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Short Communication

Awareness of attenuated mucopolysaccharidoses in a pediatric orthopedic clinic

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1. Introduction

Mucopolysaccharidosis (MPS) I is an autosomal recessive lysosomal storage disorder caused by deficient activity of the enzyme α-L-iduronidase, leading to widespread accumulation of the glycosaminoglycans (GAGs) dermatan sulfate and heparan sulfate in all tissues and organs. The clinical presentations of MPS I include learning difficulties (severe form), corneal clouding, coarse facial features, recurrent ear, nose, and throat infections, airway obstruction, valvular heart disease, umbilical and inguinal hernias, joint stiffness and skeletal deformities. This genetic disorder has a wide spectrum of clinical severity and is classified into three syndromes: Hurler syndrome (severe), Hurler-Scheie syndrome (intermediate), and Scheie syndrome (attenuated).[1] The incidence of MPS I differs among different populations, ranging from 1 in 60,000 live births in Northern Ireland to 1 in 900,000 live births in Taiwan.[2]

2. Case report

A 7-month-old girl was referred to our genetic clinic by a pediatric orthopedic surgeon due to mildly stiff joints and a somewhat coarse face. The postnatal course was smooth except for a limited range of motion of bilateral hips noted by the pediatrician at 5 months of age. An X-ray of her pelvis showed lower than average bilateral greater trochanters and deformed lesser trochanters. Bilateral

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developmental dislocation of the hips was suspected at that time. A dysmorphologic evaluation by a geneticist revealed coarse and curly hair, an upturned nose, somewhat depressed nasal bridge, mildly coarse face, some faint Mongolian spots over the buttocks, prominent lower costal margins, mild lumbar gibbus of the spine, mild limitation of extension of bilateral elbow joints, and mildly prominent joints (Fig. S1). She had normal neurodevelopmental milestones. These findings suggested MPS or a related disorder. The urinary GAG level was elevated at 159.5 mg/mmol creatinine (reference range 15.3 ± 13), and qualitative analysis of urinary GAG by two-dimensional electrophoresis revealed excess dermatan sulfate. The levels of urinary dermatan sulfate and heparan sulfate determined using liquid chromatography/tandem mass spectrometry were 174 μg/mL (reference range <0.80 μg/mL) and 3.9 μg/mL (reference range <0.41 μg/mL), respectively.[3] Blood leukocyte α-L-iduronidase activity was markedly reduced at 0.39 μmol/mg protein/h (reference range 6.8—37), confirming the diagnosis of MPS I (Hurler-Scheie syndrome). The patient was found to be a compound heterozygote for a deletion and an insertion mutation in the *IDUA* gene: c.1192_1194delGAG, p.E398del from a paternal allele, and c.1634delA, c.1634_1635insGGG, p.E545Gfs*16 from a maternal allele (Fig. S2). After she had been diagnosed with MPS I, she began enzyme replacement therapy (ERT) with laronidase from 13 months of age. After 2.8 years of ERT, her urinary GAG excretion showed an 83% reduction.

3. Discussion

We report a 7-month-old girl who was referred to our genetic clinic by a pediatric orthopedic surgeon due to mildly stiff joints and a somewhat coarse face, and was subsequently diagnosed with MPS I. MPS I is a progressive and multisystemic disorder with a wide spectrum of clinical severity. The reported clinical manifestations and related investigations of MPS I in Taiwanese patients include airway changes, pulmonary function impairment, hearing loss assessments, cardiovascular changes, polysomnographic studies, bone mineral density assessments, diagnostic screening methods, ERT effects, and newborn screening. In 2003, ERT with laronidase (Aldurazyme®; Genzyme, a Sanofi company, Cambridge, MA, USA), a recombinant human form of α-L-iduronidase, was shown to improve endurance, joint mobility, and lung function, and potentially be beneficial for patients with MPS I, especially if started early in the course of the disease.[4,5]

Since MPS I is a rare, progressive and multisystemic disease with insidious initial manifestations, making an early diagnosis can be a challenge for the first-line medical practitioner.[6] Patients with attenuated MPS I typically first present with joint stiffness or hernia. Tracing back the medical history, these children are usually brought to various medical specialists due to their various presentations before the confirmative diagnosis of MPS I. A mean delay from the time of initial symptom presentation to diagnosis of 2.7 years has been reported for patients with attenuated disease, with a mean of five physicians being consulted before the correct diagnosis is made.[7] Identification of the early signs and symptoms could help make an early diagnosis and provide timely appropriate treatment for this disease, which may then lead to a better clinical outcome.

Conflict of interest statement

The authors declare that they have no competing interests.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at doi:10.1016/j.pedneo.2018.01.004

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