Case Study

Early Infantile Gangliosidosis GM1 with B/L pitting edema of lower Limbs

Abstract:

Gangliosidosis is an inherited enzyme deficiency of beta-galactosidase, which results in the accumulation of glycosphingolipids within the lysosomes. It leads to neurological, skeletal, and dermatological manifestations. Inferred gm1 gangliosidosis is a lysosomal storage disorder affected by mutations in glb1, encoding β-galactosidase. The range of severity is from type i infantile disease, lethal in early childhood, to type iii adult onset, resulting in gradually progressive neurological symptoms in adulthood. We relate to 13 months old patient with early infantile type of gangliosidosis.

Key Words: *Gangliosidosis, inherited enzyme, beta-galactosidase, glycosphingolipids, Lysosomes*

Introduction

Landing et al. (1964) gave the first definitive description of this disease, it was previously used to call as hurler variant, pseudo hurler variant and tay – sachs disease with visceral involvement.[1] O' brein et al (1965) suggested the term "generalized gangliosidosis.[2] gangliosidosis is an autosomal recessive lysosomal storage disease characterized by accumulation of ganglioside substrate in lysosomes due to deficiency of human beta-galactosidase enzyme.[3] clinically patients show variable degrees of neurodegeneration and skeletal abnormalities. Type 1 or infantile form shows rapid psychomotor deterioration beginning within 6 months of birth, generalized central nervous system involvement, skeletal dysplasia, hepatosplenomegaly, facial dysmorphism, macular cherry red spots, and early death. Dysplastic changes in long bones and vertebrae has been observed.[4] General edema [5] or pitting edema of hands and feet is also significant [6]

Infantile is the most frequent form of gm1 gangliosidosis but the exact prevalence is not known. About 200 cases have been reported to date. Over all prevalence at birth of gm1 gangliosidosis is estimated to occur in one in 100,000 to 300,000.[7] the prevalence in brazil (1:17,000), in persons of roma ancestry (1:10,000), and in the maltese islands (1:3,700) is much higher than in other areas and likely represents founder effects.[8] it involves cardiac manifestations. Ekg showed an incomplete bundle branch block and pathology showed vacuolated and hypertrophied myofibers. The mitral valve leaflets were thick and nodular with vacuolated histiocytes and fibrous tissue. In some cases, the right coronary artery was partially occluded by an atherosclerotic plague containing ballooned cells.[9]

Skin manifestations include angiokeratoma corporis diffusum appears with gm1-gangliosidosis. The angiokeratomas did not form clusters but were scattered widely over the body and proximal extremities. No angiokeratomas were observed on the penis and scrotum.[10]

Extensive dermal melanocytosis has been reported in association with gm1-gangliosidosis type i, clinically, dermal melanocytosis associated with lysosomal storage disease is characterized by extensive blue cutaneous pigmentation with dorsal and ventral distribution, indistinct borders, and persistent and/or 'progressive' behavior.[11]
Gm1 also involves glomerular epithelium, a renal biopsy revealed storage of mucopolysachharide in vacuoles of glomerular epithelium, vacuoles were considered as lysosomes.[12].
Currently no effective medical treatment is available for gm1 gangliosidosis. Bone marrow transplantation was successful in an individual with infant lie gm1 gangliosidosis, however no long-term benefit was reported. [13]
Presymptomatic cord-blood hematopoietic stem cell transplantation has been advocated by some as a possible treatment because of success in other lysosomal storage disorders.[14].
Prognosis is not good. Death usually occurs during the second year of life because of infection and cardiopulmonary failure.[7]

Presentation of Case :

13 months old Baby girl was attended and History was narrated by mother, mother complained of non-bloody Diarrhea for 1 month, 3 episodes /day, contains mucous, grade 3-4, partially alleviated with medicine. Associated with non-documented and low-grade fever which was sudden in onset, intermittent, aggravated at morning and night had no alleviating factors. Mother denied history of vomiting, dysuria, fits, loss of consciousness, cyanosis.
She was born at term by Simple Vaginal Delivery at hospital, mother had no history of prenatal/ Natal/ postnatal complications. She had cried well soon after birth though his family had noticed the dysmorphic facies and increased weight of 4.5 kg. Parents considered increased weight to be normal. Patient at age of 12 months, developed Respiratory infection and was treated for it. Patient had normal developmental milestones but was unable to stand. Patient is third child of contagious parents, 1 child passed away due to meningitis at age of 1.

On Examination the baby had dysmorphic face. She was pale, Head circumference is 50 cm, anterior fontanelle is open and flat which measures 1.5 cm x 1.5 cm. There is frontal bossing, and patient is squint. Depressed nasal bridge. upper and lower limb asymmetry with B/L pitting edema of lower limbs up till thighs, wrinkles on arms, Rocker Bottom feet. Harrison sulcus was noted, hepatomegaly with liver span of 8 cm below costal margin, No splenomegaly. Cardiac and Chest exams were normal. X-Ray Skeletal survey showed J shaped Sella Turcica and anterior beaking of thoracolumbar vertebrae. Liver Trucut Biopsy showed Mild Macrovesicular steatosis. Her Echocardiogram, Ultrasound KUB (Kidney Ureter and Bladder) and Thyroid Profile were normal. Eye Examination did not show any Cherry Red Spot.

Discussion:

The patient has several clinical features which are typical of generalized GM1-gangliosidosis. These include vertebral changes which included Upper and lower limb asymmetry, dysmorphic facies[4], characteristic pitting Bilateral lower limb edema, edema, [5,6] since birth, upper respiratory tract infection.

Other unique clinical features of the patient included J shaped Sella Turcica and anterior beaking of thoracolumbar on X-Ray Skeletal survey

Conclusion :

This suggests that Vertebral changes which includes bilateral lower limb asymmetry and edema either generalized or lower limbs can give a better clinical clue in diagnosing Gangliosidosis GM1 in infants.

CONSENT :

All authors declare that 'written informed consent was obtained from the guardians of patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office/chief editor/editorial board members of this journal.

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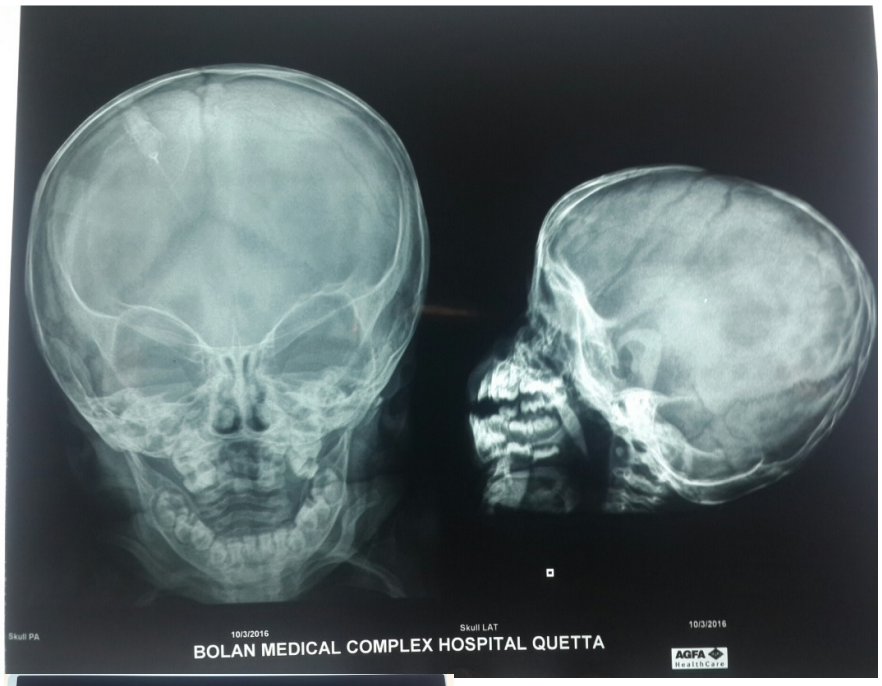
Figure 1: shows frontal bossing, Depressed nasal bridge. Upper and lower limb asymmetry with B/L pitting edema of lower limbs, Rocker Bottom feet and Frontal Bossing



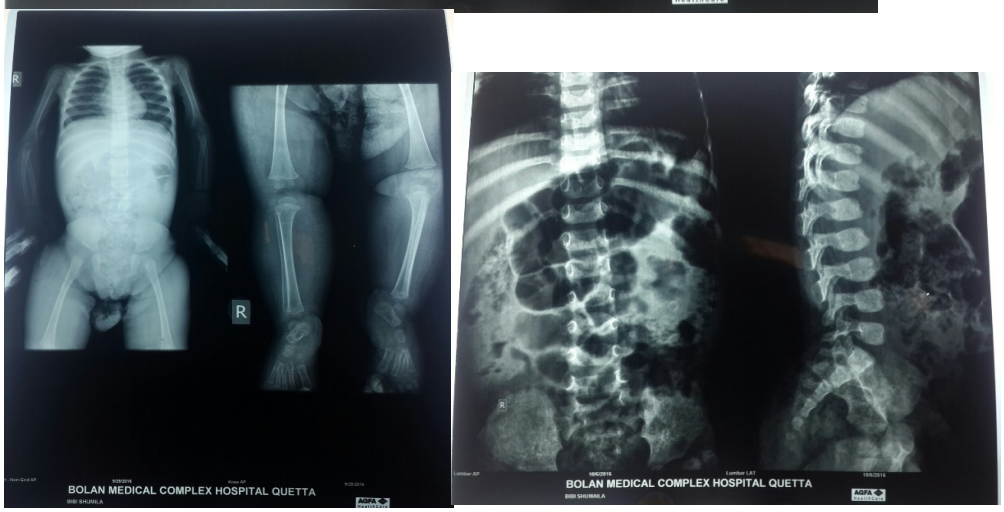


Figure 2: Skeletal survey, J shaped Sella turcica is prominent, skeletal asymmetry and Skeletal survey showing Anterior Beaking of Thoracolumbar vertebrae

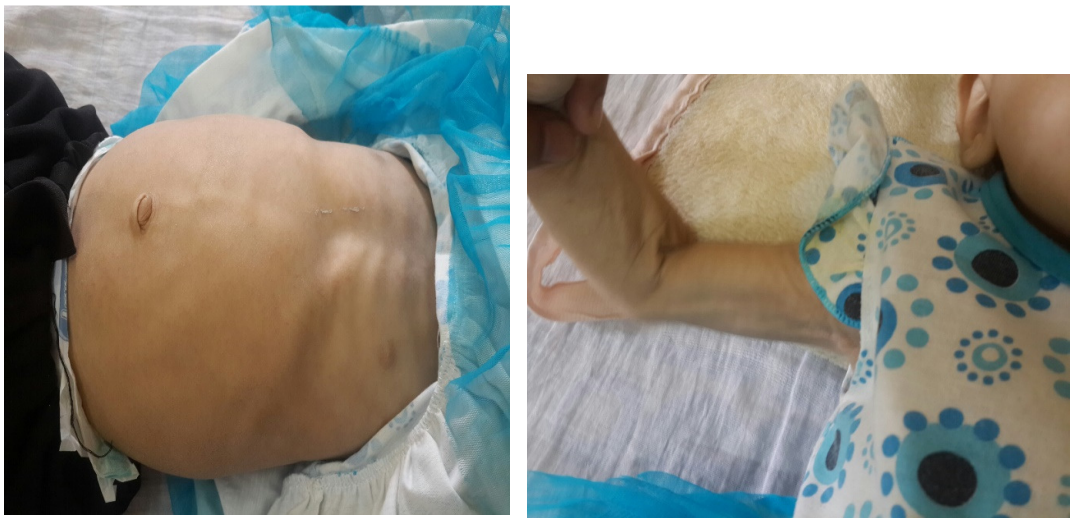


Figure 3: showing Harrison's sulcus and wrinkling of Skin.