Physical health perspective and mental subnormality of a child with Hunter's disease

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ABSTRACT

Hunter's disease or mucopolysaccharidosis (MPS II) is a rare X-linked recessive disorder caused by deficiency or malfunctioning of the lysosomal enzyme iduronate-2-sulfatase (IDS), leading to progressive accumulation of glycosaminoglycans in almost all cell types, tissues and organs which result in permanent, progressive cellular damage that affects the appearance, physical abilities, organ and system functioning and, in most cases, mental development. The common clinical presentations include facial dysmorphism, pulmonary dysfunction, hepatosplenomegaly, and skeletal defects including joint stiffness and contractures, cardiomyopathies, and neuropsychiatric manifestations. We present this case of MPS II with clinical presentation including coarse facies, short stature, and mental retardation. The diagnosis was confirmed by demonstrating the deficiency of IDS in plasma. We report this case to highlight the clinical features and to specify the mental and physical health perspective of a child with Hunter's disease. Mental subnormality includes progressive cognitive deterioration that is not manageable with enzyme replacement therapy. Hence, the patient should undergo regular assessment and should be trained accordingly.

Key words: *Enzyme replacement therapy, Hunter's disease, Joint stiffness, Mental subnormality*

Hunter's disease or mucopolysaccharidosis (MPS II) is a hereditary metabolic disorder manifesting almost exclusively in males caused by deficiency of iduronate-2-sulfatase (IDS) enzyme whose gene is mapped to Xq 28 [1]. It was first described by Hunter, in 1917 [2]. The common clinical features include facial dysmorphism, joint stiffness, contractures, hepatosplenomegaly, pulmonary dysfunction, valvular dysfunction, cardiomyopathies, and neurological involvement [3]. Care of MPS II is predominantly palliative, as there is no effective therapy for the same. However, enzyme replacement therapy (ERT) with recombinant human iduronate-2-sulfatase has now been introduced. We report this case to highlight the physical perspective and mental subnormality in a child with Hunter's disease.

CASE REPORT

A 10-year-old boy born to a non-consanguineous marriage presented with complaints of growth retardation and joint stiffness with progressive restriction of movements in hands and legs for past 6 years (Fig. 1). The child was apparently well till 3 years of age when mother noticed abdomen distension which was gradual and associated with intermittent diarrhea and breathing difficulty which used to increase in lying down posture. There was no history of pain in abdomen and bladder alterations. He had a history of recurrent cough, cold, and decreased hearing for past 5 years with associated speech delay. He had delayed milestones and impaired adaptive functioning. There was no history of trauma and any deformity in back/spine. His birth history was unremarkable.

On examination, the child was conscious, afebrile, and well oriented with stable vitals. He was underweight and short stature, had coarse facies, macroglossia, prominent frontal bulge, depressed nasal bridge, short neck, and short fingers with flexion of distal interphalangeal joint (Fig. 2). He had limitation of extension at knee, ankle (Fig. 3), elbow, and wrist joints (Fig. 2). Mild abdomen distension with umbilical herniation (Fig. 1) was noted. Cardiovascular system examination was normal except an ejection systolic murmur in aortic area. His abdomen was soft with firm liver, which was 5 cm below the right costal margin in the midclavicular line having span of 8 cm; spleen was 1 cm below the left costal margin in midclavicular line. Respiratory examination was normal.

His investigations including complete hemogram, serum calcium, phosphorus, liver and renal function tests, thyroid, and lipid profile were normal. X-ray of limbs showed delayed appearance of carpal bones with bullet-shaped phalanges and V-shaped epiphysis of long bones (Fig. 4). Echocardiography revealed mild aortic regurgitation with thickening of valves and

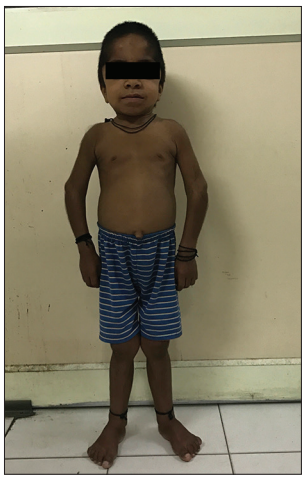

Figure 1: Growth retardation and joint stiffness

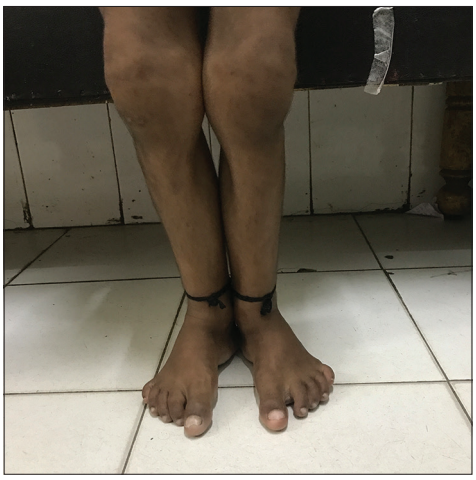

Figure 3: Limitation of extension of knee and ankle joint

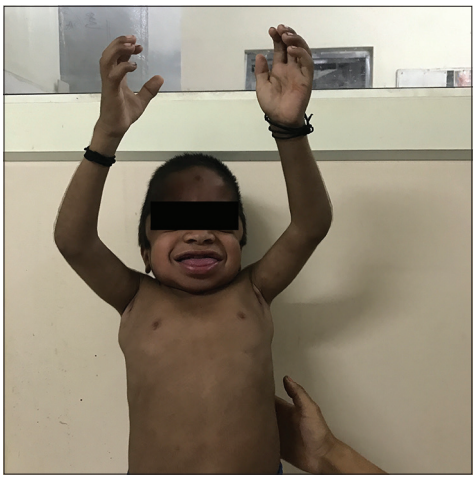

Figure 2: Coarse facies, short neck, broad nose, flexion of distal interphalangeal joint and limitation of extension of elbow joint

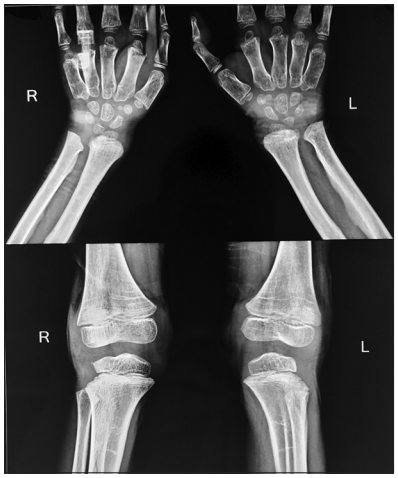

Figure 4: Radiograph of limbs showing bullet shaped phalanges, V shaped epiphysis of long bones and deayed appearance of carpal bones

moderate mitral regurgitation. Head imaging was suggestive of inherited metabolic disorder (Fig. 5). The pure tone audiometry detected moderate sensorineural hearing loss. Ophthalmological examination was normal. Assessment of intellectual functioning revealed an intelligence quotient (IQ) of 50–55.

On the basis of clinical findings and radiological examination, probable diagnosis of MPS was made and we decided to perform enzyme assay which showed deficiency of IDS, thus confirming our diagnosis. Counseling of the parents was done and the management options were explained including bone marrow transplant. Other supportive management such as physiotherapy to mobilize the joint and hearing aid was advised.

DISCUSSION

Hunter's disease is an X-linked recessive condition; it is not expected in females. Despite this, a few cases are reported in girls [4]. Conventionally, MPS II was classified into mild and severe. Wraith *et al.* classified it as severe and attenuated [5]. Our patient was male who appeared normal at birth; this is the classical presentation of Hunter's disease. The severe form manifests at early age between 18 months and 4 years and has life expectancy of 10–15 years while mild form manifests in the second decade with a life expectancy of 30–50 years [1,6,7]. The symptoms in our case manifested in early life, denoting it to be of severe subtype having a poor life expectancy. Patients with severe form have mental retardation with loss of skills, which was seen in our patient and while those of milder form may have mild mental retardation, but their intelligence usually is normal. Death in both the forms usually occurs due to cardiac failure or obstructive airway disease.

The patient of MPS II is short with coarse facial features. Thickening of the alae nasi, lips, ear lobules, and tongue becomes progressively more obvious. Significant arthropathy leads to joint contractures and skeletal defects. A combination of hepatomegaly and lax abdominal muscles leads to abdominal distension. Other features include pulmonary dysfunction, cardiomyopathies, and neuropsychiatric manifestations. Facial and body hypertrichosis are often seen and the scalp hair becomes coarse [8]. Much of the physical features mentioned above were evident in our patient in the form of growth retardation with short stature, coarse facies, macroglossia, prominent frontal bulge, depressed nasal bridge,

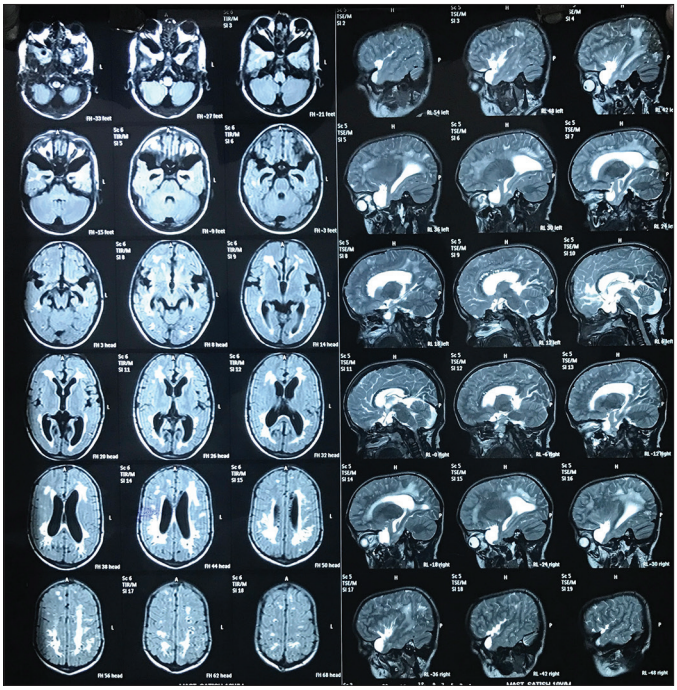

Figure 5: Neuroimaging of head showing paucity of white matter with prominence of ventricle and hypodensities

short neck, short broad and stubby fingers with joint contractures, hepatosplenomegaly with umbilical hernia, cardiac defect with mental retardation, speech abnormality, and hearing deficit.

MPS II patients are normal at birth and early developmental milestones may also be normal, even in the presence of significant somatic disease. Our case had normal birth history, but manifestations occurred during early childhood with speech abnormality, hearing deficit, and intellectual disability, radioimaging of head was remarkable for paucity of white matter with prominence of ventricles with hypodensities (Fig. 5). Communicating hydrocephalus, common in MPS I, is rare in MPS II.

The prevalence and severity of cardiovascular disease in MPS is 60–100% [9]. It includes incompetence of the valves, mitral valve prolapse, ischemic heart disease, and cardiomegaly resulting in heart failure [1,6,7]. Orthopedic complications because of direct bone involvement and severe arthropathy can lead to significant disability. The role of physical therapy in MPS II is not well studied, but range of motion exercises offer some benefit in preserving joint function and should be started at an early age. If significant joint movement restriction has already occurred, range of motion exercises may slow further progression [10]. As seen in our patient, chronic recurrent rhinitis and persistent copious nasal discharge are common in these patients. In severe MPS II, rhinorrhea tends to improve with age, but upper airway obstruction and sleep apnea become more troublesome as the age progresses. Sleep studies should form part of the regular assessment plan and significant episodes of hypoxia should be managed by continuous or bilevel positive airway pressure devices. Early placement of ventilating tubes is recommended in severe forms [10].

As in our patient, MPS II cases are prone to bouts of watery diarrhea, which are not associated with malabsorption. Diarrhea can be controlled by diet and the use of antimotility drugs [10]. Rectal biopsies have demonstrated storage within gut neural cells [11]. With age, loss of muscle strength and physical inactivity lead to constipation.

The screening test is analysis of glycosaminoglycans. The presence of excess heparan and dermatan sulfates in the urine is suggestive of MPS I, II, and VII. Confirmatory diagnosis is made by enzyme assay, using substrates specific for iduronate-2-sulfatase. Absent or low iduronate-2-sulfatase activity in males is diagnostic of Hunter syndrome [1].

Approved treatment is ERT using a recombinant human iduronate-2-sulfatase produced in the human cell line [12], and the definitive treatments are bone marrow transplantation and umbilical cord blood transplantation. However, these definitive treatments are not readily available in most of the developing countries, and supportive management is mainstay of therapy to improve the quality of life such as physiotherapy to mobilize the joints, nutritional management, and treatment of infections, blood transfusion, and management of cardiac and respiratory complications [13].

A comprehensive initial assessment of patient at diagnosis should, therefore, be undertaken and should be followed regularly. As far as physical perspective is concerned, supportive management and the anticipation of possible complications can greatly improve the quality of life. Mental subnormality is a very common feature in Hunter syndrome. Progressive cognitive decline is not amenable to the ERT due to the non-penetrance of blood–brain barrier to the large protein molecules. Thus, even on training, a good quality of life might not be achieved. The families of this patient need considerable motivation, psychological, and social support. They should be offered genetic counseling and contact with other affected families, patients, and support groups. Hence, it is the role of clinician to provide a good quality of life, to counsel them for regular IQ assessment, and to make them aware about the future prospects of these patients.

CONCLUSION

Hunter's disease is a multisystemic disease with constellation of physical findings. Its definitive treatment is not available but multidisciplinary and a holistic approach, especially for those who have severe neurological involvement can improve the quality of life. Central nervous system disease remains a major challenge, and an innovative approach to treatment with regular evaluation of IQ is needed to assess the comorbidities. The child with MPS II should be provided a stimulating environment to encourage as much learning as possible during the early stages, as some skills may be retained during the later period of general deterioration.

REFERENCES

1. Kliegman RM, Behrman RE, Jenson HB, Stanton FB. Nelson Textbook of Pediatrics. 20th ed. Philadelphia, PA: Saunders; 2016. p. 737-41.
2. Hunter C. A rare disease in two brothers. Proc R Soc Med 1917;10:104-6.
3. Shah SG, Mahal T, Sharma S. Atypical clinical presentation of mucopolysaccharidosis Type II (Hunter syndrome): A case report. J Med

Case Rep 2010;4:154.
4. Tuschl K, Gal A, Paschke E, Kircher S, Bodamer OA. Mucopolysaccharidosis Type II in females: Case report and review of literature. Pediatr Neurol 2005;32:270-2.
5. Wraith JE, Beck M, Giugliani R, Clarke J, Martin R, Muenzer J. Initial report from the hunter outcome survey. Genet Med 2008;10:e508-16.
6. Martin R, Beck M, Eng C, Giugliani R, Harmatz P, Mufioz V, *et al*. Recognition and diagnosis of mucopolysaccharidosis II (hunter syndrome). Pediatrics 2008;121:377-86.
7. Tylki-Szymańska A. Mucopolysaccharidosis type II, hunter's syndrome. Pediatr Endocrinol Rev 2014;12 Suppl 1:107-13.
8. Thappa DM, Singh A, Jaisankar TJ, Rao R, Ratnakar C. Pebbling of the skin: A marker of hunter's syndrome. Pediatr Dermatol 1998;15:e370-3.
9. Fesslova V, Corti P, Sersale G, Rovelli A, Russo P, Mannarino S, *et al*. The natural course and the impact of therapies of cardiac involvement in the mucopolysaccharidoses. Cardiol Young 2009;19:e170-8.
10. Wraith JE, Scarpa M, Beck M, Bodamer OA, De Meirleir L, Guffon N, *et al*. Mucopolysaccharidosis Type II (Hunter syndrome): A clinical review and recommendations for treatment in the era of enzyme replacement therapy. Eur J Pediatr 2008;167:267-77.
11. Elsner B. Ultrastructure of the rectal wall in hunter's syndrome. Gastroenterology 1970;58:856-62.
12. Muenzer J, Bodamer O, Burton B, Clarke L, Frenking GS, Giugliani R, *et al*. The role of enzyme replacement therapy in severe hunter syndrome-an expert panel consensus. Eur J Pediatr 2012;171:181-8.
13. Muenzer J, Beck M, Eng CM, Escolar ML, Giugliani R, Guffon NH, *et al.* Multidisciplinary management of hunter syndrome. Pediatrics 2009;124:e1228-39.

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