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Fukuyama Congenital Muscular Dystrophy: A Rare Case Report

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ABSTRACT: Fukuyama CMD constitutes a part of a spectrum of closely overlapping Congenital Muscular Dystrophies (CMD) and neuronal migration disorders. Here, we present a child with Fukuyama CMD with hypotonia, developmental delay and epilepsy. We hereby highlight the rarity of the syndrome per say, its presentation and the radiological characteristics which help in diagnosing Fukuyama accurately obviating the need for an invasive procedure like muscle biopsy and molecular genetic studies in centers with limited infrastructure.

Keywords: Fukuyama muscular dystrophy, Congenital muscular dystrophy, Muscle-Eye-Brain disease, Walker Warburg syndrome.

I. INTRODUCTION

Congenital muscular dystrophies (CMDs) are a group of phenotypically and genotypically heterogeneous muscular disorders with early infantile onset. Commonly encountered CMDs include Walker Warburg CMD, Fukuyama CMD, Muscle–eye–brain disease and Merosin-deficient CMD. Most of these diseases show autosomal recessive pattern of inheritance with varying presentation of muscle weakness, hypotonia, mental retardation and ocular involvement. Fukuyama type is a unique form of CMD with high predilection for the Japanese population. MRI is the modality of choice to evaluate the brain anomalies in this disorder. Characteristic changes on brain MRI aid in differentiating this disorder from other clinically simulating CMDs. We report a rare case of Fukayama CMD seen in a 9 month old male child.

II. CASE REPORT:

A nine month-old baby boy born of non-consanguineous marriage, with unremarkable birth history and family history presented with global developmental delay, hypotonia, inability to lift his head or roll over, presented to department of Radio diagnosis for MRI brain. His neurologic examination demonstrated diffuse hypotonia, weakness (including facial muscles), muscle weakness was more marked in distal muscles than proximal group, hyporeflexia, had poor visual aquity on both eyes with no significant abnormality in fundus. His mother also gives history of feeding difficulty in early infancy.

He had multiple episodes of seizures since three months of age. The seizures were initially characterized by head deviation to right followed by right hemiclonic seizures during sleep occurring 1-2 episodes per month lasting 2-3 min each and had gradually ran up over time to 2-3episodes per week. His parents also noticed events with eye deviation to one side followed by facial twitches lasting 10-15 sec. Child had been on sodium valproate with little improvement in seizures. An electroencephalogram was normal.

Local examination revealed microcephaly, strabismus, generalised hypotonia and absent deep tendon reflexes. There were no neurocutaneous markers or remarkable musculoskeletal or systemic anomalies. There is enlargement of calf muscle noted. His serum creatine kinase was elevated (4216 µ/L).

The patient was further evaluated with MRI brain. MRI findings were suggestive of Fukayama type of CMD. Genetic testing was suggested but the patient could not afford.

MRI shows-

- Diffuse edema and T2/FLAIR hyperintensity involving cerebral white matter bilaterally predominantly in fronto-occipital region with sparing of subcortical U fibres consistent with **abnormal myelination**.
- Thickened, bumpy dysplastic gyri with shallow sulci in both cerebral hemispheres predominantly involving bilateral temporal lobes consistent with **polymicrogyria**.
- Multiple hyperintense cerebellar **cysts**.

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- Hypoplastic **pons** with a prominent fourth ventricle with fusion of superior and inferior **colliculus**.
- Mild protrusion of scleral-uveal coat of bilateral orbits consistent with posterior **staphyloma**.

Child was diagnosed as Fukayama CMD and has been initiated on valproate and lamotrigine combination and rehabilitative measures.

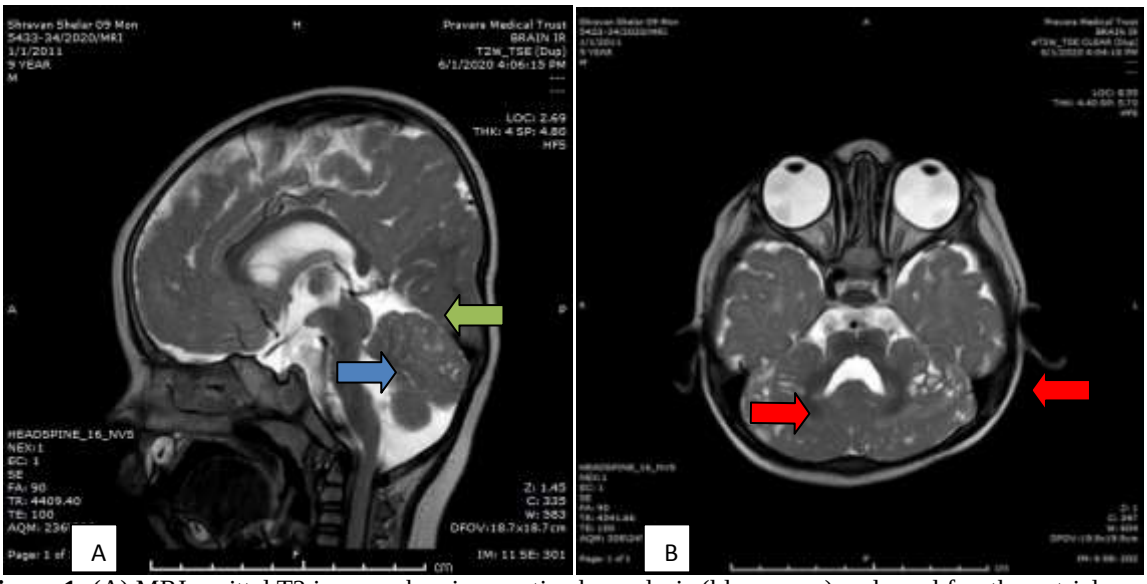

Figure 1: (A) MRI sagittal T2 images showing pontine hypoplasia (blue arrow), enlarged fourth ventricle, and fusion of superior and inferior colliculi (green arrow) (B) Axial T2 image shows lateral cerebellar cysts (red arrows).

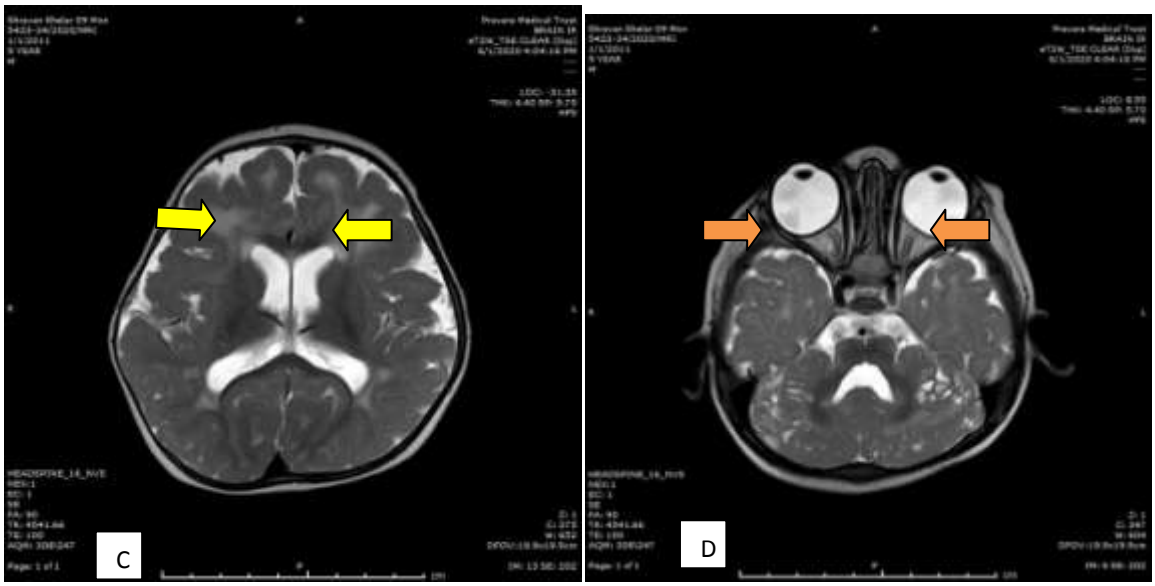

Figure 2: (C) Axial T2 images showing periventricular white matter hyperintensities representing hypomyelination in cerebral white matter, more pronounced over frontal and occipital region (yellow arrow) (D). Axial T2 image showing posterior staphyloma of orbit (orange arrow).

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III. DISCUSSION

Fukayama CMD is a rare autosomal recessive form of CMD, first described by Fukayama in 1960 in Japan [1]. Mutation in gene Fukutin is responsible for this disorder and is located on chromosome 9q31 [2]. Affected children present with insidious onset of progressive hypotonia and facial muscle weakness beginning in infantile period ultimately resulting in contractures. The affected children show delayed motor and language milestones with decreased intellectual performance. Visual impairment is seen in about half of the cases and ocular changes like retinal dysplasia, retinal detachment, optic nerve atrophy, myopia and strabismus can be seen on ophthalmological examination [3]. Other features include pseudohypertrophy of muscles of calf and forearms and convulsions. The clinical course is complicated by respiratory and cardiac failure in second decade of life due to secondary involvement by the disease process and is the common cause of death. Laboratory investigations show increased creatine phosphokinase levels and myopathic pattern in electromyogram [2, 4]. Muscle biopsy shows myopathic changes with fibrosis suggestive of muscular dystrophy, but it cannot categorize the type of CMD. MRI is the modality of choice to diagnose this disorder. Hallmark changes on MR include cerebral and cerebellar cortical dysplasia, cerebellar cysts, brainstem abnormality and white matter changes. Cerebral cortical dysplasia has two patterns of involvement. The first pattern is that of polymicrogyria with shallow sulci, slightly thickened cortices and bumpy gray-white matter junction while the second pattern shows thickened cortex with smooth graywhite matter junction [5]. Polymicrogyria seen in FCMD is not distinctive as it is also seen in other CMDs like WalkerWarburg syndrome (WWS) and muscle–eye–brain disease. Symmetrical polymicrogyria is also described in several entities like familial polymicrogyria, congenital bilateral perisylvian syndrome, Aicardi syndrome, Zellweger syndrome and in congenital Cytomegalovirus infection [6].Cerebellar cortical dysplasia manifests as disarrayed cerebellar foliation with polymicrogyria. Cerebellar cysts are also commonly seen on MR. Brainstem abnormalities include pontine and midbrain hypoplasia [5]. Periventricular and subcortical white matter changes are commonly seen and are thought to be secondary to dysmyelination than due to delayed myelination. The dysmyelination changes in white matter improve with time [7]. Other abnormalities include fusion of mid brain colliculi and ventriculomegaly. MRI also aids in differentiating this entity from other CMDs like WWS and muscle–eye–brain disease [8]. WWS is a severe form of CMD with diffuse cobblestone type of lissencephaly and marked white matter abnormality with complete lack of myelination. Brainstem is significantly deformed with flattening or kinking of it. Callosal dysgenesis and ventriculomegaly are the associated features of this disorder [9]. Muscle–eye–brain disease has less extensive cortical dysplasia and patchy or absent white matter abnormality. Clinically, these patients have microcephaly and marked eye abnormality in the form of myopia[10].

Classifications of these clinical syndromes are now being annotated with unique clinical, neuroimaging findings and specific loss-of-function gene mutations, some of which can exhibit genetic and phenotypic heterogeneity. Despite this heterogeneity, these conditions are characterized by generally unique features within a broad spectrum. [11]

CMD can be seen with or without cerebellar abnormalities such as cysts or hypoplasia/dysplasia with or without mental retardation, and in a CMD subtype of merosin-deficiency, MCD1D, there can be diffuse white matter signal abnormality on brain magnetic resonance imaging scan without mental retardation.[11]

However, dominant presentation as seizures is not a well characterized feature of CMD. Also, the diagnosis of CMD relies on clinical findings, brain and muscle imaging, muscle biopsy histology (dystrophic features without the hallmarks of the structural changes seen in the congenital myopathies), muscle and/or skin immune histochemical staining, and molecular genetic testing. But here we emphasize the fact that careful analysis of clinical features, simple laboratory investigations and neuroimaging will help clinching the diagnosis and thereby may help avoid muscle biopsy and sophisticated genetic testing in countries with limited resources.

IV. CONCLUSION

Fukuyama muscular dystrophy shows characteristic unique MRI findings which aid in early diagnosis and differentiating it from other clinically simulating congenital muscular dystrophies.

Conflict of interest: None.

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