Cardiovascular Therapy: Open Access

Case Report Open Access

Dysostosis Multiplex (Gm-1 Gangliosidosis: Type II)

Madhu KJ[1]*, Vijyalakshmi IB[2], Chitra Narsimhan[2] and CN Manjunath[1]

[1]Department of Cardiology, Sri Jayadeva Institute of Cardiovascular Sciences and Research, India
[2]Department of Pediatrics Cardiology, Sri Jayadeva Institute of cardiovascular Sciences and Research, India

: Mucopolysachroid; Keratan sulphate; Dermal melanocytosis;Autosomal recessive.

A

G_{M1} gangliosidosis is an autosomal recessive lysosomal storage disorder characterized by the generalized accumulation of G_{M1} ganglioside, oligosaccharides, and the mucopolysaccharidekeratan sulfate (and their derivatives). De ciency of the lysosomal hydrolase, acid β-galactosidase, causes G_{M1} gangliosidosis [1]. G_{M1} gangliosidosis is a rare disorder, and the estimated incidence is 1:100,000-200,000 live births [2]. G_{M1} gangliosidosis is found in all races, although speci c alleles can be identi ed in certain ethnic groups. A high frequency of G_{M1} gangliosidosis has been reported from Southern Brazil, and a large number of Japanese patients with the adult form have been reported [3]. All 3 types of G_{M1} gangliosidosis are inherited as autosomal recessive traits and have equal sex distributions.

C

5 years old boy with normal birth history born to a non-consanginous parents, presented with mild developmental delay, gait di culties and sti ness of limbs since 4 year of age. Initially parents noticed child had tiptoe walking, later he had sti ness of both upper and lower limbs which is gradually progressive. Child is still able to walk but unable to run. ere is history of febrile seizures at 1.5 year of age. Younger sibling also having similar complaints

P

Boy is alert, cooperative GPE revealed, Coarse facial features, proptosis, prominent forehead, tented upper lip, hepatosplenomegaly, melanotic patches over back, elbow, nger & hamstrings contracture, protrubrent abdomen with umbilical hernia, brisk re exes, power 5/5 and spastic gait.

A

CBC showed normocytic hypochromic with mild relative monocytosis, LFT' & RFT's were normal, Urine test positive for MPS, Serum Hexosaminidase. A enzyme levels raised above normal limits, Aryl sulfatase negative, Beta galactosidase enzyme levels were reduced.

C

Mild MR, MVP, dilated LV, pericardial thickening, depositions over heart valves, chordae, endocardium and pericardium

***Corresponding author:**

Received:

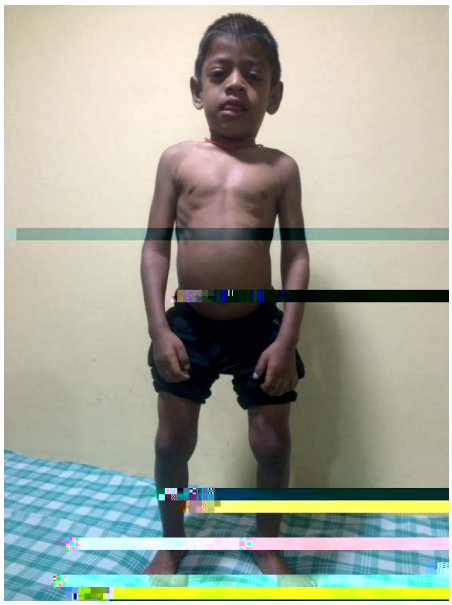

Figure 1: Showing prominent forehead, hypertelorism, proptosis, fat nasal

Figure 2
larosis, hamstrings contracture, fnger contracture, protrubrent abdomen with

age 6 months with progressive organomegaly, dysostosis multiplex, facial coarsening, and rapid neurologic deterioration withi the rst year of life. Death usually occurs during the second year of life because of infection (usually due to pneumonia that results from recurrent aspiration) and cardiopulmonary failure [10]

2): Typically presents at age 1-2 years with progressive psychomotor retardation. Little visceromegaly and milder skeletal disease are present compared to the infantile form. Death usually occurs before the second decade of life.

e adult form (Type 3): Typically presents during childhood or adolescence as a slowly progressive dementia with prominent parkinsonian features and extrapyramidal disease, particularly dystonia. Marked phenotypic variability may occur. Age at death may widely vary.

: Developmental delay [11], arrest, and regression, Generalized hypotonia initially, developing into spasticity, Exaggerated startle response, Hyperre exia, Seizures, Extrapyramidal disease, Generalized dystonia (adult subtype) [12], Ataxia, Dementia, Speech and swallowing disturbance [13].

: Macular cherry-red spots, Optic atrophy, Corneal clouding

: Frontal bossing, Depressed nasal bridge and broad nasal tip, Large low-set ears, Long philtrum, Gingival hypertrophy and macroglossia [1], Coarse skin, Hirsutism, Cardiovascular - Dilated and/or hypertrophic cardiomyopathy, valvulopathy.

: Hepatosplenomegaly, Inguinal hernia.

: Lumbar gibbus deformity and kyphoscoliosis, Dysostosis multiplex, Broad hands and feet, Brachydactyly, Joint contractures, Prominent dermal melanocytosis [14-17].

Diagnosis of G_{M1} gangliosidosis can be con rmed by measurement of acid β-galactosidase activity in peripheral blood leukocytes. Patients with the infantile form have almost no enzyme activity, whereas patients with the adult form may have residual activity of 5-10% of reference values.

Galactose-containing oligosaccharides are excreted in the urine. Their presence may be used as an ancillary diagnostic

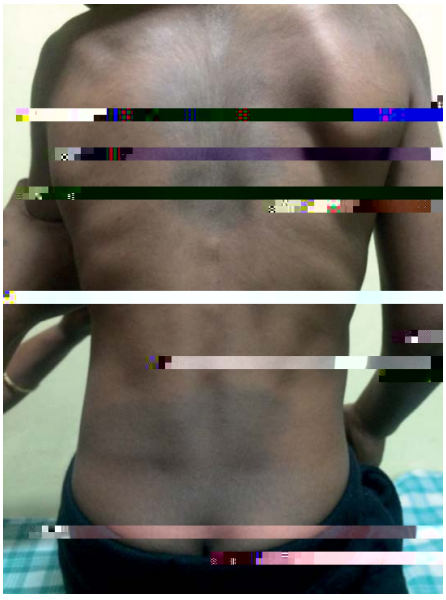

Figure 3

test, and the concentration of the metabolites is proportional to disease severity.

CBC

Vacuolation of lymphocytes may be present in patients with G_{M1} gangliosidosis but is a nonspeci c.

Diagnosis of G_{M1} gangliosidosis has been made based on dried blood spots from newborn screening lter paper, even a er 15 months in storage [18].

Molecular analysis of the β-1 galactosidase gene (GLB1) is clinically available [9].

Prenatal diagnosis has been performed successfully by assay of β-galactosidase activity in cultured amniocytes or amniotic chorionic villi [1]. Mutation identi cation allows prenatal or preimplantation genetic diagnosis [19,20].

Currently, no effective medical treatment is available for the underlying disorder in patients with G_{M1} gangliosidosis. Bone marrow transplantation was successful in an individual with infantile/juvenile G_{M1} gangliosidosis; however, no long-term benefit was reported [21]. Presymptomatic cord-blood hematopoietic stem-cell transplantation has been advocated by some as a possible treatment because of success in other lysosomal storage disorders [22]. Symptomatic treatment for some neurologic sequelae is available but does not significantly alter the clinical course. Active research in the areas of enzyme replacement and gene therapy for