Mucolipidosis Type II Secondary to GNPTAB Gene Deletion from India

Dear Sir,

Mucolipidosis II (ML II) is a rare autosomal recessive disorder of lysosomal metabolism. It has often been clinically misdiagnosed as mucopolysaccharidosis. ML II is characterized by developmental delay, short stature, coarse facial features, and dysostosis multiplex.[1] We are reporting 9-month-old girl born to a second degree consanguineously married couple presented with developmental delay and noisy breathing. Examination revealed coarse facies, thick eyebrows, hypertelorism, bilateral corneal clouding, pectus excavatum, and kyphosis. There was hepatosplenomegaly but no cherry red spot. On investigations, thyroid function test and urine glycosaminoglycans were normal. Skeletal survey shows kyphosis of dorsal spine. Magnetic resonance imaging brain shows mild cerebral atrophy. Enzyme analysis in plasma shows elevated, alpha-mannosidase12,970 (normal: 20–120)-nmol/h/ml, alpha-fucosidase-6624 (normal: 90–610)-nmol/h/ml, and beta-hexosaminidase-T-23090 (normal: 620–4990) nmol/h/ml. High levels are suggestive of ML II/III. GNPTAB gene testing revealed a homozygotic deletion in exon 19 (c_3503_3504delTC). Based on severe MPS phenotype in early infancy, enzyme assay, and genetic testing, we diagnosed the case as ML II.

ML II is caused by deficiency of N-acetylglucosamine-1-phosphotransferase. This enzyme deficiency can produce two different phenotypes, ML II and ML III (pseudo-Hurler polydystrophy).[2] ML II and III differ in age of onset with ML II being present at birth and ML III starting clinical symptoms between 3 and 5 years of age. ML II causes severe intellectual disability, coarse facial features, skeletal abnormalities, and an early death during first decade. ML III is a late onset with variations in intellectual disability (normal to decreased), skeletal abnormalities which are prominent and these individuals may live for a number of decades. Based on above differences, we considered possibility of ML II in our child.[3]

We excluded MPS based on early infancy presentation and absent of glycosaminoglycans in the urine. We ruled out congenital hypothyroidism based on normal thyroid function tests. We also excluded GM1 gangliosidosis and Sialidosis as child had no startle response, epilepsy, and cherry red spot in the fundus. Cury et al. reported mutation c_3503_3504delTC located in exon 19 was most common mutation (n = 11/24) in ML II and III in Brazil.[4] This mutation from Indian subcontinent is useful for the molecular diagnosis of ML II in India.

ML II should be considered as one of the differential diagnoses in patients presenting in early infancy with MPS phenotype. ML II is differentiated from ML III based on severe and early presentation in former.

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Conflicts of interest
There are no conflicts of interest.

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In view of the clinical profile, a possibility of CDKL5 was no cerebrospinal fluid hypoglycorrhachia. Investigations revealed a normal brain magnetic resonance imaging. The electroencephalogram showed multifocal spike-wave discharges. The metabolic testing (blood ammonia, arterial lactate, blood acylcarnitine profile, urinary organic acids) revealed no abnormalities. There were no hypoglycaemia, hyperammonaemia, seizures. She had not achieved social smile, was not able to speak, had reduced eye contact and had stereotypies, microcephaly, head control, grasping, or vocalization. She also had poor muscle tone and had central hypotonia. Seizures were generalized tonic and hypomotor, and some patients had intractable seizures accompanied by severe developmental delay and in the long term. The perinatal period was uneventful. She had not achieved social smile, was not able to speak, had reduced eye contact and had stereotypies, microcephaly, head control, grasping, or vocalization. She also had poor muscle tone and had central hypotonia. Seizures were generalized tonic and hypomotor, and some patients had intractable seizures accompanied by severe developmental delay and in the long term. The perinatal period was uneventful.

Dear Sir,

The results of a genetic testing for CDKL-5 was performed as previously described. The diagnosis of a CDKL5-encephalopathy.

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