

# Congenital Muscular Dystrophy

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## Citation

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## Abstract

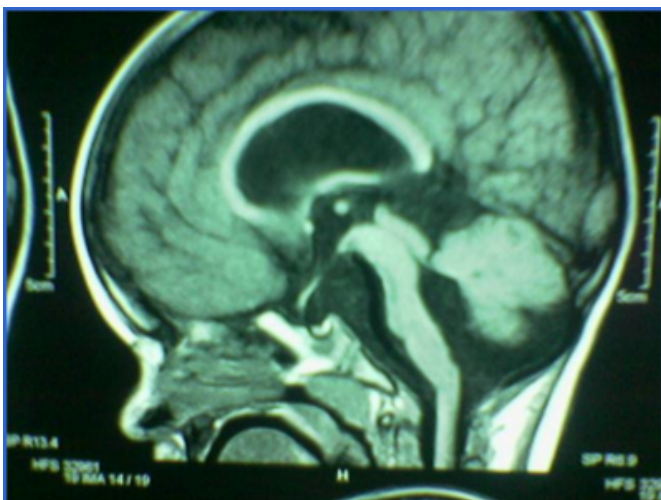
We report a case of a 11 month old male child born of non-consanguinous marriage presented with severely delayed milestones and occasional seizures. There was inability to sit and head holding had developed at 8 months. Marked hypotonia was present in all muscles. Profound mental retardation was also seen. Nystagmus was present and there was marked visual loss( light perception was present). Ears were low set and bilateral cryptorchidism was present. MRI brain showed thick, pachygyric cerebral cortex. The cerebellum was hypoplastic with multiple tiny cysts in the cerebellar hemisphere as well as vermis.

## CASE REPORT

A 11 month old male child born of non-consanguinous marriage presented with severely delayed milestones and occasional seizures. There was inability to sit and head holding had developed at 8 months. Marked hypotonia was present in all muscles. Profound mental retardation was also seen. Nystagmus was present and there was marked visual loss( light perception was present). Ears were low set and bilateral cryptorchidism was present. MRI brain showed thick, pachygyric cerebral cortex. The cerebellum was hypoplastic with multiple tiny cysts in the cerebellar hemisphere as well as vermis(Figure 1).

### Figure 1

Figure 1. T1 Weighted saggital MR image shows markedly thinned pons with characteristic anterior notch. Corpus callosum is stretched, cerebellum is also hypoplastic.

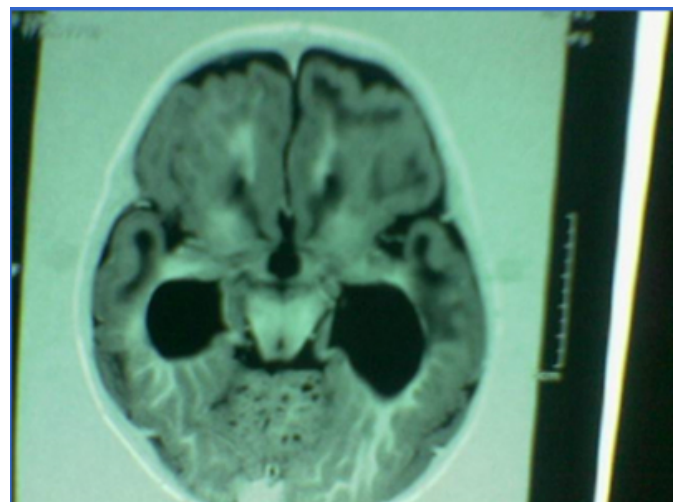


However the most striking abnormality was an extremely hypoplastic pons with a distinct notch on its ventral aspect(

Figure 2).

### Figure 2

Figure 2. True inversion recovery MR image shows multiple small cerebellar cysts. Hydrocephalus is present with white matter hypointensity .Note the pachygyric cerebral cortex



USG abdomen showed normal kidneys. Blood tests showed markedly creatine kinase levels( 3000 U/L). A muscle biopsy was done which showed small, short muscle fibres,diffuse degeneration,necrosis and scattered regeneration of muscle fibres,endo and perimysial fibrosis. In view of the clinicoradiological and pathologic features a diagnosis of Walker-Warburg syndrome was considered most appropriate. Genetic studies were postponed as the patient was non affording . Two weeks later the patient succumbed to respiratory infection and failure.

## DISCUSSION

Congenital muscular dystrophies(CMDs) are a heterogenous

group of autosomal recessive myopathies presenting at birth with hypotonia. Several different classifications have been proposed including a biochemical one by Muntoni and Voit<sup>2</sup>.

CMDs can be broadly divided into:

(i) CMDs without major CNS malformations which can be either merosin(-), which show only white matter hypointensities or merosin (+) which can show either normal brain or only mild cerebellar hypoplasia. A common type is merosin positive CMD due to Fukutin related protein deficiency (FKRP)

(ii) CMD with major CNS abnormalities

- Fukuyama congenital muscular dystrophy (FCMD) which is the least severe, common in Japan.
- Muscle-eye-brain disease (MEB, Finnish variant)
- Walker-Warburg syndrome (WWS)- the most severe form.

These CMDs are caused by mutations in the glycosyltransferase genes causing abnormal glycosylation of  $\beta$ -dystroglycan. Considerable phenotypic overlap can occur and diagnosis is by a combination of clinical, radiological and laboratory data. Genetic information is being increasingly used.

Walker-Warburg syndrome is the most severe CMD. It is due to mutation in the POMT1 gene O-methyltransferase 1 that catalyses first step in the Ser/Thr O-mannosylation<sup>3</sup>. Presentation is in utero or at birth with hypotonia, poor suck and swallow, and contractures. Progressive disease results in almost no developmental progress. Severe mental retardation is seen in all cases and seizures occur in more than half. The average time of death is 9 months<sup>4</sup>. Ocular abnormalities include microphthalmos, hypoplastic optic nerve, colobomas, retinal detachments, cataract, glaucoma and corneal opacities all of which lead to blindness<sup>5</sup>. Brain abnormalities seen are pachygyria or even an agyric cortex with complete type 2 lissencephaly, a thin cortical mantle, cobblestone cortex, focal interhemispheric fusions, dysplastic corpus callosum and severe hypomyelination. However posterior fossa abnormalities are most striking and often help in arriving at a specific diagnosis. The midbrain and especially the pons is elongated, stretched with a cleft/notch on its ventral surface

giving the appearance of kinked brainstem or z-shaped brainstem<sup>6</sup>. Cerebellar pachygyria, polymicrogyria with disorganized foliation is seen in most patients. Severe vermian hypogenesis is seen with multiple small cerebellar cysts. Such small cerebellar cysts are rarely seen on other conditions and are relatively specific for CMD in the given clinical set up. Microcephaly, ventricular dilatation and obstructive hydrocephalus are common. Small penis, cryptorchism, hydronephrosis, pelviureteric junction obstruction, anoperineal fistula, and talipes are also often associated with WWS.

Laboratory studies show a markedly elevated creatine kinase levels (20-15 times normal). EMG shows typical small amplitude, narrow duration motor unit potentials with early recruitment. Muscle biopsy is indicated in all cases and shows characteristic changes.  $\beta$ -dystroglycan staining is absent in the muscles.

The differential diagnosis of WWS includes differentiating the disease from the other CMDs as well as other causes of the floppy infant syndrome. The severity of disease in the other CMDs with CNS malformations is lesser – MEB being moderate and FCMD being lesser. In FCMD the ocular changes are rare and although patient become bed ridden by the age of 10 yrs due to muscle atrophy and joint contracture, average age of survival is 20 years. The CMDs without brain malformations have much better clinical course and some them especially with FKRP defect could have relatively normal life span. No specific treatment is available for these group of disorders. Supportive care to preserve muscle activity is essential. Pulmonary complications are often the main concern and the cause of death.

### References

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