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CASE REPORT VIII OPEN ACCESS

A rare Case Report of Hurler syndrome with multisystem involvement including glucose intolerance

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Abstract

Background: Mucopolysaccharidosis type I (Hurler syndrome) is a rare autosomal recessive inborn deficiency in the metabolism of glycosaminoglycans (GAGs) heparan sulfate and dermatan sulfate, resulting from deficiency of Alpha-L-iduronidaseenzyme.An interesting case of a 19 year oldmale with a combination of skeletal, neurological, ophthalmologic, and radiological findings with MPS I-(Hurler syndrome) has been presented here in this case report.

Key words: glycosaminoglycans, Hurler syndrome, Mucopolysaccharidosis type I , glucose intolerance

Introduction

Mucopolysaccharidosis are an inborn heterogeneous group of rare metabolic disorders inherent as autosomal recessive traits, due to deficiency or absence of lysosomal hydrolase - iduronidase enzyme activity.[1–3] The defect has been mapped to the chromosome band 4p16.3.[1,2]Hurler syndrome (MPS I - H) is the most common and severe form of mucopolysaccharidosis.[4] Deficiency of this enzyme results into a wide range of phenotypes including Hurler's (severe), Scheie's (mild) and Hurler-Scheie (intermediate) syndromes. [4]Incidence of MPS I-H Hurler syndrome has been reported to be 1:100,000 per child birth, and no predilection for sex and ethnicity has been found.[3,5]

Case Report

A 19-year-oldadolescence male reported to the department of Internal medicine of GMCTH with the chief complaint of Abdominal distension for last 6 month and Shortness of breathing for last 1month,Examination revealed that the boy had stunted growth and a short neck, shape of the head was dolichocephalic with marked macrocephaly, very prominent occipital and frontal bone was present with frontal bossing. Lateral view of the patient head revealed hypertelorism of fronto-occipital area. Coarse facial features like depressed nasal bridge, flaring of both nostrils, prominent supra orbital rim bilaterally, Macroglossia, dental malocclusion with ocular hypertelorism, thick eye lids, full and thick lips were observed. Joint stiffness was also observed. Abdominal examination revealed distended abdomen, herniated umbilicusand hepatosplenomegaly. Respiratory system examination revealed pectus carinatum deformity of chest wall, there was B/L VBS with fine crackles heard over bilateral basal lung field. CVS examination revealed normal S1S2 withholosystolic murmur best heard over left lower sternal border. CNS examination was grossly normal. Intraoral

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examination revealed a large tongue, broad arches with interdental spacing, and moderate anterior open bite with thick gingivae. Prenatal and postnatal history was not available. Family history was not significant. Medical history revealed weak eye sight, recurrent respiratory infections and breathing problems.

On investigation WBC and RBC was within normal limits with thrombocytopenia. RBS was 160mg/dl with FBS 112 mg/dl and PPBS 160mg/dl, c peptide level was normal and HbA1c level was 6.2 %.RFT and LFT were within normal limits. Ophthalmic examination revealed corneal cloudiness with vision(Right Eye 6/36, Left Eye 6/24). Lateral and PA view of the skull radiograph showed features of dysostosis multiplex which included a large skull with thickened and sclerotic calvarium and base of the skull, frontal and occipital hyperostosis, hypertelorism and Sella turcica with J sign.Chest radiograph showed oar-shaped ribs with narrowing at the vertebral ends and broadening at the sternal ends. Hand-wrist radiograph showed bullet-shaped phalanges with proximal pointing of the second to the fifth metacarpals.

Echocardiography was done which revealedModerate TR with PAH with LVEF 40%. Blood investigation for alpha-L-iduronidaseenzyme activity and Urine examination for increased amount of heparan sulfate and dermatan sulfatecould not be done as it was unavailable. Based on clinical and radiological findings the diagnosis was confirmed as Hurler syndrome.

Discussion

Hurler syndrome a rare autosomal recessive disorder which is caused by deficiency of enzyme alpha-L-iduronidasewhich is responsible for the degradation of the glycosaminoglycans (GAGs), and its absence results into accumulation of heparan sulfate and dermatan sulfate in lysosomes of various tissues of the body, resulting in organ damage and causing mental retardation, stunted growth, skeletal malformations, stiff joints, corneal clouding, effect on cardiorespiratory system, thick lips, macroglossia with spaced and hypoplastic teeth, and excessive excretion of the heparan sulfate and dermatan sulfate in the urine,[2,3]. Our patient had most of the characteristic clinically as well as radiologically suggesting the diagnosis of Hurler syndrome, the test could have been further confirmed by blood and urine test which was not available.

Children with Hurler's syndrome appear nearly normal at birth except for the presence of umbilical hernia, and if it is left untreated, a progressive deterioration leading to death due to cardiorespiratory involvement before second decade of life takes place. Hurler syndrome is considered to be incurable; however, as multiple organs are involved a multidisciplinary approach is needed to sustain and improve the quality of life. There are currently two different well-established approaches for the treatment of Hurler syndrome if diagnozed early, and these includes Hematopoietic stem cell transplantation (HSCT) and enzyme replacement therapy with alpha-L iduronidase enzyme to stabilize or reverse many aspects of Hurler syndrome.[1,2,4,5]

As our case of Hurler syndromewas diagnosed with Heart failure with rEF (NYHA grade) and he also had impaired fasting as well as post prandial blood glucose level,we managed him according to recent ESC guidelines including SGLT2 inhibitors.Patient is planned for regular follow up and if needed other hypoglycaemic agents will be added, other treatments are conservative as long as proper treatment will follow up in future.

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It is also important for couples with a family history of Hurler syndrome to undergo genetic counselling and genetic testing when they consider having children.

Conclusion

There exists a need for prevention, early diagnosis and management of Hurler Syndrome through a multidisciplinary approach to improve the quality of life. In context of Nepal where molecular tests are not readily available clinical and radiological features can aid in the proper diagnosis of Hurler syndrome.

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