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CASE REPORT

AN APPROACH TO RESOLVE BILATERAL GENU VALGUM DEFORMITY AMONGST VARIOUS SKELETAL COMPLICATIONS IN A MUCOPOLYSACCHARIDOSIS PATIENT

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ABSTRACT: Mucopolysaccharidosis (MPS) VI is an inheritable lysosomal storage disorder that is often associated with orthopedic problems such as hip dysplasia, spinal deformities, and deformities in the skull, knees and hands. We describe the progression and management of three MPS VI cases with focus on their orthopedic problems.

KEYWORDS: Bone, mucopolysaccharidosis VI, orthopedics, skeleton.

INTRODUCTION: Mucopolysaccharidosis VI (Maroteaux-Lamy syndrome, MPS VI) is a lysosomal storage disorder caused by mutations in the N-acetylgalactosamine-4-sulfatase (Arylsulfatase B, ARSB) gene, resulting in the accumulation of glycosaminoglycans (GAGs) in cells and tissues all over the body.[1] Disease onset and rate of progression are variable, producing a spectrum of systemic clinical manifestations with significant functional impairment.[2] The skeleton is generally one of the most severely affected organs, causing severe morbidity. MPS VI patients typically show dysostosis multiplex, a specific radiologic expression involving the skull, thorax, pelvis, hands and spine.[1,3]

Complications that result from skeletal disease include disproportionate short stature, kyphoscoliosis, joint abnormalities (Stiffness and flexion contractures of elbows, shoulders, hips, knees, and fingers), spinal cord or nerve root compression.[4,3]

We describe one Indian MPS VI patient, focusing on the most important skeletal problems, in order to illustrate the wide spectrum of possible manifestations and to discuss the individual management of the case. We could only provide the orthopaedic management, unfortunately not the enzyme replacement therapy (ERT) with recombinant human gal-sulfase, which has recently become available for MPS VI[4] since the parents could not afford it.

CASE REPORT: This 10 year-old girl is the only child of healthy non-consanguineous parents with irrelevant family history. At 1 year of her age, the parents noticed a lumbar gibbus deformity and later, their concerns increased as she did not walk independently at 16 months of age. She was sent to the Paediatric Medicine Unit with the clinical suspicion of MPS, based on radiographic abnormalities and coarse facies. A diagnosis of MPS was made at the age of 6 years. Multi-organ evaluation disclosed corneal opacity without glaucoma, hepatosplenomegaly and cardiac valvular dysplasia, mainly at the mitral level, controlled with lisinopril and furosemide. The girl had also developed macrocephaly and short stature. Her height is presently below the 5th percentile. Radiological assessments revealed typical dysostosis multiplex. In the spine, she has mild cervical bone abnormalities and anterior hypoplasia of the L1–L2 vertebral bodies. Bracing was used between 5 and 7 years. Her thoraco-lumbar kyphosis has stabilized gradually without significant scoliosis with age. She has mild contractures at the shoulders, wrists, hands, elbows, ankles and knees. This

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patient's main skeletal problems are the degeneration and contracture of the hips and the progressive, symmetric genu valgum (knock knees), that have affected the way she walked. The patient underwent bilateral lower femoral and proximal tibial medial hemiepiphysiodesis. The surgical procedure was uneventful and walking functionality recovered. However, we could not provide enzyme replacement therapy (ERT) with recombinant human gal-sulfase, which has recently become available for MPS VI.[4]

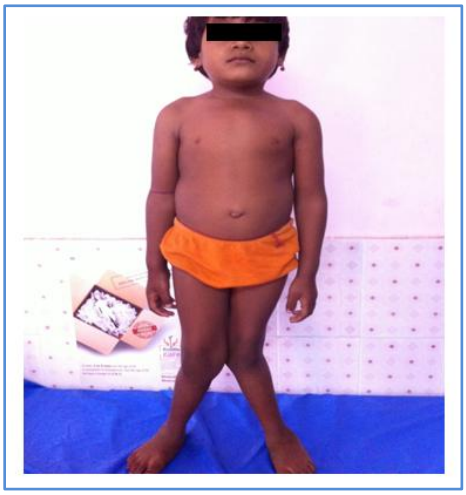
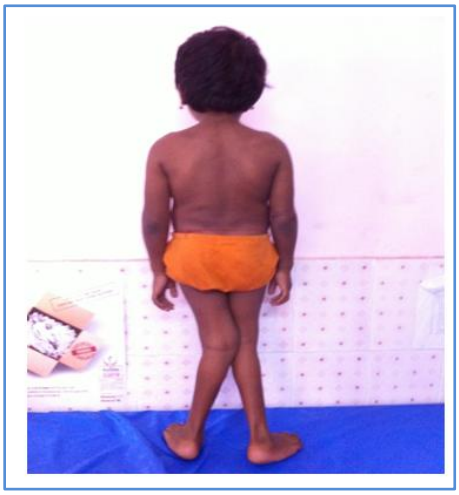


Figure 1



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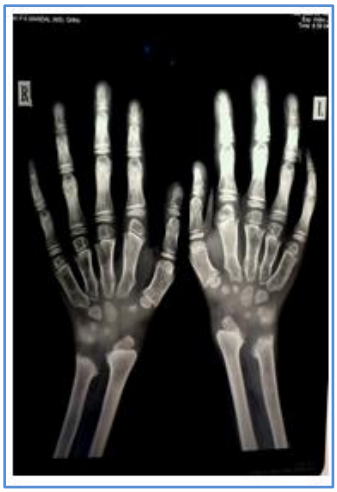

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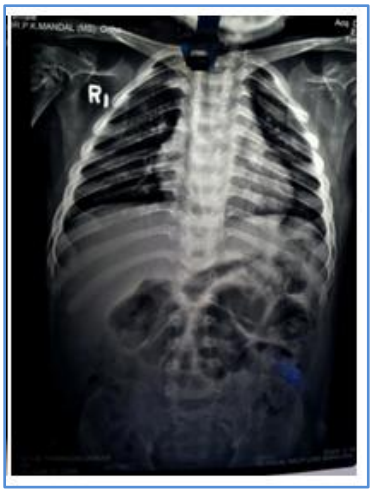

Figure 5

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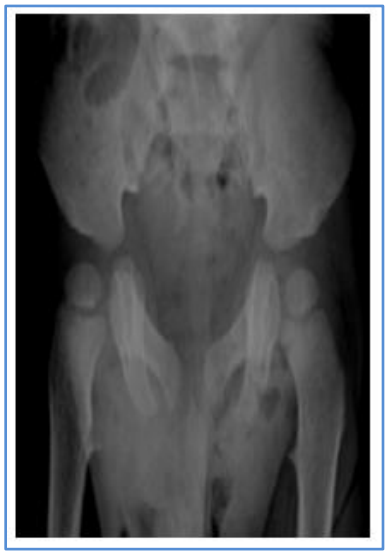

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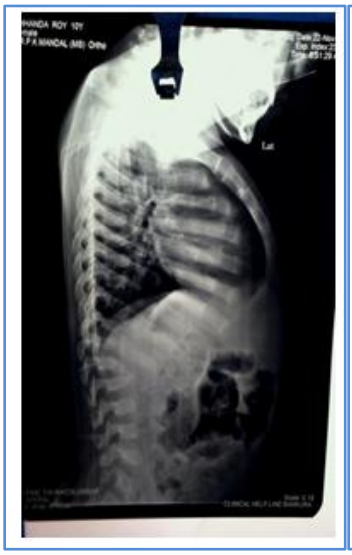

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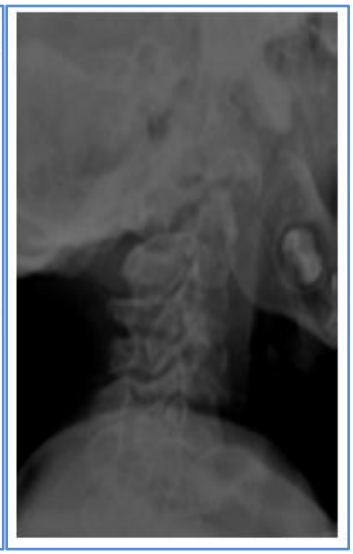

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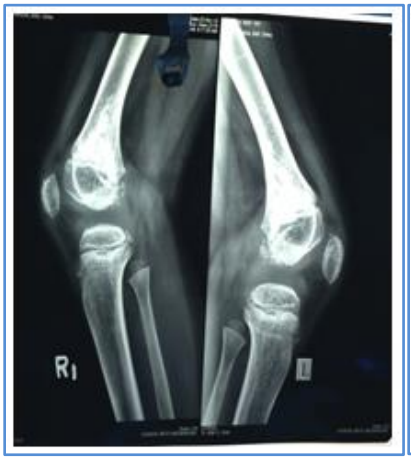

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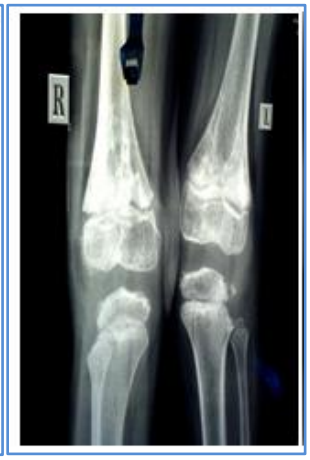

Figure 10

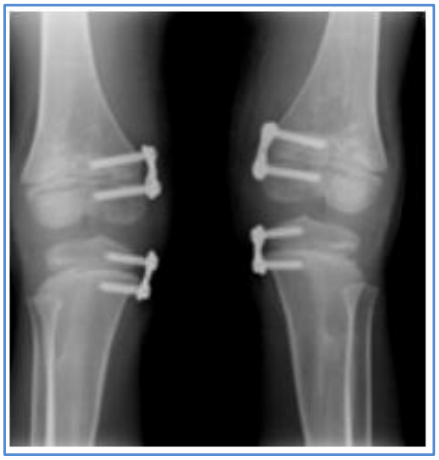

Figure 11

BIOCHEMISTRY

INVESTIGATION	RESULT		NORMAL VALUE
PLASMA GLUCOSE (FASTING)	80.11	mg/dL.	[70 - 110 mg/dL.
SERUM CALCIUM	7.80	mg/dL.	[8.6 - 10.3 mg/dL.
PHOSPHORUS (PO4)	4.50	mg/dl	Adult 2.5 - 5.0 mg Children 4.0 - 6.50 m

** End of Report. **

Table 1

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DISCUSSION: The central focus of this case is the surgical care of the genu valgum deformity. Medial hemiepiphysiodesis has been shown to be quite successful in children with Hurler syndrome (MPS IH) after hematopoietic stem cell transplant.[5] The implants shown here utilize a tension band plate and screws and represent a fairly new device in the care of angular deformities in children.[6] "Guided growth" or "growth modulation" as originally described by Walter Blount in the 1940's, utilized staples to this end.[7] Failure of staples was common in MPS (As in other conditions), due to back out of the staples, often requiring revision surgery. The tension band plates offer hope for fewer implant related complications, and have had a very good track record in other skeletal dysplasias. Because this technique relies on growth to be effective, patients must have at minimum one year of growth remaining in order to be considered candidates for this procedure. Some orthopedists, unfamiliar with MPS disorders, may wait too long for medial hemi-epiphysiodesis, assuming that MPS patients mature at the same age as uninvolved patients. However, because growth may terminate at an early age, surgical intervention that relies on continued growth should not be delayed.

The above-described case clearly illustrates that MPS VI can lead to significant skeletal deformities that require careful surveillance. As a result of bone and joint abnormalities, MPS VI patients often develop hip dysplasia, genu valgum, growth retardation, and gross abnormalities of the spine such as kyphosis or scoliosis.[2]

Appropriate treatment of orthopedic problems can decrease the patients' morbidity and improve their quality of life considerably. Several complications, such as spinal cord or carpal tunnel compression, which require awareness and timely intervention, may develop secondary to bone disease. Clinical examination and imaging techniques should be used on a regular basis to follow these patients and detect complications of skeletal disease as early as possible. In fact, carpal tunnel compression of the median nerve and triggering of the flexor tendons is a situation that is often overlooked due to unusual absence of typical symptom of hand numbness or tingling and the difficulty in obtaining a detailed neurological exam including nerve conduction studies in the patients' age group. If treatment for triggering or median nerve compression is delayed, permanent damage to the median nerve and fixed contractures of the distal interphalangeal joints may occur. Besides carpal tunnel syndrome, cervical spine complications are an important issue. In addition to the possibility of cervical instability due to odontoid hypoplasia, GAG storage, inflammation, and fibrosis in the posterior longitudinal ligament and in dura (pachymeningitis cervicali) can cause compression of the spinal cord, particularly at the C1–C2 level. Ultimately, patients can become wheelchair-bound.

Neurological assessment and a sagittal magnetic resonance imaging of the spine can monitor for this complication and suggest intervention before cervical myelopathy occurs. All three patients are currently being treated with ERT (galsulfase). Galsulfase has been shown to increase endurance in a 12-min walk test and 3-min stair climb test in phase 2 and 3 clinical trials.[4,8,9] Secondary analyses of the galsulfase clinical studies and case reports have suggested that ERT can improve joint mobility.[4,10,11] As bone deformities are irreversible and often start to develop very early in life in MPS VI patients, early onset of ERT might be indicated in order to delay the development of severe skeletal dysplasia. Studies in cats have shown that ERT has a positive impact on bone development, particularly when started early in life. So far, no studies on the impact of ERT on bone development in humans have been completed. Additional data are expected from several studies in sibling pairs and a clinical study in infants that are currently ongoing.

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CONCLUSIONS: Orthopedic problems are common in MPS VI patients and can be extremely disabling. Early detection and management of these problems are warranted and can significantly improve the quality of life of these patients.

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REFERENCES:

1. E. F. Neufeld and J. Muenzer, The mucopolysaccharidoses, in: The Metabolic and Molecular Bases of Inherited Disease, C.R. Scriver, A. L. Beaudet, W.S. Sly and D. Valle, eds, McGraw- Hill Medical Publishing Division, New York, 2001, pp. 3421–3452.
2. R. Giugliani, P. Harmatz and J.E. Wraith, Management guidelines for mucopolysaccharidosis VI, Pediatrics 120(2007), 405–418.
3. R. Lachman, K.W. Martin, S. Castro, M.A. Basto, A. Adams and E. Le˜ao Teles, Radiologic and neuroradiologic findings in the mucopolysaccharidoses, Journal of Pediatric Rehabilitation Medicine, Submitted (reference to another paper of these proceedings).
4. P. Harmatz, C.B. Whitley, L. Waber, R. Pais, R. Steiner, B. Plecko, P. Kaplan, J. Simon, E. Butensky and J. J. Hopwood, Enzyme replacement therapy in mucopolysaccharidosis VI (Maroteaux-Lamy syndrome), J Pediatr 144(2004), 574–580.
5. E. Odunusi, C. Peters, W. Krivit and J. Ogilvie, Genu valgum deformity in Hurler syndrome after hematopoietic stem cell transplantation: correction by surgical intervention, J PediatrOrthop 19(1999), 270–274.
6. P.M. Stevens, Guided growth for angular correction: a preliminary series using a tension band plate, J Pediatr Orthop 27 (2007), 253–259.12D. Auclair, J.J. Hopwood, D.A. Brooks, J.F. Lemontt and A.C. Crawley, Replacement therapy in Mucopolysaccharidosis typeVI: advantages of early onset of therapy, Mol Genet Metab 78(2003), 163–174.
7. W.P. Blount and G.R. Clarke, Control of bone growth by epiphyseal stapling: a preliminary report, J Bone Joint Surg Am31A (1949), 464–478.
8. P. Harmatz, C.B. Whitley, L. Waber, R. Pais, R. Steiner, B. Plecko, P. Kaplan, J. Simon, J. Waterson and J.J. Hopwood,A phase I/II study of enzyme replacement therapy (ERT) for mucoploysaccharidosis VI (MPS VI; maroteaux-lamy syndrome): 48 week progress report, Am J Hum Genet 71(2002), 582.
9. P. Harmatz, R. Giugliani, I. Schwartz, N. Guffon, E.L. Teles, M.C. S´a Miranda, J.E. Wraith, M. Beck, L. Arash, M. Scarpa,Z.F. Yu, J.Wittes, K.I. Berger, M.S. Newman and A.M. Lowe, Enzyme replacement therapy for mucopolysaccharidosis VI: a phase 3, randomized, double-blind, placebo-controlled, multinational study of recombinant human N-acetylgalactosamine 4-sulfatase (recombinant human arylsulfataseBor rhASB) and follow-on, open-label extension study, J Pediatr 148(2006), 533–539.
10. P.J. Belmont, Jr. and D.W. Polly, Jr., Early diagnosis of Hurler's syndrome with the aid of the identification of the characteristicgibbus deformity, Mil Med 163 (1998), 711–714.
11. M. Scarpa, R. Barone, A. Fiumara, L. Astarita, G. Parenti, A. Rampazzo, S. Sala, G. Sorge and R. Parini, MucopolysaccharidosisVI: the Italian experience, Eur J Pediatr 168(2009), 1203–1206.

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