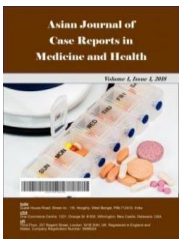

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Early Infantile Gangliosidosis GM1, a Rare Clinical Entity

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Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Gangliosidosis is a rare lysosomal storage disease. There have been about 200 cases reported, to date. The Overall prevalence at birth of GM1 Gangliosidosis is estimated to be 1 in 100,000 to 300,000. It 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 beta-galactosidase. The range of severity is from type 1 infantile disease, lethal in early childhood, to type 3 adult on set, resulting in gradually progressive neurological symptoms in adulthood. The case report relates to a 13 months old patient with early infantile type of Gangliosidosis.

Keywords: Gangliosidosis; autosomal recessive inherited enzyme deficiency; beta-galactosidase; glycosphingolipids; lysosomes.

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1. INTRODUCTION

Landing et al. [1] gave the first definitive description of this disease, it used to be previously called as Hurler variant, pseudo hurler variant and Tay – Sachs disease with visceral involvement. O' Brein et al. (1965) suggested the term "generalized Gangliosidosis [2]. Gangliosidosis is an autosomal recessive lysosomal storage disease, characterized by accumulation of ganglioside substrates 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 that begins within 6 months of birth, presenting with generalized central nervous system involvement, skeletal dysplasia, hepatosplenomegaly, facial dysmorphism, macular cherry red spots and early death. Dysplastic changes in long bones and vertebrae have been observed [4]. General edema [5] or pitting edema of hands and feet is also significant [6].

Gangliosidosis is a rare clinical disorder, the exact prevalence is not known. About 200 cases have been reported to date. Overall 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]. Infantile form is the most frequent form of GM1 gangliosidosis. It involves cardiac manifestations. EKG (Electrocardiogram) shows an incomplete bundle branch block, and pathology shows vacuolated and hypertrophied myofibers. The mitral valve leaflets are thick and nodular with vacuolated histiocytes and fibrous tissue. In some cases, the right coronary artery is partially occluded by an atherosclerotic plague containing ballooned cells [9].

Skin manifestations include angiokeratoma corporis diffisum which appears with GM1-gangliosidosis. The angiokeratomas don't form clusters but scattered widely over the body and proximal extremities. No angiokeratomas are observed on the penis and scrotum [9].

Extensive dermal melanocytosis is reported in association with GM1-gangliosidosis type 1. Clinically, dermal melanocytosis is associated with lysosomal storage disease. It is characterized by extensive blue cutaneous pigmentation with dorsal and ventral distribution, indistinct borders, and persistent and/or 'progressive' behavior [10].

GM1 also involves glomerular epithelium, a renal biopsy reveals storage of mucopolysachharide in vacuoles of glomerular epithelium, the vacuoles are considered as lysosomes [11].

Currently no effective medical treatment is available for infantileGM1 gangliosidosis. Bone marrow transplantation was successful in an individual with infantile GM1 gangliosidosis, however no long-term benefit was reported [12].

Presymptomatic cord-blood hematopoietic stem cell transplantation has been advocated by some as a possible treatment because of success in other lysosomal storage disorders.

Prognosis is not good. Death usually occurs during the second year of life because of infection and cardiopulmonary failure [7].

2. PRESENTATION OF CASE

History of a 13 months old baby girl was narrated by her mother. Mother complained that patient had non-bloody Diarrhea from 1 month. The frequency happened to be 3 episodes in a day which contained mucous and was graded 3-4. It was partially alleviated with use of over the counter medicine. Diarrhea was associated with non-documented, low-grade fever. Fever was sudden in onset, remained intermittent but had not any appreciated alleviating factors. It was aggravated with time of the day specially at morning and night. Mother denied any history of vomiting, dysuria, fits, loss of consciousness or cyanosis in the child.

Mother had no history of prenatal, Natal or any postnatal complications. Patient was born at term by Simple Vaginal Delivery at hospital. Patient cried soon after birth. After Birth APGAR score was 7 in 1 minute and 8 after 5 minutes. Parents noticed the presence of dysmorphic face. Weight of the patient seemed to be higher and when measured it was noted to be 4.5 kg. Parents considered increased weight to be normal. She developed respiratory infection at the age of 12 months which was treated successfully. She was unable to stand or walk but had achieved other developmental milestones. Patient was third child of consanguineous parents. The eldest child passed away due to the complication of meningitis at age of 1, while the second child is alive and doing fine.

On Examination the baby had a dysmorphic face and had a pale look. Head circumference was measured to be 50 cm. Anterior fontanelle was open and flat which measured as 1.5 cm x 1.5 cm. There was frontal bossing and depressed nasal bridge. On musculoskeletal examination, it showed asymmetry of both upper and lower limb, rocker bottom feet and B/L (Bilateral) pitting edema of lower limbs till the level of thighs [Fig. 1]. There were wrinkles on arms. Abdominal examination showed Harrison sulcus [Fig. 3] she had hepatomegaly with liver span of 8 cm below costal margin but no splenomegaly. Examination of the eyes revealed squinted eyes but did not show any Cherry Red Spot. Cardiac and Chest exams were otherwise normal.

Imaging studies were planned. X-Ray Skeletal survey showed J shaped Sella Turcica and anterior beaking of thoracolumbar vertebrae [Fig. 2]. Liver Trucut Biopsy showed Mild Macrovesicular steatosis. Her Echocardiogram, Ultrasound KUB (Kidney Ureter and Bladder) and Thyroid Profile both were normal.

At the end of history parents were counselled to undergo testing and the scope of prenatal diagnosis was discussed for next pregnancy.

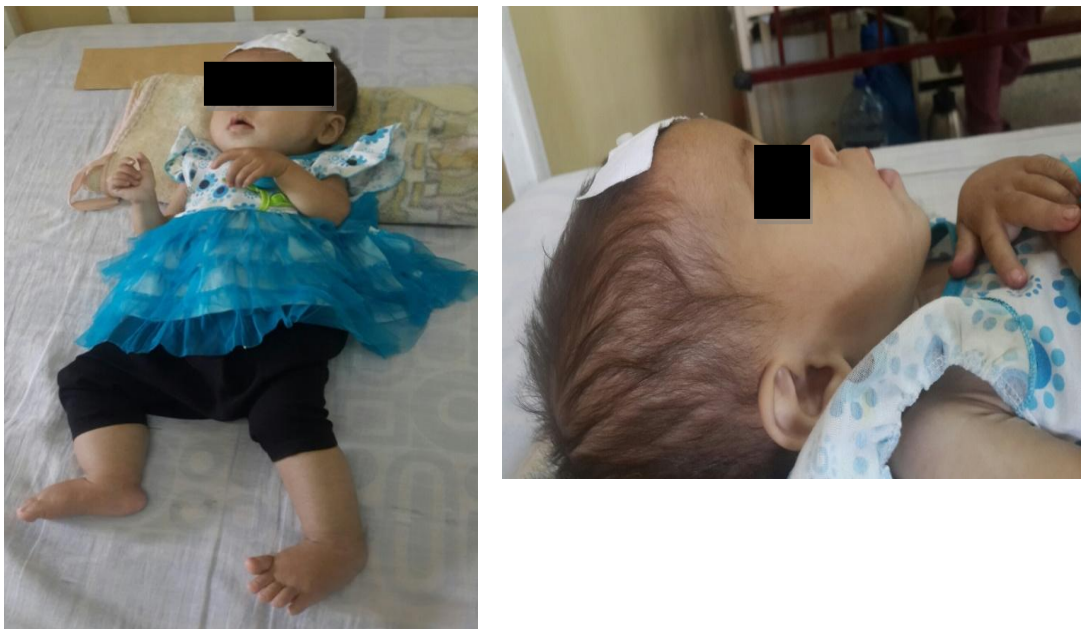

Fig. 1. Shows frontal bossing, depressed nasal bridge. Upper and lower limb asymmetry with B/Lpitting edema of lower limbs, rocker bottom feet and frontal bossing

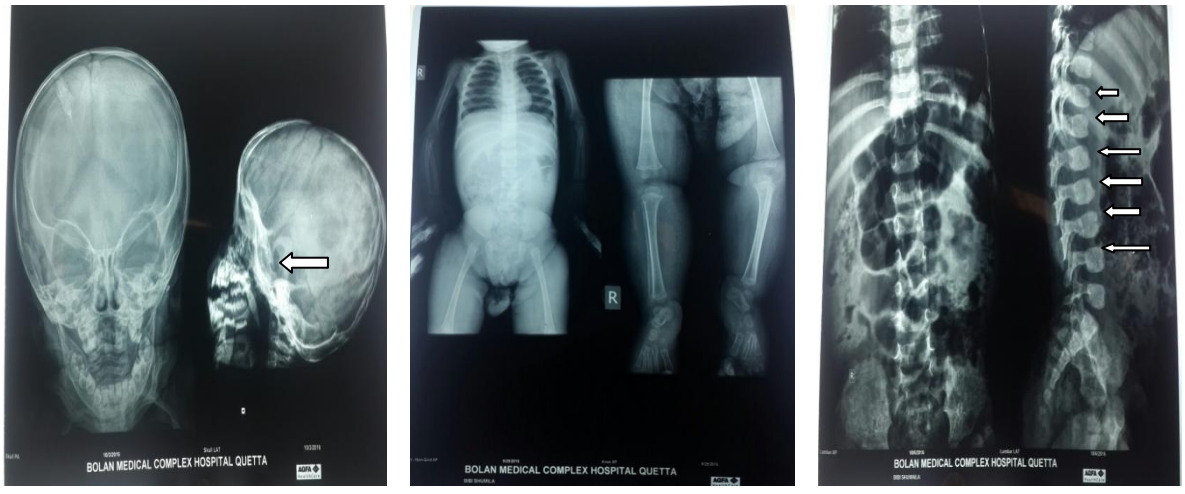

Fig. 2. Skeletal survey, J shaped sellaturcica is prominent, skeletal asymmetry and skeletal survey showing anterior beaking of thoracolumbar vertebrae

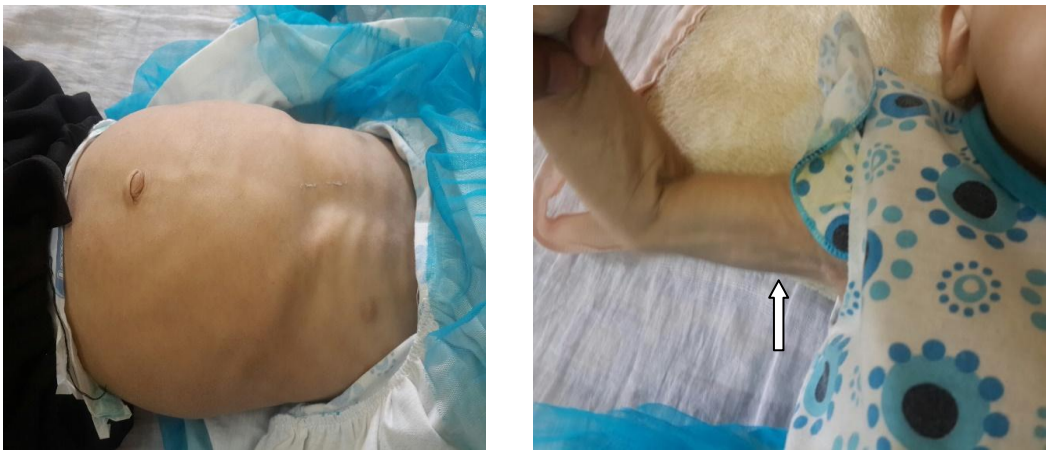

Fig. 3. Showing Harrison's Sulcus and wrinkling of skin

3. DISCUSSION

Gangliosidosis 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 beta-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.

Gangliosidosis is a rare clinical disorder. About 200 cases have been reported to date. The prevalence of GM1 gangliosidosis at birth is estimated to occur in one in 100,000 to 300,000 Childs.

The patient is diagnosed on the basis of 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 [5,6] since birth and 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.

4. CONCLUSION

This case report emphasizes on reporting of a rare, inherited enzyme deficiency disorder. It also focuses on the clinical and radiological aspects that can help in diagnosing Gangliosidosis.

CONSENT

All authors declare that written informed consent was obtained from the guardians of patient for publication of this case report and accompanying images.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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