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MRI FINDINGS SUGGESTIVE OF METACHROMATIC LEUKODYSTROPHY IN A CHILD WITH DEVELOPMENTAL REGRESSION AND EPILEPSY: A RADIOLOGICAL CASE REPORT

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AUTHOR AND AFFILIATION

Lina Lasri[1], Alia Yassine Kassab[1], Samia Obilat[1], Houda Bennani[1], Lina Belkouchi[1], Siham El Haddad[1], Nazik Allali[1], Latifa Chat[1]

[1] Department of Radiology, Children's Hospital, Ibn Sina University Hospital, Mohammed V University, Rabat, Morocco

Corresponding author: Lina Lasri | Email: lasrilina@gmail.com

ABSTRACT

Metachromatic leukodystrophy (MLD) is a progressive lysosomal storage disorder in which brain magnetic resonance imaging (MRI) may provide the first clue to an inherited white matter disease. We report the radiological findings of a 6-year-old girl with delayed development since birth, a history of fetal distress, longstanding spasticity, inability to walk, and caregiver-reported developmental regression beginning at approximately 18 months of age. She was referred for brain MRI after epileptic seizures. MRI demonstrated bilateral, symmetric, confluent T2- and fluid-attenuated inversion recovery hyperintensity of the periventricular and deep cerebral white matter, most pronounced in the parieto-occipital regions with frontal involvement. The subcortical U-fibers were relatively spared. No corresponding diffusion restriction was identified, and the deep gray nuclei and corpus callosum were preserved. This distribution raised suspicion of a leukodystrophy, particularly MLD. However, the absence of a definite tigroid pattern or callosal involvement, together with the history of fetal distress and early developmental impairment, required careful consideration of chronic perinatal white matter injury. Arylsulfatase A activity, urinary sulfatide analysis, molecular testing, and serial MRI were not available; therefore, MLD could not be confirmed. This case emphasizes that developmental regression is not explained by the static brain disturbance underlying cerebral palsy and should prompt renewed diagnostic evaluation. Symmetry, confluence, and relative U-fiber sparing can orient the radiologist toward a leukodystrophy, but definitive attribution to MLD requires biochemical and genetic confirmation.

KEYWORDS

Metachromatic leukodystrophy; developmental regression; epilepsy; magnetic resonance imaging; cerebral palsy

MAIN ARTICLE

INTRODUCTION

Metachromatic leukodystrophy (MLD) is an autosomal recessive lysosomal sphingolipid storage disorder caused most commonly by deficient arylsulfatase A activity, leading to sulfatide accumulation and progressive demyelination in the central and peripheral nervous systems [1]. Clinical subtypes are classified according to age at symptom onset. The late-infantile form generally begins before 3 years of age and is characterized by rapid motor regression, whereas juvenile and adult forms may initially present with cognitive, behavioral, or motor abnormalities [1,2].

Brain MRI is central to the evaluation of suspected leukodystrophy because lesion distribution can narrow the differential diagnosis and direct laboratory testing. Nevertheless, MRI is not sufficient to establish MLD. Current consensus recommendations require biochemical and molecular confirmation, typically combining arylsulfatase A activity, urinary sulfatide analysis, and identification of pathogenic ARSA variants [3].

The distinction from cerebral palsy can be particularly challenging in children with early motor impairment and a history of perinatal distress. Cerebral palsy describes permanent motor and postural disorders attributable to a non-progressive disturbance of the developing fetal or infant brain [4]. A genuine loss of previously acquired abilities therefore represents a diagnostic warning sign and should prompt reconsideration of a purely static encephalopathy. We describe a child with early motor delay, subsequent regression, epilepsy, and a symmetrical white matter MRI pattern suggestive of MLD, while emphasizing the limitations of a radiology-only diagnosis.

CASE PRESENTATION

A 6-year-old girl was referred for brain MRI following epileptic seizures. Her medical history included fetal distress and delayed neurodevelopment recognized from early life. The initial motor phenotype was dominated by stiffness and progressive spasticity, and she never achieved independent walking. On this basis, she had previously been considered to have cerebral palsy.

According to the caregivers, her course was not entirely static. At approximately 18 months of age, they observed a definite decline with loss of previously acquired developmental abilities rather than simple developmental stagnation. This progressive component, together with the later occurrence of seizures, raised concern for an underlying disorder beyond a fixed perinatal motor injury.

MRI Findings

Axial fluid-attenuated inversion recovery and axial and coronal T2-weighted images demonstrated bilateral, symmetric, confluent hyperintensity involving the periventricular and deep cerebral white matter. The abnormalities were most conspicuous in the parieto-occipital regions, with additional frontal involvement. The subcortical U-fibers were relatively spared. No corresponding restriction was identified on diffusion-weighted imaging.

The deep gray nuclei and corpus callosum were preserved on the available examination. No definite tigroid pattern, focal mass effect, or overt cerebral atrophy was identified. The symmetrical confluent distribution and relative sparing of the subcortical white matter suggested an inherited leukodystrophy, with MLD considered the leading radiological possibility. Given the perinatal history, chronic hypoxic-ischemic white matter injury, particularly periventricular leukomalacia, remained an important differential diagnosis.

At the time of manuscript preparation, no result was available for leukocyte arylsulfatase A activity, urinary sulfatides, ARSA molecular analysis, or nerve conduction studies. No serial MRI was available to document progression. The imaging diagnosis therefore remained suggestive rather than confirmatory.

DISCUSSION

The interpretation of pediatric white matter abnormalities requires a pattern-based approach incorporating lesion symmetry, confluence, predominant location, involvement of specific tracts, and the presence of enhancement, rarefaction, or atrophy [5]. MLD typically produces bilateral, symmetric, confluent T2 hyperintensity in the periventricular and deep white matter, often with posterior predominance and relative sparing of the subcortical U-fibers during earlier stages [5,6]. Radially oriented bands or dots of relatively preserved tissue can create the characteristic tigroid or leopard-skin appearance. With progression, the corpus callosum, internal capsules, corticospinal tracts, cerebellar white matter, and subcortical regions may become involved [6,7].

Several findings in the present case support the radiological consideration of MLD: the abnormalities were bilateral, highly symmetric, confluent, centered in the periventricular and deep white matter, and relatively spared the U-fibers. The reported onset of regression at approximately 18 months also overlaps with the late-infantile phenotype, in which gait disturbance and loss of motor abilities are common early manifestations [1,2]. Epilepsy can occur as the disease advances [2].

However, important limitations reduce diagnostic specificity. No definite tigroid pattern was visible, and the corpus callosum was preserved. In a large cohort examining MRI near diagnosis, callosal involvement was identified as a frequent early sign, particularly in symptomatic juvenile disease, although early symptomatic late-infantile cases could have mild or nonspecific MRI abnormalities [8]. Furthermore, after several years of reported neurological decline, the absence of overt atrophy or more extensive tract involvement is not the most typical appearance of advanced late-infantile MLD. These discrepancies make it essential to describe the examination as suggestive rather than diagnostic.

The main acquired differential diagnosis is chronic perinatal white matter injury. The history of fetal distress, developmental delay from birth, spasticity, and inability to walk can all be explained by a static hypoxic-ischemic injury. Established periventricular leukomalacia generally demonstrates loss of periventricular white matter volume, ventriculomegaly with irregular ventricular contours, deep sulci approaching the ventricles, and variable cerebral or callosal atrophy [9,10]. These destructive and volume-loss features were not prominent on the displayed MRI, whereas the white matter signal abnormality was conspicuously symmetric and confluent. Nonetheless, noncystic perinatal injury cannot be excluded from a limited single examination.

Clinical evolution is therefore decisive. Cerebral palsy is attributed to a non-progressive disturbance of the developing brain [4]. Motor function can change with growth, orthopedic complications, intercurrent illness, or epilepsy, but a true loss of previously acquired developmental skills should not automatically be attributed to cerebral palsy. In the present patient, objective documentation of which milestones were acquired and subsequently lost would strengthen the distinction between progressive regression and severe early developmental impairment.

Confirmation of MLD requires more than reduced arylsulfatase A activity alone because pseudodeficiency can produce low enzyme values without clinical disease. Diagnostic evaluation should combine enzyme testing with urinary sulfatide measurement and molecular analysis of ARSA; alternative pathways, including saposin B deficiency, may require additional testing when clinical and biochemical findings are discordant [3]. Peripheral nerve conduction studies can also provide supportive evidence of demyelinating neuropathy. Histological confirmation is not routinely required.

This report is limited by the absence of biochemical and genetic confirmation, detailed standardized developmental assessment, electrophysiological testing, serial imaging, and documented follow-up. Accordingly, it does not establish a definitive diagnosis of MLD. Its value lies in illustrating how a symmetric confluent MRI pattern and a history of regression can alert the radiologist to a possible progressive white matter disorder in a child previously labeled as having cerebral palsy and can direct the appropriate confirmatory work-up.

CONCLUSION

Bilateral symmetric periventricular and deep white matter abnormalities with relative sparing of the subcortical U-fibers are suggestive of a leukodystrophy and may raise particular concern for MLD. In a child with a perinatal risk history, the imaging findings must be weighed against chronic perinatal white matter injury. Developmental regression is the critical clinical warning sign that argues against attributing the entire course to a static cerebral palsy phenotype. MRI should guide, but not replace, biochemical and genetic confirmation.

FIGURES

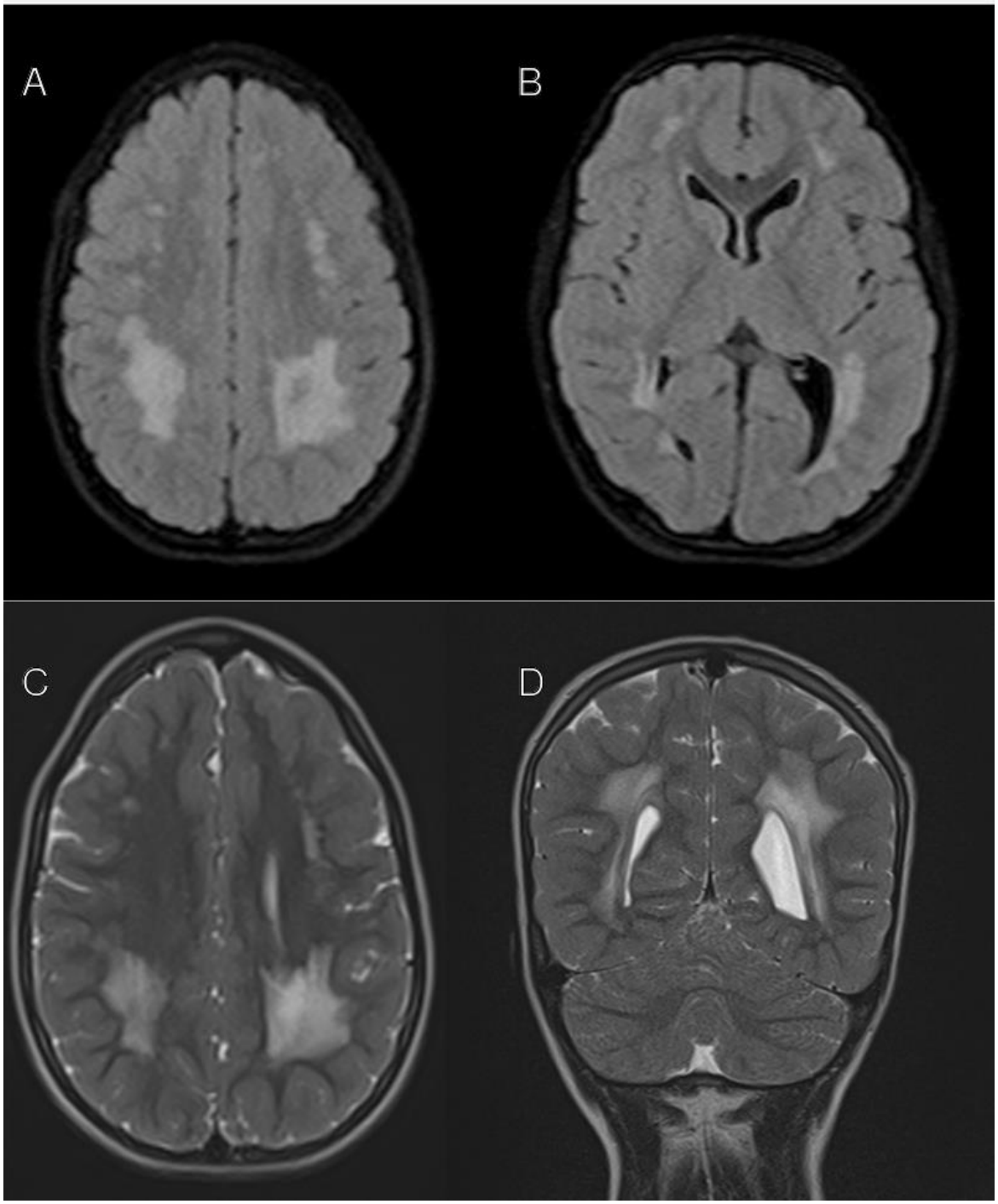

Figure 1: Brain MRI in a 6-year-old girl with developmental regression and seizures. Axial FLAIR images (A, B) and axial (C) and coronal (D) T2-weighted images demonstrate bilateral, symmetric, confluent hyperintensity of the periventricular and deep white matter, with parieto-occipital predominance and frontal extension. The subcortical U-fibers are relatively spared. The deep gray nuclei and corpus callosum are preserved on the displayed images.

DECLARATIONS

Consent. Written informed consent for publication of this case and the anonymized images was obtained from the child's legal guardians.
Conflicts of interest. The authors declare no conflicts of interest.
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