

Clinical manifestation of Hurler syndrome in a 7 year old child

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Abstract

Mucopolysaccharidosis type I (MPS I H, 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-iduronidase enzyme. This condition is characterized by accumulation of incompletely degraded glycosaminoglycans into various organs of body, which leads to impairment of organs and body functions. Such children appear nearly normal at birth; however, if left untreated, show a progressive mental and physical deterioration leading to death due to cardiorespiratory failure before the second decade of life. Pedodontists have a role for early diagnosis, rendering corrective and preventive treatment to the developing dentition, and referring the patient to the concerned specialities. An interesting case of a seven year old boy with a combination of skeletal, neurological, ophthalmologic, oro-dental and radiological findings of this diverse and devastating clinical entity with MPS I-(Hurler syndrome) has been presented here in this case report.

Keywords: Dentist, glycosaminoglycans, Hurler syndrome, Mucopolysaccharidosis type I, oro-dental features

Introduction

Mucopolysaccharidoses 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 mucopolysaccharidoses.^[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 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 seven year old child reported to the department of

Pedodontics with the chief complaint of dull pain and bilateral facial asymmetry in the lower jaw since past one month. Examination revealed that the child 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 [Figure 1]. Coarse facial features like depressed and broad nasal bridge, flaring of both nostrils, prominent supra orbital rim bilaterally, ptosis of eye balls with ocular hypertelorism, thick eye lids, full and thick lips were observed. Facial asymmetry was more marked on the right side due to diffuse swelling at angle and body of mandible [Figure 2]. Partial trismus was also observed. Child had an enlarged abdomen, herniated umbilicus and massive hepatosplenomegaly [Figure 3]. Both the hands were short and stubby with clawed fingers, which he was unable to straighten [Figure 4]. Intraoral examination revealed a large tongue, broad arches with interdental spacing, and moderate anterior open bite with thick gingivae [Figure 5].

Teeth present were

55 54 53 52 51 61 62 63 64 65
85 84 83 82 41 31 73 74 75

Tooth number 85 and 75 were carious with root stumps. The enamel of the primary teeth was slightly hypoplastic with pitting of enamel. Oral hygiene was moderate. Expansion of the buccal cortical plate at the angle and the body of mandible in the region of the canines, premolars and molars was observed bilaterally; however, was more marked on the right side. Egg shell crackling was present on the right side of the buccal cortical plate with an area of osteolysis of approximately 1 sq cm in diameter [Figure 1, Figure 6, and Figure 7]. The history of the present condition revealed mild pain and swelling in the angle and the body of mandible in the region of the canines, premolars and

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Figure 1: Hypertelorism of fronto-occipital region of head in the patient included in the case report



Figure 2: Coarse facial features and facial asymmetry of the patient included in the case report



Figure 3: Enlarged abdomen and herniated umbilicus of the patient included in the case report



Figure 4: Clawed fingers of both hands of the patient included in the case report



Figure 5: Broad arches, spaced dentition and large tongue of the patient included in the case report



Figure 6: Expansion of buccal cortical plates of the patient included in the case report

molars bilaterally, of over one month duration. Past dental history was not significant. Prenatal and postnatal history

was not available. Family history was noncontributing. Medical history revealed discharge from ears, repeated ear infections, weak eye sight, stiffness of joints and breathing problem with frequent episodes of respiratory infections.

Investigations

Panoramic radiograph revealed a large cyst-like area of bone destruction surrounding unerupted permanent canine, premolar and molar regions and the angle of mandible bilaterally leading to marked displacement of 47 and 37. Very thin lower border of mandible was left on the right side in 47

and 46 region due to bone destruction. Root stumps of 85 and 75 were present. Hypoplastic mandibular condyles with short neck and rami with flattening of superior surface of condyles were observed [Figure 7]. 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 [Figure 8]. Chest radiograph (PA and lateral view) showed oar-shaped ribs with narrowing at the vertebral ends and broadening at the sternal ends [Figure 9]. Hand-wrist radiograph showed bullet-shaped phalanges with proximal pointing of the second to the fifth metacarpals [Figure 10]. Urine examination revealed an increased amount of heparan sulfate and dermatan sulfate. Blood was investigated for alpha-Liduronidase enzyme activity to confirm the diagnosis of MPS I H. The investigation is a Fluometric test and reduced or absence of alpha L-iduronidase activity in blood or its constituents confirms the diagnosis of MPS I H. Dried blood spots on filter paper (DBFP – Whatmans 903 filter paper) technique was used to analyze the activity of alpha L-iduronidase in blood



Figure 7: Panoramic radiograph shows cystic lesion due to bone destruction and hypoplastic condyles of the patient included in the case report

and white blood cells. Blood and white blood cells showed deficiency of alpha – Liduronidase enzyme and their values were $0.57 \mu\text{mol/l}$ blood/h and $0.02 \text{ nmol/mg protein/hr}$ respectively. Based on clinical findings, radiological findings, presence of glycosaminoglycans in urine and deficiency of alpha-Liduronidase enzyme in white blood cells, the diagnosis was confirmed as Hurler syndrome.

Discussion

Enzyme Alpha-L-iduronidase 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] as observed in our case. Radiological finding of hypoplastic condyles^[6] appears to be the cause of partial trismus in this case and



Figure 8: Radiographic examination (PA and Lateral view) of the skull showing a large skull with features of dysostosis multiplex of the patient included in the case report



Figure 9: Oar-shaped ribs with narrowing at the vertebral ends and broadening at the sternal ends of the patient included in the case report

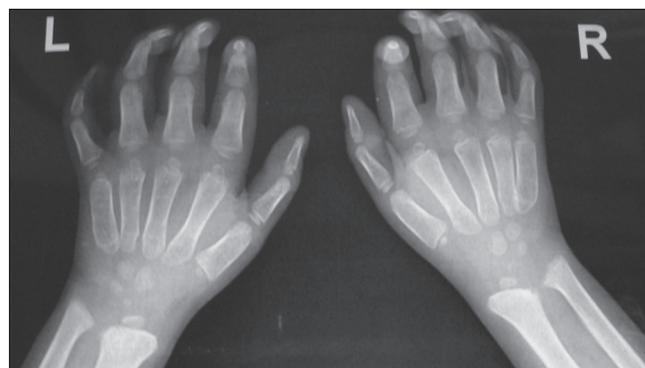


Figure 10: AP radiograph of hand and wrist shows widened metaphyses and diaphyses with bullet-shaped phalanges with proximal pointing of the second to fifth metacarpals of the patient included in the case report

may pose difficulties in dental treatments and delivery of general anesthesia. Wide mandibular and maxillary arches with interdental spacing results from the pressure of the tongue with macroglossia due to deposition of GAGs within tongue^[3,7,8] Dentigerous cyst-like lesions observed in current case resulting from progressive destruction of the bone are common in other cases as well and generally affect the mandible bilaterally.^[3,6-8] The remaining root stumps of 85 75 were extracted and oral hygiene instructions were given. Marsupialization was planned later as the extent of osseous support was greatly compromised especially on the right side. This technique was adopted as it would help to maintain the osseous support and promote eruption of the impacted teeth.^[6,9]

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 diagnosed 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.^[1,2,4,10]

Developing dentition may also get affected due to chemotherapy and radiotherapy before HSCT, and results into delayed dental development, malocclusion, dental anomalies, enamel hypoplasia, disruption of root development and agenesis of some teeth.^[2] Oral healthcare professionals should know the dento-skeletal anomalies in Hurler syndrome, and effects of chemotherapy and radiotherapy on the developing dentition to optimize dental development and oral health. It is also important for couples with a family history of Hurler syndrome to undergo genetic counseling 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. The timing of bone marrow therapy has significant and variable effect on the stages of tooth development with implications for the long-term maintenance of the dentition. Pediatric dentists should be aware of the problems posed by Hurler syndrome on oral health, and should provide an effective oral health care in such children.

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