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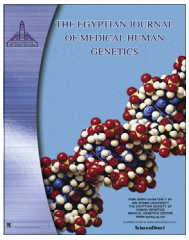

CASE REPORT

Alpha-fucosidosis – Two brothers presenting with dysostosis multiplex

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Abstract α-Fucosidosis is a rare inherited neuro-degenerative disorder causing progressive neurological deterioration leading to early death. Definitive diagnosis requires α-fucosidase enzyme assay or FUCA1 gene testing, which being expensive limits the definitive diagnosis in resource limited countries. We present two siblings with classic symptoms, radiological and MRI brain findings suggestive of α-fucosidosis and a clinical approach to reach to the diagnosis.

1. Introduction

α-Fucosidosis (OMIM # 230000) is an autosomal recessive lysosomal storage disorder caused by the deficiency of fucosidase enzyme due to mutations in *FUCA1* gene [1]. It was first reported in 1966 [2] and since then less than 120 cases have been reported [3]. Patients present with broad clinical spectrum of progressive psychomotor regression, coarse facies, dysostosis multiplex, angio-keratoma, visceromegaly and seizures [4]. The definitive diagnosis of α-fucosidosis is established based on either the decreased activity of fucosidase enzyme or the detection of a mutation in *FUCA1* gene. Both approaches are expensive and often limit the definitive diagnosis in countries with limited resources. We present two siblings with α-fucosidosis from Pakistan, focusing on radiological findings as a diagnostic tool to develop an approach to a patient with dysostosis multiplex, in neuro-degenerative disorders including α-fucosidosis (Fig. 1).

2. Case report

2.1. Patient 1

A 6.5 year old boy, third child of first-cousin parents, was seen at the metabolic clinic for psychomotor regression noted at 11 months of age. He was born after a full-term, uneventful pregnancy. The parents reported normal growth and development till 11 months of age, after which initial stagnation of development followed by progressive spasticity of body was noted. Eventually his ability to sit unsupported and cruise was lost. Parents also reported progressive deterioration in his ability to understand and respond socially. Frequent aspiration during feeding was a significant issue. However, no sei-

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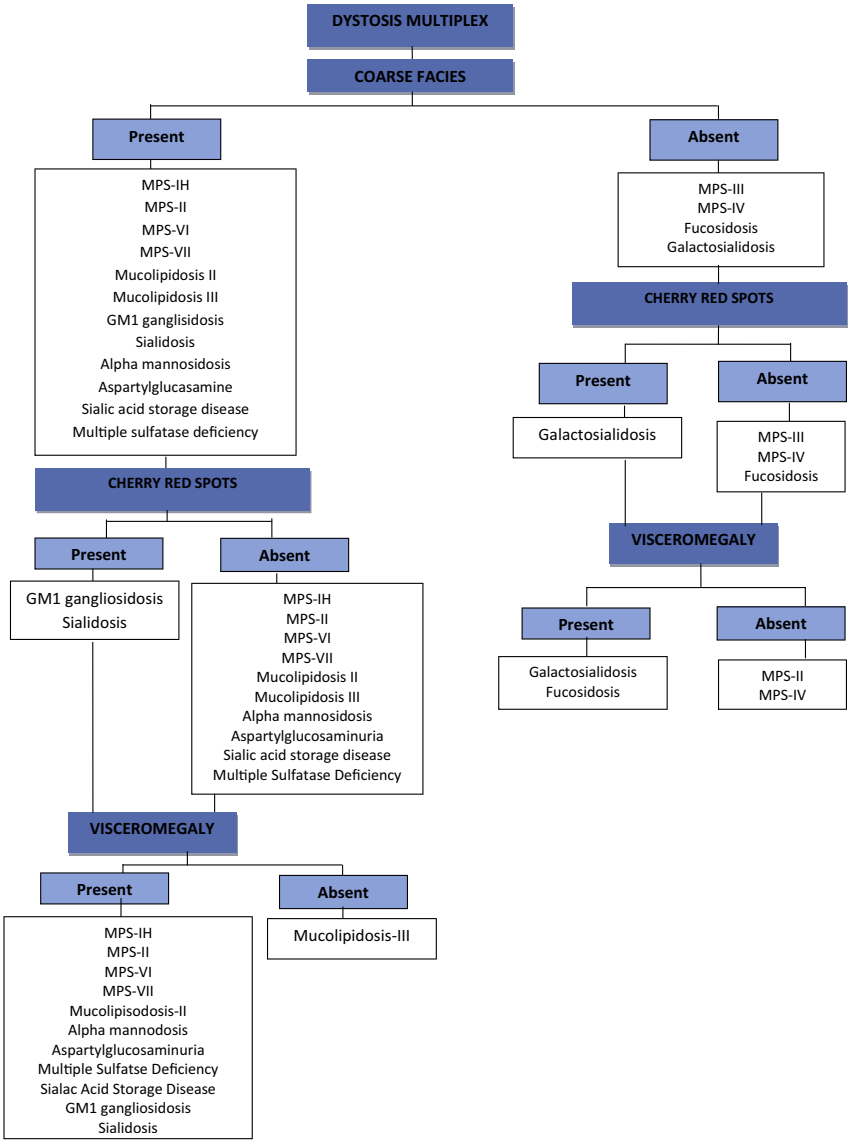

Figure 1 Approach to dysostosis multiplex.

zures were reported. At the time of his assessment weight, height and head circumference was 11 kg, 91 cm and 46.5 cm respectively (all < 5th percentile). He was noted to have no facial coarsening but a scissoring posture along with hepatosplenomegaly was noted on physical examination; liver was 5 cms below right coastal margin and spleen 3 cms in the long axis, (Fig. 2a). He was also noted to have spastic quadraparesis with increased deep tendon reflexes. However, no corneal clouding, contractures or cutaneous changes including angiokeratoma were noted. Ophthalmologic evaluation did not reveal cherry red spots. X-ray of the spine showed an anterior breaking of lumbar vertebrae, (Fig. 3a). The MRI brain was done, which showed a significant loss of white matter causing cerebral atrophy and enlarging CSF spaces (Fig. 3b).

Based on the clinical features of hepatosplenomegaly, dysostosis multiplex on X-rays, classical MRI brain features along with the absence of facial coarsening and cherry red spots; our differential diagnosis included Alpha-fucosidosis, Mucopolysaccharidosis type III & type IV. In our patients, psychomotor regression and the presence of organomegaly led us to the diagnose Alpha-fucosidosis as Psychomotor regression is not a feature of Mucopolysaccharidosis type IV and organomegaly is not noted in Mucopolysaccharidosis type III and type IV. To evaluate for the cause, his urine oligosaccharide analysis was performed at Institute Medical Research, Kuala Lumpur, which showed densely-staining band at the origin and other distinct bands above it showing pattern similar to positive control of α-fucosidosis (Fig. 4). Enzyme activity of α-fucosidase in leukocytes was 1 nmol/h/mg protein which was less than 1% from normal mean. These two laboratory methods confirmed the diagnosis.

2.2. Patient 2

Patient 2 was the younger brother of patient 1. He was 3 year old at the time of evaluation for psychomotor regression, which started at 12 months of age.