Cardiac Calcifications in Aicardi-Goutieres Syndrome: An Unusual Prenatal Presentation

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Aicardi–Goutieres syndrome (AGS) is a rare genetic disease arising during the first year of life mainly affecting the central nervous system. Fetal AGS mimics in-utero infection and presents with microcephaly and cerebral calcifications.

We report on prenatal myocardial calcifications as the first manifestation of AGS. The parents are consanguineous with two healthy children and one who suffered from severe intellectual disability, epilepsy and diffuse brain calcifications on CT scan. He died at 4 years of age without a definitive diagnosis.

At 21 weeks of the current pregnancy, myocardial calcification with premature atrial beats and pericardial effusion were observed. No calcifications were detected in the brain, liver, spleen, or placenta. Maternal serology for intrauterine infection, ANA, anti-SSA and anti-SSB were negative. Ultrasound at 27 weeks revealed calcifications of the myocardium, caudothalamic groove and liver. At 32 weeks, reduced cardiac contractility, multiple cardiac, thalamic, brainstem and striatal calcifications and a parenchymal temporal lobe cyst were detected.

The couple chose to terminate the pregnancy. Genetic analysis of the amniotic fluid revealed biallelic mutations in TREX1 gene compatible with AGS. AGS is associated with a high risk of recurrence, and notably, this same mutation was detected in the preserved DNA of the deceased sibling.

Intrauterine cardiac calcifications are uncommon; differential diagnosis includes chromosomal abnormalities (e.g., trisomy 13), infectious agents (STORCH, parvovirus, adenovirus, varicella, and enterovirus), autoantibodies (SSA, SSB), cardiac tumors (rhabdomyoma, teratoma and fibroma), and cocaine exposure (hypoxic cardiac injury). The prognosis of affected fetuses is guarded.

Cardiac involvement in ASG is rare. A negative work-up for the aforementioned differential diagnosis of cardiac calcifications, particularly STORCH, together with cerebral calcifications, behooves consideration of AGS. An abnormal myocardial contractility, calcifications, pericardial effusion and arrhythmia may be the earliest manifestation of AGS resulting from TREX1 mutation.