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Congenital Muscular Dystrophy: Report of Two Cases

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ABSTRACT *Central nervous system abnormalities are often striking and useful in diagnosis in patients with congenital muscular dystrophy (CMD). Two cases of congenital muscular dystrophy are reported with abnormal neuroimaging findings especially in posterior fossa structures.*

Introduction
Congenital muscular dystrophy (CMD) comprises a heterogeneous group of muscular disorders that present with hypotonia at birth and variable muscle weakness and contractures. Many patients have associated central nervous system and ocular abnormalities. Elevation of serum creatine kinase is seen and muscle biopsy show changes of dystrophy. Two cases of congenital muscular dystrophy are reported with their neuroimaging features.

Case 1
A four year old preterm female first born child of non-consanguineous marriage presented with global developmental delay and mental retardation. She had hypotonia of all muscles, wasting of limbs and contractures of knee and ankle. Her weight and head circumference were below 5th percentile. Magnetic resonance imaging (MRI) of brain revealed multiple small cysts in bilateral cerebellar hemispheres and vermis with thickened disorganized cerebellar cortex (Fig. 1A and B) and pachygyria in bilateral frontal regions (Fig. 1B). Patchy T2 and FLAIR hyperintensities were seen in posterior periventricular white matter (Fig.2A). Inferior vermian hypoplasia and dilated fourth ventricle with elongation of brainstem was seen (Fig. 2B) with normal lateral and third ventricles. Blood analysis showed markedly increased serum creatine kinase levels (1390 U/L). Electromyography (EMG) of left lower limb showed myopathic pattern representing intrinsic muscle disease. Muscle biopsy revealed few residual and scattered small atrophic skeletal muscle fibers with fibroadipose tissue in between and surrounding the muscle fibers. The clinical profile, imaging and pathological findings favored diagnosis of congenital muscular dystrophy without hydrocephalus.

Case 2
A six month old second borne female child of consanguineous marriage presented with recurrent upper respiratory tract infection. Marked hypotonia was present in all muscles with absent neck holding. Patient had increased head circumference (44 cms) with nystagmus and white eye reflex was seen in both eyes. Ocular ultrasound revealed persistent hypoplastic primary vitreous in both globes. MRI brain showed hypoplastic cerebellar hemispheres and vermis and thickened dysplastic cerebellar cortex with numerous small subcortical cysts (Fig.3A and 4A). Marked hypomyelination was present (Fig. 3A and B) with moderate hydrocephalus and stretching of corpus callosum (Fig. 3B and 4B). Shallow sulcations in cerebral cortex with pachygyria in both frontal lobes was seen (Fig.4A). Irregular inner surface of the cerebral cortex giving cobblestone appearance was noted in bilateral parieto-occipital regions (Fig. 3 B). Hypoplasia of pons was seen with dorsal kink at the pontomesencephalic junction and fusion of colliculi (Fig. 4 B). Blood tests showed elevated creatine kinase levels (1970 U/L). Muscle biopsy was done which showed short muscle fibers, few interspersed necrotic and regenerated immature muscle fibers with increased endomysial and perimysial connective tissue was seen. Based on clinical, neuroimaging and pathologic features diagnosis of Santavuori Muscle-eye-brain disease was considered.

Discussion
Congenital muscular dystrophies (CMDs) are autosomal recessive diseases comprising heterogeneous group of muscular disorders that present with slowly progressive or nonprogressive hypotonia at birth and variable muscle weakness and joint contractures[1]. CMD shows two well recognized forms, one which have abnormalities primarily confined to muscle with normal or near-normal intelligence, also called classic or pure muscular dystrophies[1], whereas others also have severe mental retardation with anomalies of the brain and eyes [2-5]. CMDs without major brain malformations are either merosin positive, common type occurring due to Fukutin related protein deficiency or merosin negative. Merosin negative CMDs have significant dysmyelination or hypomyelination of white matter[6]. Merosin positive CMDs have normal or very mild imaging findings like cerebellar hypoplasia, non-specific white matter changes and focal polymicrogyria[7]. CMDs with major brain abnormalities have spectrum of overlapping imaging findings including abnormal white matter, cortical, brainstem and cerebellar anomalies and ocular abnormalities[2-5, 8]. They are divided into (i) Fukuyama congenital muscular dystrophy (FCMD), a least severe form seen primarily in Japanese children, (ii) Santavuori Muscle-eye-brain disease (MEB), a Finnish variant and (iii) Walker-Warburg syndrome (WWS) which is the most severe form. Merosin is reduced in patients with Fukuyama CMD and MEB disease. CMDs result from mutations in a variety of different genes, including those encoding for structural proteins and putative or demonstrated glycosyltransferases which affect the glycosylation of Dystroglycan. Muntoni and Voit in 2004 proposed a classification for CMDs based on genetic mutation leading to defects of structural proteins and defects of glycosylation[9]. Barkovich et al[10] classified the CMDs based on the genes implicated in the cobblestone complex disorders (Lissencephaly type II) with imaging findings of reduced sulcation with cobblestone cortical surface, polymicrogyria, pachygyria, hypomyelination, brain-

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stem hypoplasia, cerebellar hypoplasia or dysplasia and cerebellar cysts. Major phenotypes included are WWS, FCMD and MEB disease.

Classic or pure form of CMD shows hypomyelination, mild hypogenesis of the cerebellar vermis, hypoplastic pons with normal brain cortices and white matter of the brain stem and cerebellum[2]. Walker-Warburg Syndrome[2, 8, 11] shows diffuse abnormal thickened cortex with few shallow sulci, with an irregular gray matter–white matter junction possibly due to extension of bundles of disorganized cortical neurons into the underlying white matter giving appearance of "cobblestone" cortex. Severe hypomyelination of white matter of cerebral or cerebellar hemispheres is seen. The cerebellar hemispheres and vermis are hypoplastic with cerebellar cortex shows polymicrogyria and multiple cysts. Pontine hypoplasia with distinct dorsal kink at the pontomesencephalic junction, fused colliculi, congenital hydrocephalus and callosal hypogenesis are usually seen. Posterior cephaloceles, progressive macrocephaly and testicular defects are common. Ocular malformations like retinal dysplasia, persistent hypoplastic primary vitreous, congenital glaucoma or microphthalmos, optic nerve hypoplasia are commonly seen in WWS[11, 12]. Patients have absent psychomotor development and die in the first year of life secondary to recurrent aspiration and respiratory illnesses.

Santavuori MED disease[2, 5, 11] shows severity and imaging pattern intermediate between the WWS and FCMD. Hypoplastic pons, fused colliculi, vermian hypoplasia, cerebellar polymicrogyria and cerebellar cysts are seen. Pachygyria, more severe in frontal lobes and polymicrogyria, irregular gray-white matter junction, callosal hypogenesis, hydrocephalus, absent septum pellucidum and delayed myelination may also be present. In FCMD cobblestone lissencephaly is more prominent in the parieto-occipital region while polymicrogyria is present mostly in the frontal lobes[2, 11]. Myelination is often delayed and follows reverse of the normal myelination pattern. Posterior fossa abnormalities include hypoplasia of the pons, cerebellar polymicrogyria, and cerebellar cysts[3, 4, 13]. Callosal abnormalities and cephaloceles are unusual with FCMD, while ocular abnormalities may be seen but are less severe[11]. CMDs not fitting into these major phenotypes have also been described including CMD with occipital agyria, CMD with cerebellar cysts and leukodystrophy without cortical malformations or hydrocephalus[11]. Posterior fossa abnormalities in CMDs are often striking and useful in reaching the diagnosis. Multiple small cerebellar cysts are relatively diagnostic for CMD and are rarely seen in other diseases. Significant elevation of serum creatine kinase levels is seen in CMDs while muscle biopsy will show dystrophic changes. Marked phenotypic overlap can occur amongst CMDs and diagnosis is made by a combination of clinical profile, imaging finding, genetic information, laboratory tests and muscle biopsy.

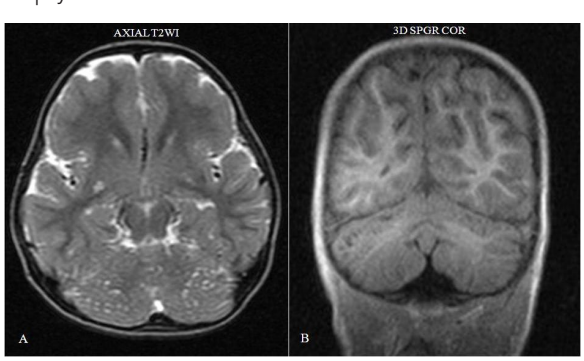

Figure 1A and B: Axial T2W image reveals multiple small cysts in bilateral cerebellar hemispheres and vermis with pachygyria in bilateral frontal regions (1A). Coronal 3D-SPGR image shows thickened dysplastic cerebellar cortex with multiple small subcortical cysts (1B).

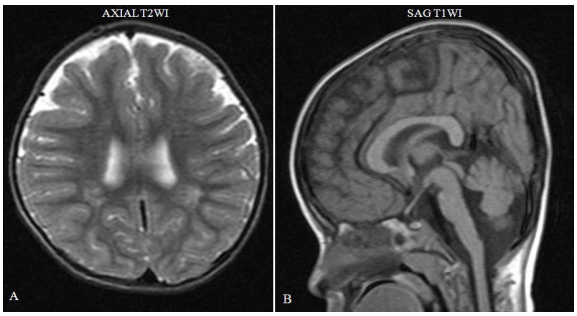

Figure 2A and B: Axial T2W image shows hyperintensities in bilateral posterior periventricular white matter (2A). Sagittal T1W image reveals inferior vermian hypoplasia and dilatation of fourth ventricle with elongation of brainstem (2B).

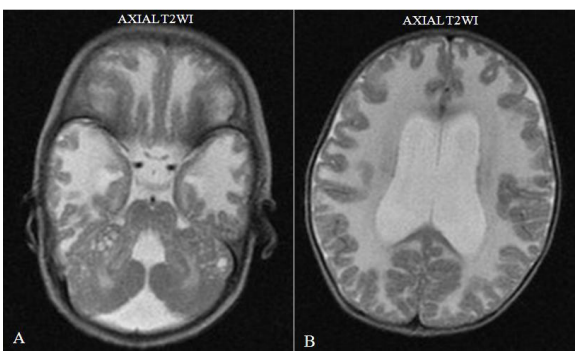

Figure 3A and B: Axial T2W images show hypoplastic cerebellar hemispheres and vermis with thickened dysplastic cerebellar cortex and multiple cerebellar subcortical cysts (3A). Moderate hydrocephalus and marked hypomyelination are seen with irregular inner surface of the cerebral cortex in bilateral parieto-occipital regions (3B).

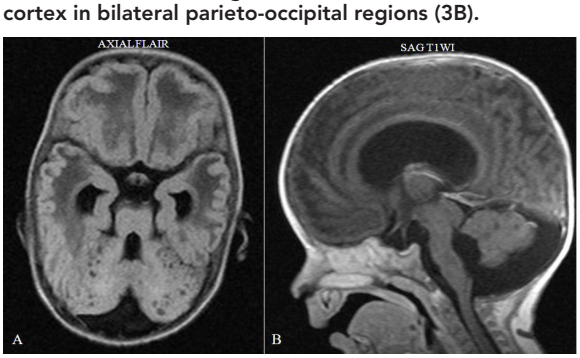

Figure 4A and B: Axial FLAIR image reveal multiple small cerebellar subcortical cysts with pachygyria in bilateral frontal regions (4A). Hypoplasia of pons and cerebellum noted with dorsal kink at the pontomesencephalic junction and fusion of colliculi (Fig. 4 B). Moderate hydrocephalus is seen with stretching of corpus callosum.

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REFERENCE

1. Cwik VA, Brooke MH. Disorders of muscle dystrophies and myopathies. In: Berg BO, ed. Principles of Child Neurology. New York: McGraw-Hill; 1996:1665–1702 | 2. Barkovich A. Neuroimaging manifestations and classification of congenital muscular dystrophies. AJNR19:1389-96, 1998 | 3. Fukuyama Y, Kawazura M, Haruna H. A peculiar form of congenital muscular dystrophy. Report of fifteen cases. Paediart Universit (Tokyo) 1960; 4:5-8. | 4. Fukuyama Y, Osawa M, Suzuki H. Congenital progressive muscular dystrophy of the Fukuyama type: clinical, genetic, and pathological considerations. Brain Dev 1981;3:1–29 | 5. Santavuori P, Somer H, Sainio K, et al. Muscle-eye-brain disease. Brain Dev 1989;11:147–153 | 6. Mercuri E, Rutherford M et al. Early white matter changes on brain magnetic resonance imaging in a newborn affected by merosin-deficient congenital muscular dystrophy. Neuromuscul Disord 11(3):297-9, 2001 | 7. Philpot J, Pennock J et al. Brain magnetic resonance imaging abnormalities in merosin-positive congenital muscular dystrophy. Eur J Paediatr Neurol4(3):109-14, 2000 | 8. Rhodes RE, Hatten HP et al. Walker-Warburg syndrome. AJNR Am J Neuroradiol1992; 13:123-126. | 9. Muntoni F,Voit T :The congenital muscular dystrophies in 2004:a century of ecciting progress.Neuromuscl Disord 2004Oct;14(10):635-49. | 10. Barkovich A, Kuzniecky R, Jackson G, et al. A developmental and genetic classification for malformations of cortical development. Neurology 2005; 65: 1873–1887. | 11. Barkovich AJ. Congenital Malformations of the Brain and Skull. In: Barkovich AJ, ed. Pediatric neuroimaging. 4th ed. Philadelphia: Lippincott, Williams & Wilkins 2005; 291-439. | 12. Gerding H, Gullotta F, Kuchelmeister K, Busse H. Ocular findings in Walker-Warburg syndrome. Childs Nerv Syst 1993; 9:418-420. | 13. Aida N, Tamagawa K, Takada K, et al. Brain MR in Fukuyama congenital muscular dystrophy. AJNR Am J Neuroradiol 1996; 17:605–613. |