

2019. *N Engl J Med.* 2020;382:727-33.

- Cai J, Xu J, Lin D, Yang Z, Xu L, Qu Z, *et al.* A case series of children with 2019 novel coronavirus infection: Clinical and epidemiological features. *Clin Infect Dis.* 2020 Feb 28 [Online ahead of print]. Available from: [https://academic.oup.com/cid/advance-article/doi/10.1093/cid/](https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa198/5766430)

[ciaa198/5766430](https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa198/5766430). Accessed April 2, 2020.

- Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, *et al.* Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med.* 2020 Feb 28. Available from: <https://www.nejm.org/doi/full/10.1056/NEJMoa2002032>. Accessed April 2, 2020.

## Urolithiasis due to Hereditary Xanthinuria Type II: A Long-term Follow-up report

**H**ereditary xanthinuria (HX) is a rare autosomal recessive disorder of purine metabolism. It results from deficiency of the enzyme 'xanthine dehydrogenase/oxidase (XDH/XO)' which catalyzes the final two steps in the purine degradation pathway (conversion of hypoxanthine and xanthine to uric acid). The resultant plasma accumulation and excess urinary excretion of xanthine is responsible for the arthropathy, myopathy, crystal nephropathy, urolithiasis, and renal failure seen in this disorder. Most patients belong to Middle East or Mediterranean region, and the disorder is rare in other parts of the world [1,2]. Two types of HX have been described; type I and type II, based on distinct mutation loci. It is difficult to distinguish the two subtypes on clinical and biochemical grounds, and molecular testing is needed for accurate phenotyping [1].

A 13-month-old male child, presented with recurrent episodes of orange colored graveluria and hematuria since the age of nine months. The child was born of a second-degree consanguineous marriage and family history was negative. Examination revealed a healthy appearing child with length 78 cm (75th centile) and weight 8.8 kg (10th-25th centile). The general and systemic examination was unremarkable.

Investigations revealed serum calcium 10.2 mg/dL, phosphorus 5.6mg/dL, alkaline phosphatase 678 IU/L, creatinine 0.4 mg/dL, blood urea 10 mg/dL, hypouricemia (serum uric acid <0.01 mg/dL) and hypouricosuria (24 hour urinary uric acid 0.4 mg/day, normal 250-750 mg/day; 24 hour urinary creatinine 88 mg/day, normal 88-106 mg/day). Radiograph of kidney ureter and bladder was normal, while ultrasonography revealed two calculi in the urinary bladder and concretions in the lower pole of left kidney. In view of low serum and urinary uric acid levels

and radiolucent nature of renal stones, xanthinuria was suspected. His hospital course was complicated by urethral obstruction which was relieved by catheterization followed by cystolithotomy at a later date. The bladder stones retrieved were subjected to X-ray diffraction study, revealing them to be of xanthine origin. A targeted gene sequencing revealed compound heterozygous mutation in the enzyme molybdenum cofactor sulfuryase (*MOCOS*) gene [heterozygous two base pair deletion in exon 6 (chr18:33785104\_33785105delCT) and heterozygous nonsense mutation in exon 11 (chr18:33831134T>G)]. Patient was diagnosed to be having HX type II and advised dietary purine restriction (avoidance of purine-rich foods including red and organ meat, shell fish, oily fish, seafood, sweetened beverages such as fruit juices and colas, yeast and mushroom, spinach, peas and whole pulses), and adequate oral hydration.

On follow-up, he had no further episodes of renal colic, graveluria or hematuria. The child maintained good compliance to dietary restrictions advised. His height and weight at nine years were 138.7cm (75th-97th percentile), and 32.1 kg (75th-97th percentile), respectively. Serial annual ultrasonography imaging and renal functions have remained normal with serum uric acid <0.01 mg/dL.

HX is a rare disorder of the purine metabolism that leads to urolithiasis. Renal stones can occur at any age, even in infancy [2]. The stones are radiolucent, and are seen in about 40-50% patients with this disorder. The diagnosis may be established with stone analysis, demonstration of an elevated urinary xanthine or hypoxanthine excretion, and measurement of XDH/XO activity in liver or intestinal biopsy sample. The finding of an orange-brown urinary sediment, orange-stained diapers, and profound hypouricemia are other important indicators. However, it is difficult to characterize the exact phenotype of the disorder (type I or II) based on these clinical and biochemical indicators alone, necessitating the use of molecular tests.

The mainstay of treatment is institution of a low-purine diet, and intake of plenty of oral fluids [3]. Urinary

alkalinization is of minimal therapeutic value, as the solubility of xanthine is only minimally enhanced at alkaline pH. Our patient showed excellent treatment response over a long follow up of nine years, which is in line with the short-term follow-up response reported in the literature [4,5].

To conclude, HX is a rare disorder of purine metabolism which should be suspected in children presenting with orange colored graveluria, hypouricemia, hypouricosuria and radiolucent renal stones. Molecular testing is essential for exact phenotyping, and should be pursued in all cases. Such children show excellent response to treatment with low purine diet and increased oral hydration, as exemplified in the case described.

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## REFERENCES

1. Mraz M, Hurba O, Bartl J, Dolezel Z, Marinaki A, Fairbanks L, *et al.* Modern diagnostic approach to hereditary xanthinuria. *Urolithiasis.* 2015;43:61-7.
2. Badertscher E, Robson WL, Leung AK, Trevenen CL. Xanthine calculi presenting at 1 month of age. *Eur J Pediatr.* 1993;152:252-54.
3. Gargah T, Essid A, Labassi A, Hamzaoui M, Lakhoua MR. Xanthine urolithiasis. *Saudi J Kidney Dis Transpl.* 2010; 21:328-31.
4. Fujiwara Y, Kawakami Y, Shinohara Y, Ichida K. A case of hereditary xanthinuria type I accompanied by bilateral renal calculi. *Intern Med.* 2012;51:1879-84.
5. Arikyants N, Sarkissian A, Hesse A, Eggermann T, Leumann E, Steinmann B. Xanthinuria type I: a rare cause of urolithiasis. *Pediatr Nephrol.* 2007;22:310-4.

## Developmental Delay with Intermittent Twisting of Neck

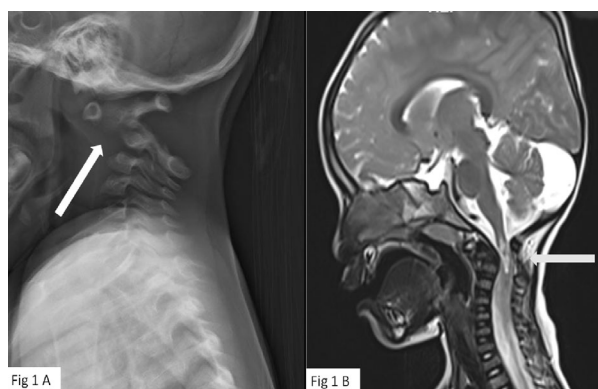
The hallmark of cerebral palsy (CP) is the presence of pyramidal or extra-pyramidal signs [1]. There are many disorders that can mimic CP [2]. One such mimicking condition is high cervical cord compression due to anomalies of the spinal cord [3].

A two-year-old boy, second of twins born of non-consanguineous marriage, was brought with inability to stand. He was delivered at eight months of gestation with a weight of 1.5 kg and no significant neonatal complications. His motor milestones were significantly delayed compared to his twin and spasticity was noticed from six months of age. The parents reported stiffness of his neck and limbs which was more on waking up, which would decrease within a few minutes. There were no seizures or regression of milestones. He was diagnosed to have mixed (spastic-dystonic) cerebral palsy. His language and social skills were age appropriate. At presentation, he was using two- word phrases and had attained daytime bowel and bladder control.

On examination, weight, height and head circumference were within normal limits. There were no

obvious dysmorphic features. His upper segment to lower segment ratio was 0.92 suggestive of truncal shortening. His vision and hearing were normal. There was hypertonia in all the four limbs and brisk deep tendon reflexes. The plantar responses were extensor bilaterally. Examination of the other systems was unremarkable.

Lateral X-ray of the neck (**Fig. 1a**) showed anterior dislocation of C1 vertebra. The pre-dentate space was widened and measured 13 mm. MRI did not show any



**Fig. 1** (a) X-ray Cervical spine lateral view flexed position showing widened pre-dentate space (white arrow); (b) MRI T2 weighted image sagittal section showing compression of the cord at C1 level (grey arrow).