GACI - Generalized Arterial Calcification of Infancy

previously known as Idiopathic Infantile Arterial Calcification (IIAC), Idiopathic Arterial Calcification of Infancy (IACI), Occlusive Infantile Arterial Calcification, Occlusive Infantile Arteriopathy.

ULTRA RARE

At least 200 affected individuals have been described in the medical literature since 1899.

GACI affects males & females equally and occurs in populations all around the world

GENETIC

Hereditary - Autosomal Recessive

The genes known to date to cause GACI are *ENPP1* and *ABCC6*. This is sometimes referred to as *ENPP1* or *ABCC6* Deficiency.

Each baby born to carrier parents has a 25% chance (one in four) of being affected by GACI, a 50% chance of being an unaffected carrier and a 25% chance of not inheriting any mutations at all.

EARLY SYMPTOMS

In newborns symptoms can include: respiratory difficulties, high blood pressure, an enlarged heart, reduced or absent pulses and joint calcification.

Symptoms can vary greatly in different patients and siblings with the exact same genetic mutation have had markedly different outcomes.

PRENATAL DIAGNOSIS

An ultrasound may reveal polyhydramnios, pericardial effusion, or echogenicity of the major arteries. Amniocentesis & CVS can also detect GACI. Since 2013 there have been at least 5 expecting mothers who were treated prenatally.

COMPLICATIONS OF GACI

Complications include heart issues due to calcification, hypertrophy, ARHR2 Rickets, hearing loss, bone pain, joint calcification, muscle weakness, angioid streaks in the eyes, dental problems, kidney issues, PXE (skin condition), gastrointestinal problems, and high blood pressure.

Patients with GACI are usually followed by a team of specialists including: cardiology, endocrinology, nephrology, orthopedics, audiology, ophthalmology, pulmonology, otolaryngology, physiotherapy, dental and gastroenterology.

ARHR2

Many patients who survive GACI develop a rare form of rickets -Autosomal Recessive Hypophosphatemic Rickets Type 2 (ARHR2). This is usually, but not always, associated with the ENPP1 gene.

Symptoms include bone and joint pain, bone deformities, dental problems, calcification of ligaments and short stature.

Treatment for rickets involves daily phosphorus and active vitamin D supplementation. The phosphorus is typically taken every 6 hours to maintain proper levels in the body.

Regular blood and urine tests are required to ensure the correct balance is achieved and to prevent kidney damage.

TREATMENT / PROGNOSIS

GACI causes the body to have low levels of pyrophosphate – an enzyme that prevents the build up of calcium in blood vessels and arteries, leading to heart attack, heart failure and stroke. Bisphosphonates have shown limited success in replacing the pyrophosphate for patients with GACI. Sadly around 50% of babies diagnosed with GACI die in the first 6 months of life. There are only a handful of adult survivors known worldwide. There is ongoing research into the condition and new treatments, including enzyme replacement therapy, are close to clinical trial.