

## Case Reports

# A case of molybdenum cofactor deficiency

\*Dinesha Maduri Vidanapathirana<sup>1</sup>, Subashinie Jayasena<sup>1</sup>, Eresha Anandanie Jasinge<sup>1</sup>, Pyara Ratnayake<sup>1</sup>, Lynette Fairbanks<sup>2</sup>

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## Introduction

Molybdenum cofactor deficiency (MoCD) is a rare autosomal recessive inborn error of metabolism characterized by intractable seizures, microcephaly, severe and progressive neurological deterioration, facial dysmorphism and feeding difficulties<sup>1,2</sup>. MoCD leads to a combined deficiency of molybdenum cofactor dependent enzymes including xanthine dehydrogenase, sulphite oxidase, aldehyde oxidase and mitochondrial amidoxime reducing component<sup>3</sup>. Death at an early age is common and patients who survive, usually progress to severe psychomotor delay<sup>2</sup>. MoCD can be easily missed as the imaging mimics hypoxic ischaemic encephalopathy<sup>2</sup>. It is important to maintain a high degree of suspicion in order to screen for this lethal disorder which could affect a subsequent sibling. We report on the clinical presentation, ultrasound scan (USS) brain findings and biochemical results which confirmed MoCD in a Sri Lankan infant. This is the first case of MoCD identified in Sri Lanka.

## Case report

The patient is the third child of a second degree consanguineous marriage born to a healthy mother, the two older siblings being healthy. He was a term baby with a birth weight of 2.6kg (-1SD to -2SD), a length of 50.5cm (-1SD to -2SD) and a head circumference of 33.5cm (5<sup>th</sup> centile) with no antenatal complications. He was observed in the baby unit for two days for excessive crying and poor suckling and discharged on day three of life.

<sup>1</sup>Lady Ridgeway Hospital for Children, Colombo, Sri Lanka, <sup>2</sup>St Thomas' Hospital, United Kingdom

\*Correspondence: [maduri129@yahoo.com](mailto:maduri129@yahoo.com)

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Infant had two episodes of seizures at 5 months of age which settled with medication. At present, the child is 8 months old and has global developmental delay and difficulty in feeding. His clinical examination revealed microcephaly with overriding sutures, facial dysmorphism in the form of micrognathia, large right auricle and a narrow bifrontal diameter. Neurological examination revealed spasticity in all four limbs. The remainder of his physical examination was unremarkable. Eye referral revealed superonasal subluxation of lenses. His ultrasound scan of the brain revealed brain atrophy with mild encephalomalacia and prominent ventricles. The USS findings and clinical features raised the possibility of MoCD/Sulphite oxidase deficiency and the patient was subsequently subjected to biochemical investigations.

Laboratory investigations revealed a low serum uric acid level in two samples done 2 months apart (45µmol/L and 48µmol/L, the normal range being 119-428µmol/L). Uric acid to creatinine ratio as well as the fractional excretion of uric acid were also very low registering values of 0.01 (0.7 -1.5 ) and 0.48% (15% -22%) respectively. Urine blotted in a filter paper for xanthine, hypoxanthine and sulphocysteine was sent to Purine Research laboratory in London, United Kingdom. Results are shown in the table 1.

**Table I: Laboratory results of the patient**

Urine	Results (Reference range)
Sulphocysteine	188.9 (0-10) µm/mM
Hypoxanthine	0.115 (0.01-0.11) mmol/L
Xanthine	1.596 (0.01-0.09) mmol/L
Urate/creatinine ratio	0.02 (0.3-1.5) mmol/L: mmol/L

The urinary levels of xanthine, hypoxanthine and sulphocysteine were found to be high and this favoured the diagnosis of MoCD biochemically.

## Discussion

MoCD is a rare autosomal recessive inborn error of metabolism that was firstly described by Duran et al.

in 1978<sup>4</sup>. Sulphite oxidase, xanthine dehydrogenase and aldehyde oxidase are the three enzymes dependent on a molybdenum-pterin complex named molybdenum cofactor<sup>3</sup>. Absence of the cofactor leads to a combined deficiency of these three enzymes.

MoCD predominantly affects the central nervous system. The neurological injury caused by MoCD is the result of an absence of sulphite oxidase activity leading to an accumulation of the neurotoxic metabolite (sulphite) or the deficit of the product (sulphate)<sup>5</sup>.

Global cerebral oedema, cystic encephalomalacia, cortical and white matter atrophy, focal or bilateral changes within the globi pallidi and subthalamic regions, dysgenesis of corpus callosum and ventriculomegaly are the major radiological features reported of MoCD<sup>2</sup>. Some findings were consistent with our patient e.g. cystic encephalomalacia, brain atrophy, ventriculomegaly. Some cases have been reported with lens dislocation and our patient also had bilateral superonasal subluxation of lens<sup>2</sup>.

Isolated sulphite oxidase deficiency (SOD) is clinically very similar to MoCD. These two disorders can be differentiated biochemically with elevated S-sulphocysteine in both conditions and additionally excretion of xanthine and hypoxanthine in MOCD due to abnormal xanthine dehydrogenase pathway. Our patient's urine sample showed elevation of S-sulphocysteine, xanthine and hypoxanthine which biochemically confirmed MoCD. Genetic studies could further establish the diagnosis.

To date no effective treatment is available and death in early infancy is the usual outcome. A case study has shown that purified cyclic pyranopterin monophosphate (cPMP) to have resolved metabolic abnormalities and resulted in dramatic clinical improvement in an infant with MOCD<sup>1</sup>.

MoCD should be considered in children presenting with intractable seizures. Low uric acid level with radiological findings gives a clue to the diagnosis. Promising therapeutic strategies may, in future, combat this fatal condition.

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