Sodium Thiosulfate in *ABCC6* Mutated Generalized Arterial Calcification of Infancy: A Case Report

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Introduction

Generalized arterial calcification of infancy (GACI) is a rare autosomal-recessive disorder that can be caused by mutations in *ABCC6*, a gene believed to regulate pyrophosphate (PPi). Low levels of PPi have been observed with *ABCC6* associated GACI resulting in widespread arterial calcification and cardiac related mortality by 6 months of age.[1,2] No treatment options are approved, but Sodium thiosulfate (STS) is a calcium chelating agent used in other disorders to prevent and reverse vascular calcification.[3,4] We report an unusual case of GACI caused by biallelic *ABCC6* variants treated with STS.

Case Presentation

- A previously healthy 2-month-old female presented to the ED with new onset focal seizures.
- CT and MRI/MRA brain scans showed patchy diffusion restriction with cortical T2 hyperintensity and edema in the right MCA and PCA territory.
- Initial CT head showed calcification of bilateral ICAs and left vertebral arteries. MRA of brain and neck also showed diminutive flow of same arteries, consistent with the stroke territory

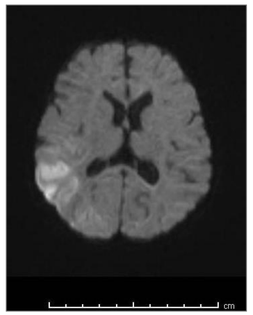

Figure 1: MRI DWI sequence showing acute watershed infarction in the right MCA and PCA territory

Evaluation

- Arterial ultrasonography and CT imaging of the chest, abdomen, and pelvis confirmed additional calcification of the bilateral extremities and renal arteries.
- Echocardiogram was normal
- Genetic testing revealed compound heterozygous variants of the *ABCC6* gene: c.742C>T and c.2294G>T. Parental testing confirmed trans configuration for the *ABCC6* variants and carrier state for one of the variants.

Treatment

- Trileptal started for seizure management and is currently being weaned due to no further seizure activity.
- Anti-platelet therapy with low-dose aspirin for stroke prevention.
- 25% STS(12.5 g/m2) started May 2020 and only interrupted twice due to central line infections. Efficacy was assessed at 3 and 6 month follow-up.

Results

- Child is tolerating infusions with minimal nausea.
- Echocardiogram continues to show no signs of calcification.
- Serial imaging by ultrasound is performed for extremities and renal vasculature. Cerebral arteries are followed by contrasted CT imaging.
- No evidence of calcification progression or worsening vasculopathy. Slight improvement in areas followed by ultrasound.

Results (Continued)

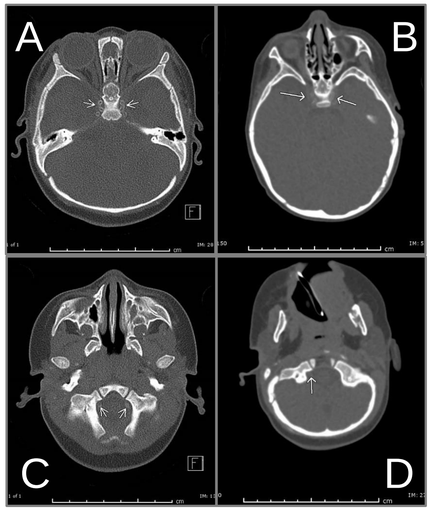

Figure 2: CT head showing calcification and narrowing of bilateral ICAs (A) and left vertebral artery (C) at case presentation; CT Angiogram head demonstrating no change in bilateral ICAs (B) and continued flow throughout the right vertebral artery (D) following 6 months of STS Therapy.

Arterial Calcification at Imaging Follow-up

Arterial Calcification	3 Month Follow-up	6 Month Follow-up
Cerebral	Stable	Stable
Upper Extremities	Stable	Stable
Renal	Stable/Slight Decrease	Stable/Slight Decrease
Lower Extremities	Stable/Slight Decrease	Decrease

Discussions

STS has been reported to reverse calcific stenosis in a case with a similar disorder that had *ENPP1 and ABCC6* mutations, but metabolic acidosis lead to treatment discontinuation at 6 months.[4] In our patient, Nausea/vomiting and occasional abnormal chloride readings were the only side effects observed. Treatment was delayed twice to manage central line infections and may have resulted in the mixed response seen at 6 month follow-up. Cerebral vasculopathy is stable overall and no new strokes have occurred. At 13 months of age, cardiac calcification is still absent and all age-appropriate developmental milestones have been met.

Conclusions

Based on the stabilization and some reversal of arterial calcification, STS may be a treatment option for ABCC6 mutated GACI.

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