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Abstract title: Prenatal Brain Damage in Isolated Sulfite Oxidase and Molybdenum Cofactor Deficiency

Background: Isolated sulfite oxidase and molybdenum cofactor deficiency, two disorders associated with sulfite intoxication, are devastating neurodegenerative conditions that typically present after birth; however, evidence of prenatal brain injury has been reported. Because dietary restriction or cyclic pyranopterin monophosphate substitution therapy may benefit patients if started at the onset of disease, a deeper understanding of the frequency and characteristics of prenatal brain involvement is needed.

Objective: To characterize radiographic and clinical signs of prenatal brain involvement in patients with isolated sulfite oxidase and molybdenum cofactor deficiency.

Study Design/Methods: We reviewed 15 brain MRIs from a cohort of isolated sulfite oxidase and molybdenum cofactor deficiency patients and performed a systematic literature review.

Results: One patient in our cohort demonstrated atrophy of the basal ganglia, brainstem, and cerebellum with cystic leukomalacia in the frontal subcortical white matter on day 3 of life. These findings were consistent with chronic injury that occurred before birth. Eleven patients with possible prenatal onset were identified in our literature review: eight patients with chronic atrophy on brain imaging performed prenatally or within the first 3 days of life, one patient with hyperechoic lesions on brain ultrasound at birth, one patient with hypoplasia of the cerebellum and corpus callosum at 35 weeks gestation, and one patient with poor cortical gyration at 21 weeks of gestation.

Conclusions: Signs of prenatal brain injury likely due to sulfite intoxication are appreciable in a subset of patients though the true frequency remains unknown. Radiographic signs in the prenatal brain that warrant further workup for isolated sulfite oxidase and molybdenum cofactor deficiency include basal ganglia atrophy, cavitary subcortical leukomalacia, hypoplasia of the cerebellum or corpus callosum and poor cortical gyration.