A case of multiple sulfatase deficiency

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Introduction

Multiple sulfatase deficiency (MSD) is an extremely rare autosomal recessive lysosomal storage disorder arising from mutations in the sulfatase-modifying factor-1 (*SUMF1*) gene located on chromosome 3p26[1]. This gene encodes the formylglycine-generating enzyme (FGE)[1]. There are seventeen sulfatases found in humans; sulfatases are a group of hydrolytic enzymes that degrade sulfated substrates[1,2]. FGE activates all sulfatases. *SUMF1* mutations impair FGE function, decreasing all sulfatase activities to variable degrees[3,4]. The clinical picture of this disease combines features of mucopolysaccharidosis (MPS), metachromatic leucodystrophy, X-linked ichthyosis and chondrodysplasia puncta in a variable spectrum[1,5]. Neonatal, late infantile and juvenile forms of MSD have been identified according to the age of onset and severity[1,2,5]. We report a girl who was initially thought to have MPS but which was later found to be MSD, a rare disease with no publications as yet in Sri Lanka.

Case report

A three-year-old dysmorphic child, born at term to healthy non-consanguineous parents, presented with the first episode of febrile status epilepticus. She has a 6-year-old female sibling who is healthy and developmentally normal. She had no seizures in the past. Milestone achievement was delayed initially, with progressive loss of all skills over the previous 5 months. Birth history was uncomplicated apart from mild jaundice. She had a history of recurrent respiratory symptoms. She also had difficulty in swallowing with gastro-oesophageal reflux.

Examination revealed a bed-bound child with weight and length well below -3SD, occipito-frontal circumference between median to -1SD and weight for length below -3SD. Coarse facial features, thickened eyebrows, flat nasal bridge, carious teeth, hypertrichosis, ichthyosis, small hands, dystonic posturing and pectus carinatum were noted (Figure 1).

Figure 1: Photograph demonstrating: A - Pectus carinatum, talipes equinovarus deformity and ichthyosis in lower limbs and B- Hypertrichosis

Cardiovascular and respiratory system examinations were unremarkable. A 3 cm hepatomegaly was found on examination of the abdomen. There were static contractures in the ankles with bilateral talipes equinovarus deformities and dynamic contractures in bilateral hips. Tone was high with exaggerated reflexes. Haematological and biochemical investigations were within the normal ranges. 2D echocardiogram was unremarkable. Ocular examination was normal with no evidence of corneal clouding. Skeletal survey showed features of dysostosis multiplex (Figure 2).

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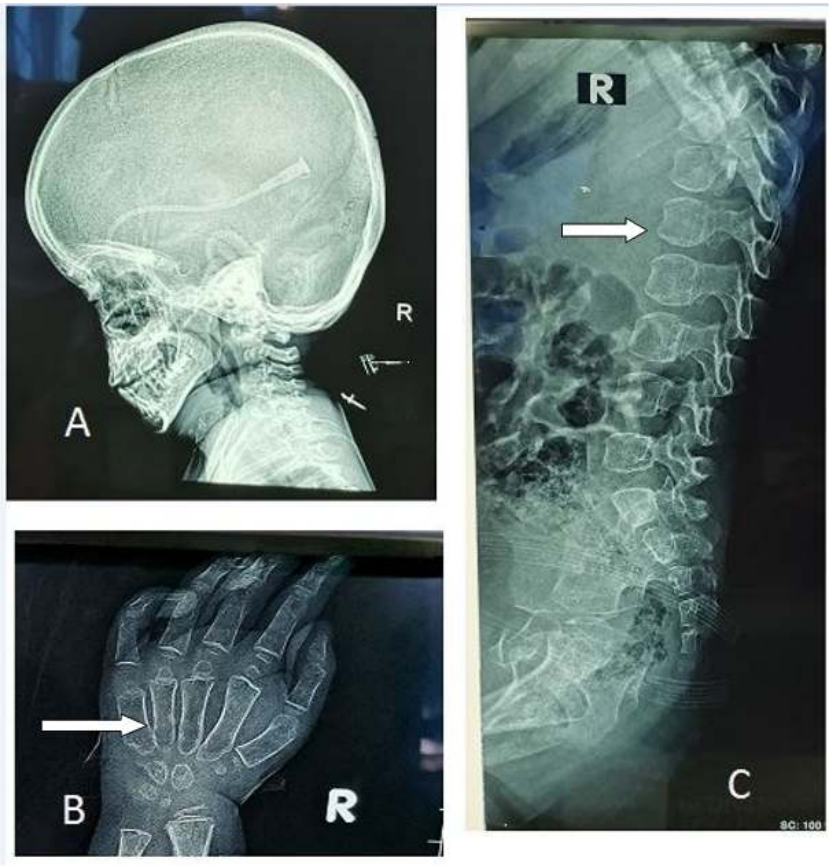

Figure 2: ***Dysostosis multiplex on x-ray: A- Macrocephaly. B- Proximal pointing of metacarpal bones (white arrow). C- Mild anterior-inferior vertebral body beaking (white arrow)***

Electroencephalogram showed immature sleep background. Magnetic resonance imaging (MRI) of the brain revealed ventriculomegaly, cerebral atrophy and bilateral white matter changes (Figure 3). Enzyme analysis revealed deficiency of three sulfatases (Table 1).

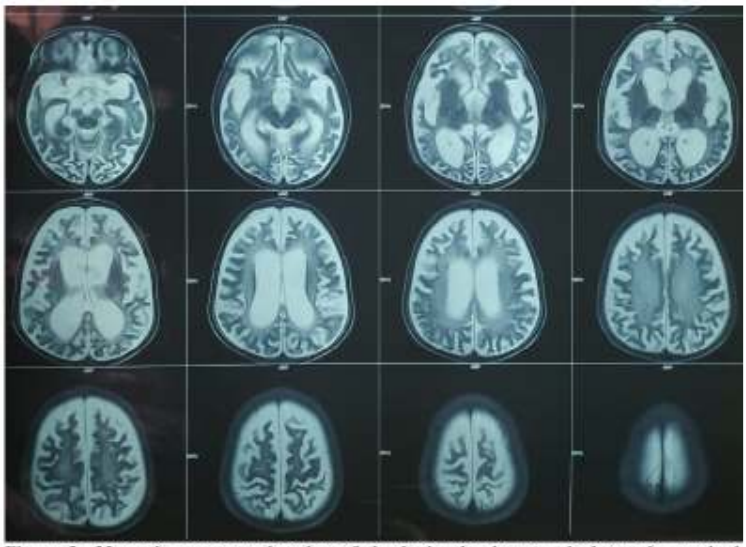

Figure 3: ***Magnetic resonance imaging of the brain showing ventriculomegaly, cerebral atrophy and hyper-intensity in bilateral periventricular, deep and subcortical white matter.***

Table 1 : *Results of enzyme analysis*

Enzyme	Value (μmol/L/hour)	Reference range
Arylsulfatase B	0.9	≥ 8.8
Galactosamine-6-sulfate sulfatase	1.6	≥ 5.3
Idorunate-2-sulfatase	< 0.8	≥5.6

Genetic analysis showed homozygous missense mutation c.1033C>T p.(Ar345Cys) on *SUMF1* gene, confirming the diagnosis of autosomal recessive MSD. We were unable to do family screening

Discussion

Many of the features in this patient were in favour of MPS. The striking ichthyosis led us to explore other differential diagnoses. Developmental regression together with ichthyosis is a significant clue to diagnose MSD[5]. Other features common to all subtypes of MSD are hepatosplenomegaly, growth restriction, epilepsy, joint stiffness with contractures, ichthyosis, hypertrichosis, dental abnormalities, dysostosis multiplex and MRI findings of ventricular enlargement with periventricular white matter changes[2]. There can be an overlap of symptoms across the different subtypes of MSD making it difficult to fit a child into one category[6]. This patient most likely has the late infantile form as she developed symptoms by one year of age and had lost most of the achieved skills by three years. There are 4 reported cases of MSD with the same mutation as this patient and having similar features[3,5,7]. Interestingly, none were from Southeast Asia, making this case report the first from this region.

There is no known treatment for MSD as yet[2,6,8]. A multidisciplinary team care is the management option available currently[8]. As this patient presented with convulsions, we started her on levetiracetam in consultation with the paediatric neurologist. Nasogastric tube was inserted to assist feeding. Neuro-rehabilitation was arranged and long term follow up was formalised to address the associated complications.

In conclusion, this case report presents a three-year-old girl with late infantile MSD. It highlights that along with the well-known storage disorders, the possibility of lesser-known diseases such as MSD should be suspected in children presenting with developmental delay, bone abnormalities and ichthyosis.

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