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CASE REPORT PEER REVIEWED | OPEN ACCESS

MR imaging findings in children with merosin-deficient congenital muscular dystrophy

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ABSTRACT

Congenital muscular dystrophy (CMD) constitutes a set of diseases which differ, sometimes very much from each other. Congenital muscular dystrophy also known as a heterogeneous group of disorders with muscle weakness, hypotonia, and contractures present at birth. This disease is essentially characterized by a complete absence of merosin. Brain magnetic resonance imaging (MRI) in children the lesions presenting with high signal intensities are often observed throughout the centrum semi-oval, periventricular, and sub-cortical white matters on T2-weighted images in MRI brain in children with merosin-deficient congenital muscular dystrophy (MDCMD). In several studies it is noted that the apparent diffusion coefficient (ADC) map may reveal increased signal intensity and at the same times it may value in the periventricular and deep white matters. In this case report we would like to demonstrate the brain MRI characteristics of MDCMD in a young child of 15 years old.

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INTRODUCTION

Congenital muscular dystrophy (CMD) defined as a group of mixed disorders that present at birth which is essentially characterized by muscle weakness, hypotonia, and contractures.

A dystrophic pattern is usually always confirmed in muscle biopsy specimens [1, 2]. The CMD has been classified in two forms well-recognized. The classic or pure form of CMD is seen in patients with normal or near-normal intelligence. The second one differs from the classic or pure form in that brain anomalies and severe mental retardation are present [2]. This second group includes other variants described in the Japanese medical science known as Fukuyama CMD, the Walker-Warburg syndrome, and the Santavuori syndrome (muscle-eye-brain disease) [3].

It is important to remember that Fukuyama, Walker-Warburg, and Santavuori syndromes both have a variety of neuro-pathologic abnormalities that include abnormal cerebral and cerebellar gyral patterns, cerebellar cysts, and white matter changes on MR images [2–9]. The white matter findings are observed in late infancy and with a tendency to decrease in severity with age [2–9]. The

pathogenesis of these changes still unclear and remains uncertain at this time. In some investigations imaging findings in the pure form of CMD have recently been reported, along with their association with abnormal sensory and visual evoked potentials [6, 7, 10].

We outline the specific MRI findings seen in patients hospitalized in one of the pediatric hospitals in the kingdom of Morocco late diagnosed with documented MDCMD.

CASE REPORT

A 15-year-old boy, weighed 37.5 kg, presented to us with isolated delayed motor milestones noticed in early infancy. His parents noted a head lag at 4-month-old and subsequent delay in attaining other motor milestones.

He was able to sit and stand only with support and was not able to walk. Although there is a slight defect in memory capacity, his mental ability and speech appeared to be normal. Vision and hearing were normal. There was no history of seizures. No respiratory difficulty was noted. His birth and family history were unremarkable. On examination, his vital signs were normal. He had classical myopathic facies with inverted "v"-shaped upper lip and shallow cheeks. There were no other dysmorphic features. With these clinical data the CDM was suspected and later confirmed by the MRI.

Brain magnetic resonance imaging (MRI) showed diffuse and symmetrical increase in T2W signal in white matter of cerebral hemispheres (Figure 1A). And also brain stem and cerebellum showed abnormally in increasing signal. Ventricles were not dilated. The major abnormality was abnormal T2 prolongation in cerebral white matter, without involvement of corpus callosum, internal capsule, or other structural abnormalities. Signal characteristic of corpus callosum, internal capsule, basal ganglia, and thalami were normal (not showed). Diffusion weighted imaging (DWI) demonstrated no evidence of restricted diffusion.

DISCUSSION

Merosin (also called α2 laminin) is an extracellular matrix protein, whose gene is mapped in the chromosome 6p2. Laminins are a family of proteins of the basement membrane, and the predominant laminin variant in the basement membrane of the adult striated muscle is the merosin (α2 laminin), which is expressed in skeletal muscle, Schwann cells, cardiac muscle, and placental villi.

Merosin binds α-dystroglycan and in turn is linked to the subsacrolemmal cytoskeleton via the dystrophin-glycoprotein complex. The deficiency of this protein can condition an interruption of the connection between the matrix extracellular tissue and the cytoskeleton subsarcolemma, muscle degeneration [11, 12]. Merosin also plays an important role in neuronal migration and precursors of oligodendrocytes [13, 14].

Some recent studies findings have suggested that myofiber injury may be the result of an inflammatory attack on muscle, followed by poor regeneration of myofibers caused mainly by a defective basal lamina [15]. Merosin is expressed in the fetal brain and its deficiency must be related to changes in white matter and with anomalies of cortical development [16].

Generally in the clinical evaluation of patients with MDCMD is possible to find congenital hypotonia and weakness, and, in late infancy, have contractures and delayed motor milestones.

Nevertheless, the clinical conditions, the patients are able to improve their health status if they survive past the neonatal period, their neuromuscular condition stabilizes and also they may have normal or near-normal intelligence as in our patient.

In this article, we describe the clinical changes and imaging findings of a 15-year-old patient with MDCMD. The patient has normal intelligence, epilepsy, and marked changes in the substance sign supra and infratentorial white matter, associated with global atrophy (Figure 1B) of the pons or cerebellum and brain stem, and small subcortical cerebellum cystic cavitation (Figure 2A and B).

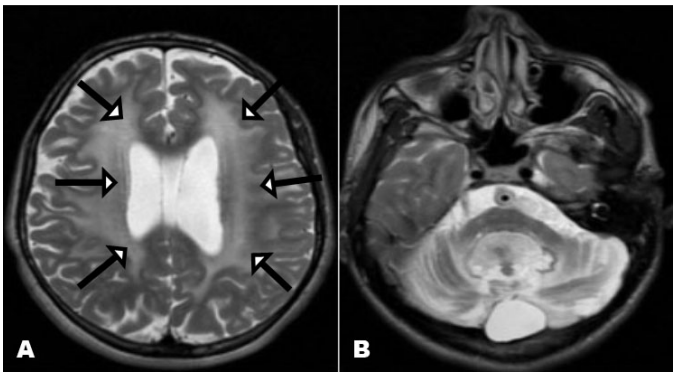

Figure 1: (A and B) Brain MRI axial T2-weighted shows diffuse and symmetrical increase in signal in the white matter of the cerebral hemispheres in (A) (arrow), and brain stem and cerebellum in (B), suggestive of dysmyelination.

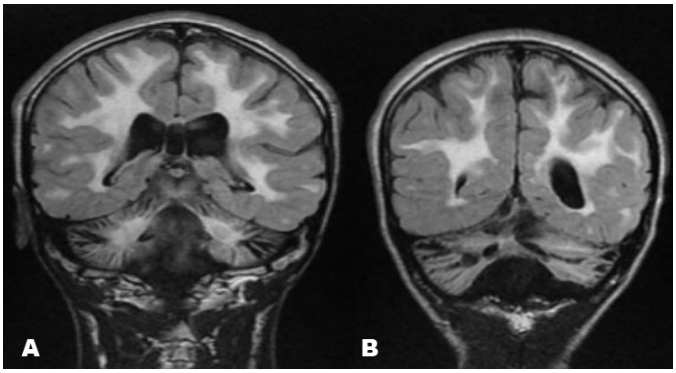

Figure 2: (A and B) Brain MRI coronal FLAIR shows diffuse, symmetrical high signal intensities in the cerebral white matter in (A) and (B).

The MRI finding was similar with the study described about three children by Pilar et al. [17]. On T2-weighted image, the patient had a diffuse and symmetrical increase in signal in the white matter of the cerebral hemispheres, same alterations of the normal white matter signal in the cerebellum, there were also evidence of white matter subcortical cerebellum cysts cavitation, global atrophy of the pons or cerebellum and brain stem, and no evidence of structural abnormalities, such as focal occipital agyria, and enlarged lateral ventricles. The signal characteristic of the white matter within the corpus callosum, internal capsule was normal in our patient.

Many changes seen in the white matter in our patient were similar to those described in the literature that there was progression of white matter disease [10]. Trevisan et al. describe one patient with MDCMD, whose imaging studies from age 2 months to 5 years showed progression of leukoencephalopathy [10].

In our patient there was no historical data of his childhood about the disease, but everything indicates to be followed for years.

Philpot described an 11-year-old child, disabled in merosin, with moderate mental retardation and epilepsy of difficult control, whose brain MRI revealed marked bilateral occipital agyria, dot-cerebellar, and mild hypoplasia dilation of the lateral ventricles [13].

On the other hand it is important to say that it is known, however, that merosin promotes neurite outgrowth and Schwann cell migration, this fact was described by Engvall and Tan et al. [18–20]. In the brain, merosin has been found in the basement membrane of blood vessels [20]. Villanova et al. postulated that this may result in an alteration in the blood-brain barrier, leading to vascular hyperpermeability and the penetration of substances into the central nervous system (CNS) [21].

CONCLUSION

This case has demonstrated the manifestations of merosin deficiency through clinical presentations and MRI findings. It is extremely important to emphasize that MR plays a very important role in confirming the diagnosis of MDCMD. In many studies the conclusions reached have revealed that subtle changes in the white matter may be seen in early infancy and aid in the diagnosis of CMD. Therefore, if changes in white matter are not seen in early childhood, due to lack of resources or other reasons, a repeated study in early childhood or in a young child (like our patient) can also be revealing and help confirm the diagnosis in a child with characteristic of CMD with merosin deficiency. Furthermore, our case recalls the possible CNS involvement in merosin-deficient patients, at least that we suggest to perform MRI for all patients with non-MDCMD.

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Arthur Semedo Insumbo – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Zakia El Yousfi – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Guarantor of Submission

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Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.