CASE REPORT

Mucolipidosis Type II (I-CELL) in two Children with Skeletal Abnormality, Dysmorphism and Hepatosplenomegaly

Jayesh J Sheth, Nrupesh Oza, Mehul Mistri, Premal Naik, Suresh Kumar, Frenny Sheth

Abstract: Mucolipidosis type II (ML-II) or I-cell disease is a rare autosomal recessive lysosomal storage disorder. This occurs due to deficiency of lysosomal transporter enzyme (phosphotransferase) with the birth incidence of 1:3,50,000. We report two cases of I-cell disease presented with dysostosis multiplex, dysmorphism and hepatosplenomegaly. Serum screening for I-cell was positive in both cases with marked elevation of lysosomal enzymes Arylsulphatase-B, β- Hexosaminidase, α-Fucosidase and α-Mannosidase. Due to its rarity and phenotypic heterogeneity present cases are reported.

Keywords: ML-II, I-cell disease, LSD, dysmorphism, Mucolipidosis

Introduction: ML-II or I-cell disease is a metabolic disorder owing to abnormal lysosomal enzyme transport in messenchymal cell (1). As a result, affected cells show dense inclusion filled with complex storage material (2). It is this property of ML that give rise to heterogeneous phenotype of an affected child mainly involving skeletal system (3). Diagnosis of the disorder can be made biochemically by estimating several lysosomal enzymes from serum or by studying characteristic pattern of lysosomal enzyme deficiencies from the fibroblast (1). Though there is no treatment option available, prenatal diagnosis is the only choice after index case confirmation. Present study is reported due to its rarity and possible genetic counseling to the family.

Case I: The child was born to non-consanguineous Hindu parents residing in Gujarat, India after three year of married life. There was no family history of any genetic disorders. Proband was a full term normal male baby with 2 kg of birth weight and normal Apgar score. At 2 month of age, parent noticed inguinal hernia and harsh breathing. At 6 months mild hepatosplenomegaly with coarse facial features and skeletal abnormality in chest region was observed. X-ray chest suggested mild interior beaking and X-ray spine suggested kyphosis in lumber region suggestive of mucopolysaccharidosis (MPS) type IV-B (Morquio disease). At this age proband has shown regression of learned skills of few words, hypotonia and deep superficial reflexes. Skin and eye finding were normal. Owing to discomfort and severity, proband was operated for inguinal hernia at the age of 1½ years. By this time, coarse facial feature with thick rough skin and mild neuroregression with characteristic gingival hyperplasia were evident. Systematic investigations were started with clinical diagnosis of MPS at 2 years of age. Confirmative investigations initially carried out from leucocytes for several lysosomal enzyme were non informative. Then after, I-cell screening was carried out from serum using p-nitrocatecholsulfate, which was positive followed by several lysosomal enzyme carried out from serum and all were markedly elevated confirming I-cell disease (Table-1).

Case II: Child was born in South India to the consanguineous Muslim parents with birth weight of 4.2 kg. Parent noticed delayed milestone since birth with large head (Head circumference 39 cm), low set ears, low hair line and depressed nose. On examination, neck, palm, chest were normal at 5 month of age with normal deep and superficial reflexes. There was lower limb deformity, left was more abducted than right lower limb and USG abdomen showed hepatosplenomegaly with spleen 3 cm and liver 5 cm below costal margins. Echocardiography study showed bicuspid aortic valve, trickle of aortic regurgitation and ascending aorta. With clinical suspicion of MPS, urine GAG was carried out which was normal (6.0 mg/mmol of creatinine) followed by positive I-cell screening from serum. Confirmative study was carried out by estimating several lysosomal enzymes (Table 1), which were markedly raised confirming I-cell disease.

Table 1: Lysosomal enzyme study carried out from serum

Enzyme	Lysosomal Enzymes Activity In serum* Of Proband		Control value*
	I	II	
β-Galactosidase	1,800	2,666	40.0
β-Hexosaminidase	30,400	38,400	1,280.0
Arylsulfatase - B	533.11	437	15.5
α- Fucosidase	26,500	32,000	266.5

* Values are expressed in nmol/hr/ml plasma.

Discussion: ML II is a rare hereditary disorder with very few reports from India (4,5). It occurs due to mutations in the GNPTA gene coding for UDP-N-acetylglucoseamine-1-phosphotransferase (6). This results in the missorting and cellular loss of lysosomal enzymes and lysosomal accumulation of storage material. As a result newly synthesized lysosomal enzymes are secreted into the extracellular medium instead being targeted to the lysosomes for degradation of intracellular storage material. Due to this, lysosomal enzymes are grossly elevated in serum while deficient in lysosomes (2). Affected individuals have severe psychomotor retardation with radiological changes that are seen in Hurler syndrome (7). In present cases, skeletal abnormality, hepatomegaly, normal urinary GAG and rapid progression of the clinical phenotype allow clinical differentiation of ML-II from Hurler syndrome. The striking gingival hyperplasia is a unique clinical feature of the I-cell disease (8) which was seen in case 1 while in case-2 cardiac valve abnormality was observed which could be due to presence of numerous vacuolated fibroblasts in heart valves (9). Both cases have shown hepatosplenomegaly that suggest damage to fibroblast in the periportal space. Neuroregression was not evident in either conceivably due to early identification of the disease by which

instance, the presence of lamellar bodies in spinal ganglia neurons are unlikely to interfere with the process of myelination. However developmental disruption of motor unit was common in both the cases which are commonly observed in ML-II patients (10). In absence of specific therapeutic option, prognostication is very important to the families. With the average life span of 2 - 6 years, presence and number of vacuolation do provide survival information (11) and would be advisable for counseling.

We observed from this case series that differential diagnosis of I-cell from MPS is essential for prognostication followed by prenatal diagnosis of the disease.

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From: FRIGE (Foundation for Research in Genetics and Endocrinology), Institute of Human Genetics, Ahmedabad

Address for Correspondence: Jayesh J Sheth, FRIGE (Foundation for Research in Genetics and Endocrinology), Institute of Human Genetics, FRIGE House, Jodhpur Road, Satellite, Ahmedabad-380015, India. Email: jshethad1@gmail.com