
2. Al Mutairi F, Alfadhel M, Nashabat M, et al. Phenotypic and molecular spectrum of Aicardi-Goutières syndrome: a study of 24 patients. Pediatr Neurol. 2018;78:35–40.