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Case Report

Megalencephalic Leukoencephalopathy with Subcortical Cysts or Van Der Knaap Disease: Magnetic Resonance Imaging Aspects of a Case Report

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Abstract

Megalencephalic leukoencephalopathy (MLC) with subcortical cysts, or Van der Knaap disease, is a very rare genetic disorder affecting the white matter. The clinical presentation is slowly progressive, with macrocrania being the most frequent mode of revelation/manifestation. Magnetic Resonance Imaging (MRI) is of great interest, for it enables the diagnosis to be made with pathognomonic signs.

Keywords: Megalencephalic leukoencephalopathy; Subcortical Cysts; Van der Knaap; MRI;

Introduction

Megalencephalic leukoencephalopathy with subcortical cysts (MLC), or Van Der Knaap disease, is a rare genetic disorder with autosomal recessive transmission leading to slowly progressive neurodegenerative disorders [1]. It is characterized by macrocephaly, epilepsy and spastic cerebellar syndrome. The magnetic resonance imaging (MRI) findings bear specific characteristics, with diffuse white matter involvement associated with frontal or parieto-temporal subcortical cysts [1]. We report an observation of this condition with its clinical, genetic and radiological aspects.

Case Presentation

This case was about a 07month-old male child presenting with macrocrania accompanied by slowly progressive and regressive signs of intracranial hypertension. He was the offspring of a first-degree consanguineous marriage. The cerebral MRI was performed under sedation with T1-, T2- and FLAIR-weighted axial sequences and a T2 sagittal sequence. The examination revealed diffuse supratentorial white matter hypertrophy, with T2 hypersignal and T1 hyposignal, more marked in the temporal regions (Figure 1), associated with bilateral frontal subcortical cysts with T2 hypersignal and FLAIR (Figure 2). There were no abnormalities in the basal ganglia or subtentorial white matter. The sagittal T2 slices showed atrophy of the corpus callosum without signal abnormalities (Figure 3). These abnormalities were characteristic of MLC or Van der Knaap disease.

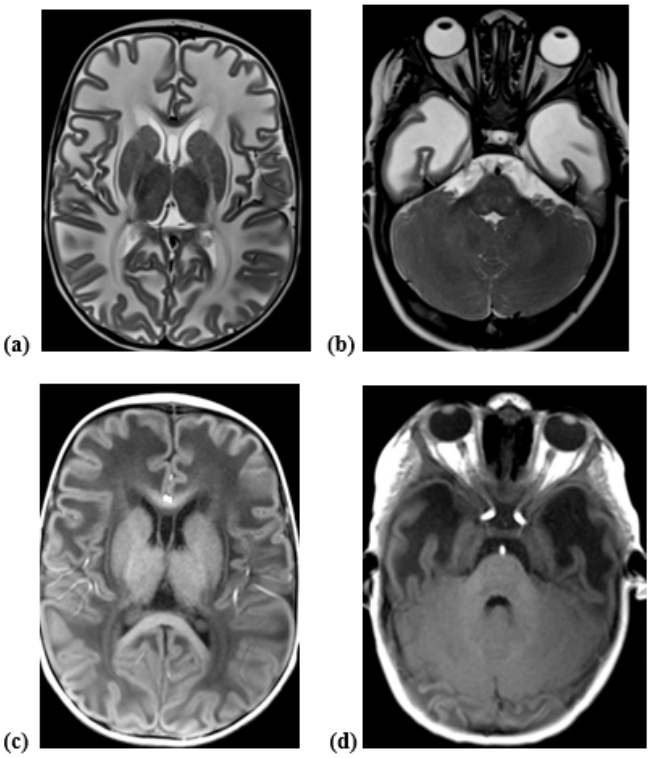

Figure 1: MRI axial sections in T2 (a and b) and T1 (c and d) weighted sequences. Diffuse supratentorial leukodystrophy in hypersignal and predominantly in the fronto-parietal and temporal regions. Integrity of basal ganglia and subtentorial white matter.

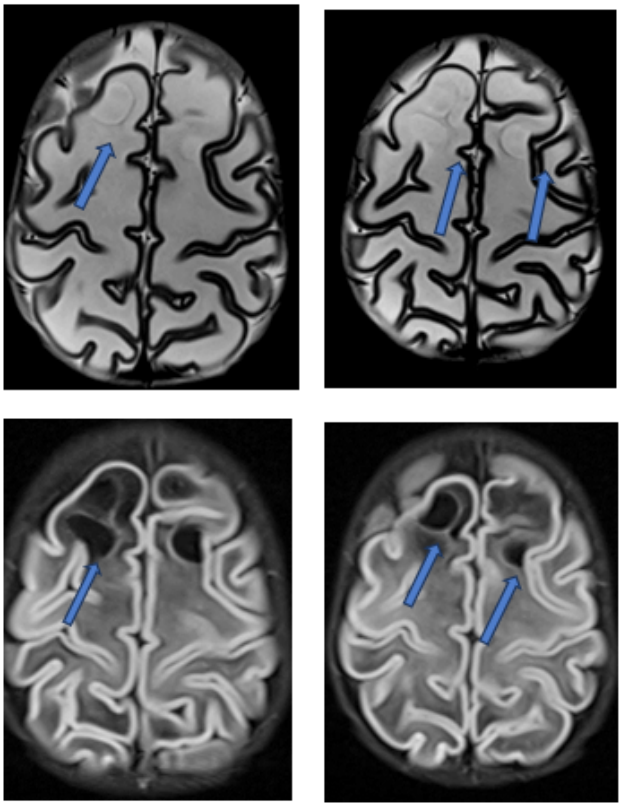

Figure 2: MRI axial sections in T2-weighted (a and b) and FLAIR-weighted (c and d) sequences. Bilateral frontal subcortical cysts (arrows) in T2 hypersignal and FLAIR hyposignal.

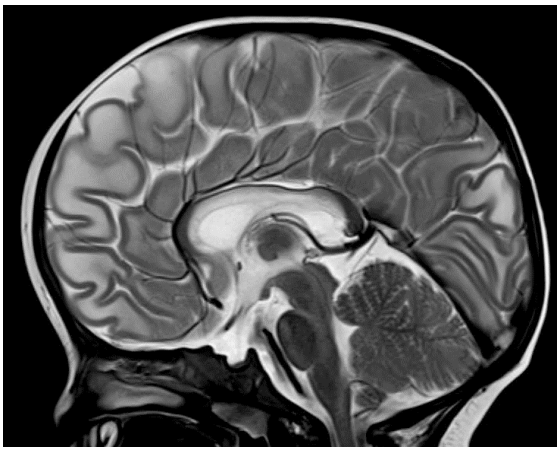

Figure 3: MRI sagittal section in T2-weighted sequence. Corpus callosum hypoplasia without signal abnormality (arrow)

Discussion

The LMC with subcortical cysts is a member of the leukodystrophy family. It is an extremely rare genetic disease. Its frequency is less than 1 per 1,000,000 births, but the disease is more frequent in certain populations with high consanguinity [2].

Our patient had first-degree consanguinity with first-cousin relatives. It is an orphan disease, meaning that there is currently no cure [2].

The disease mainly appears before the age of three, and leads to severe neurological dysfunction affecting motor and cognitive functions, which can result in death. Macrocrania is the most frequent mode of revelation/manifestation of the disease, and often evolves during the first year of a patient life [3-4]. Such was the case in our 08-month-old patient, who presented with macrocephaly in isolation.

Clinically, patients show deterioration in motor function with ataxia and spasticity, epileptic seizures and mental decline. Contrary to other leukodystrophies, the MLC with subcortical cysts progresses very slowly, but minor head trauma and common infections can exacerbate the symptoms.

Several factors are seemingly involved in the severity of the disease. Siblings with the same mutation may present different phenotypes, meaning expressing the disease differently. For example, patients having a clinical picture similar to others at the outset may show improvement or even normalization on subsequent MRI scans. This evolution of the disease falls into the category of the so-called MLC2B phenotype. These patients may also present with different phenotypes, from a benign transient form of MLC with subcortical cysts, to a form with macrocephaly and mental retardation, with or without autism.

The genes whose mutation is responsible for MLC are the MLC1 gene on chromosome 22 (at 22q13.33) and the MLC2 gene on chromosome 11 (at 11q24.2). The mutations in the MLC1 gene are recessive and present in 75% of patients. The mutations in the MLC2 gene are recessive or dominant, and account for 20% of cases. More than 20 different mutations have been identified in this second gene, and physicians distinguish between two forms, known as 2A and 2B, in these patients. In the MLC2B form, signs and symptoms improve over time, but the reasons for this improvement are not yet understood [2].

Radiologically, MRI is the key examination and is sufficient for diagnosis in typical forms. Genetic testing may be inconclusive, as other genes that have not been associated with the disease are probably involved [1,2-5], and was not performed in our patient.

On MRI, MLC is characterized by diffuse white matter lesions with T1 hyposignal and T2 hypersignal, indicating the presence of diffuse edema. The damage predominates in the fronto-parietal and anterior temporal regions and the periventricular white matter. The grey matter, the basal ganglia and thalamus are always spared [1]. The corpus callosum may be thinned or hypoplastic, but retains a normal signal [6]. The subcortical cystic lesions characterizing the disease predominate in the anterior temporal lobes and are often bilateral. Frontal cysts are less common. Our patient typically presented with MRI aspects of MLC with subcortical cysts, sufficient to retain this diagnosis.

The MRI spectroscopy provided additional diagnostic evidence, with a decrease in normal neuronal metabolites in the white matter, such as N-acetylaspartate, creatine and choline, and a decrease in the N-acetylaspartate/creatine ratio. The Myo-Inositol, a specific glial marker, may be normal, decreased or increased, depending on the severity of the disease and the patient's age [7].

Other diseases associating leukoencephalopathy with early-onset macrocephaly constitute differential diagnoses, such as Alexander disease, Canavan disease, glutaric aciduria type 1, mucopolysaccharidoses, gangliosidoses type 2 and congenital muscular dystrophies with merosine deficiency [1].

However, in these diseases, the clinical and radiological manifestations differ considerably from those observed in MLC [1].

To date, there is no definitive therapy for MLC with subcortical cysts. A lack of in-depth understanding of the molecular mechanisms of the disease is holding back therapeutic development for this leukodystrophy [2].

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Conclusion

The Megalencephalic leukoencephalopathy with subcortical cysts is a very rare genetic disorder. The MRI is of great interest in this disease. It enables the diagnosis to be made with pathognomonic signs.

References

1. Jerbi Omezzine S, Ben Ameur H, Bousoffara R, Ayedi A, Hamza HA, et al. (2008) La leucoencéphalopathie mégalencéphalique avec kystes sous corticaux: description de 04 nouveaux cas. J Radio 89: 891-4
2. ELA International [Enligne] (2023) Maladie MLC-ELA International.
3. Rajagopal KV, Ramakrishnaiah RH, Avinash KR, Lakhkar BN (2006) Van der Knaap disease, a megalencephalic leucoencephalopathy. Ind J Radiol Omag 16: 733-34
4. Sethi PK, Sethi NK (2004) Megalencephalic leukoencephalopathy with subcortical cysts. Indian J Pediatr 71: 473-5
5. Anand KS, Garg J, Valecha Y, Makar RS (2007) Megalencephalic leucoencephalopathy with subcortical cysts. Indian J Acad Clin Med 8: 250-2
6. Hari Krishman K, Leema Pauline C, Kumaresan G, Vasantha Malika TK (2005) Megalencephalic leucoencephalopathy with subcortical cysts. Indian J Pediatr 42: 60-3
7. Morita H, Imamura A, Matsu N, Tatebayashi K, Omoya K, et al. (2006) MR imaging and H-MR spectroscopy of a case of Van der Knaap disease. Brain 28:466-9