

# Molybdenum Cofactor Deficiency

William L Nyhan

Department of Pediatrics, University of California, USA

## Introduction

Molybdenum cofactor deficiency causes deficiency of sulfite oxidase and xanthine oxidase. The latter leads to the formation of urinary tract calculi, as well as elevated concentrations of hypoxanthine and xanthine. The former leads to severe deficiency of neurologic development and dislocated ocular lenses. Levels of sulfite, thiosulfite, sulfocysteine and taurine are elevated.

## Case Report

R.M. was born after an uneventful pregnancy and delivery to a 26 year old primgravid. The parents were Caucasian and not consanguineous. Birth weight was 3455 g. Apgar scores were excellent and physical examination was normal. Length was 51 cm and head circumference 39 cm. The baby appeared well for 2 days, and then was noted to suck poorly; on examination, he was dusky, mottled and floppy. On immediate transfer to the NICU, he was apneic, pH was 7.08, pCO<sub>2</sub> 69 and pO<sub>2</sub> 67. He was intubated and ventilated mechanically. There were no tonic or clonic evidences of seizures, but the EEG, revealed status epilepticus. Ultrasound of the head suggested mild cerebral edema, but CT scan of the brain was interpreted as normal. He was treated with phenobarbital. EEGs 2, 4 and 7 days later revealed a burst suppression pattern.

Phenytoin treatment was added. MRI of the brain revealed T<sub>2</sub> hyperintensities in the cortex and globi pallidi, and subdural fluid was seen along the tentorium. MRI 10 days later revealed cerebral atrophy. MRI 7 months later revealed diffuse abnormal hyperintense T<sub>2</sub> signal in the white matter bilaterally and diffuse atrophy.

Physical examination in the first week was consistently that of a flaccid infant in deep coma, being artificially ventilated. The anterior fontanel was scaphoid. Deep knee reflexes were brisk, and there was ankle clonus. He had bilateral inverted nipples. Laboratory evaluation

revealed: Na 148, K4.8, Cl 108 and HCO<sub>3</sub> 23 mEq/L; glucose 113, bilirubin 8.5; direct 0, BUN 26, creatine 1.2, calcium 8.8 and magnesium 1.7 mg/dL. The NH<sub>3</sub> was 37 μmol/L. CK was 4025 u/L.

Metabolic investigation revealed normal amino acids in plasma and CSF. The concentration of glycine was 214 μmol/L in plasma and 12 μmol/L in CSF. In plasma glutamine was 724 and alanine 343 μmol/L. Organic acid analysis of the urine was normal. Plasma total homocystine was 1.6. Qualitative dip stix test of the urine for sulfite was positive. Plasma concentration of uric acid on day 5 of life was 1.2 mg/dL, but 2 days later it was 0.3 mg/dL. Urinary oxypurines were uric acid 0, hypoxanthine 0.165 and xanthine 9.711 μmol/mol creatine (normal value 0.33-2.0, 0.022, and 0.020.09 mmol/mol creatine respectively). The urinary sulfocysteine was 233 μmol/g creatine (normal <24).

He was weaned gradually from the ventilator and did well with oral feedings. He was discharged and seen as an outpatient where he thrived physically but showed no signs of development. He was responsive to light or sound and made no purposeful movements. Deep tendon reflexes were brisk and symmetrical. EEG remained abnormal with a generalized spike pattern, and he developed a seizure pattern of myoclonic or brief flexor spasms of the shoulders and trunk. Notable in the first year were overriding of the cranial sutures.

Mutations in the MOCS gene were found at the Institute for Human Genetics by J. Reiss PhD: R67W (CGG>TGG in exon1 and G126D (GGT>GAT in exon 2, which had previously been described [1].

## Discussion

The disease in this patient appeared to be incompatible with life. He displayed no neuro development, and he died in early infancy.

## Reference

1. Reiss J, Johnson JL (2003) Mutations in the molybdenum cofactor biosynthetic genes MOCS1, MOCS2, and GEPH. *Hum Mutat* 21: 569-576. [[Crossref](#)]

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**Correspondence to:** William L. Nyhan, Professor, Department of Pediatrics, University of California, San Diego, USA, Tel: (619) 543-3580; Fax: (619) 543-3565; E-mail: wnyhan@ucsd.edu

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