SAS Journal of Medicine
Abbreviated Key Title: SAS J Med
ISSN 2454-5112
Journal homepage: https://saspublishers.com

OPEN ACCESS

Radiology

Diffuse White Matter Swelling with Subcortical Cysts in Childhood: MRI Features of Van Der Knaap Disease

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DOI: https://doi.org/10.36347/sasjm.2026.v12i05.002 | **Received:** 12.03.2026 | **Accepted:** 25.04.2026 | **Published:** 01.05.2026

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Abstract **Case Report**

Background: Megalencephalic leukoencephalopathy with subcortical cysts (MLC), also known as Van der Knaap disease, is a rare genetic leukodystrophy characterized by early-onset macrocephaly, mild initial neurological impairment, and distinctive MRI findings. ***Case presentation:*** We report the case of an 8-year-old boy presenting with motor developmental delay, progressive macrocephaly, and generalized tonic–clonic seizures. Brain MRI demonstrated diffuse, bilateral, and symmetrical supratentorial white matter abnormalities associated with subcortical cysts in the temporo-parietal regions. ***Imaging findings:*** MRI showed diffuse swelling of the cerebral white matter with hypointensity on T1-weighted images and hyperintensity on T2-weighted and FLAIR sequences, without diffusion restriction or post-contrast enhancement. Multiple bilateral temporo-parietal subcortical cysts were identified. These imaging features were highly suggestive of MLC. ***Conclusion:*** This case highlights the crucial role of MRI in the positive diagnosis of MLC and in differentiating it from other childhood leukodystrophies.

Keywords: Megalencephalic leukoencephalopathy; Van der Knaap disease; Macrocephaly; Subcortical cysts; Brain MRI; Pediatric neuroradiology.

INTRODUCTION

Megalencephalic leukoencephalopathy with subcortical cysts (MLC) is a rare inherited leukodystrophy first described by Van der Knaap *et al.,*[1]. It is characterized by early-onset macrocephaly, mild initial neurological symptoms, and a slowly progressive clinical course [2]. Epilepsy, motor delay, and cerebellar signs commonly develop during childhood [3]. MRI plays a pivotal role in diagnosis, revealing characteristic diffuse white matter abnormalities associated with subcortical cysts, predominantly in the temporal regions [4]. Recent studies have expanded the genetic and phenotypic spectrum of MLC, emphasizing the importance of imaging in guiding diagnosis and genetic testing [10].

CASE PRESENTATION

An 8-year-old male child was referred for neuroimaging evaluation due to delayed motor development, progressive macrocephaly, and recurrent generalized tonic–clonic seizures. There was no significant family history of neurological disorders. Clinical examination revealed marked macrocephaly and motor coordination impairment, without focal neurological deficit. Given the suspicion of a diffuse white matter disorder, a brain MRI was performed.

Imaging Findings

Brain MRI demonstrated diffuse, bilateral, and symmetrical abnormalities of the supratentorial white matter, resulting in a globally swollen appearance of the cerebral parenchyma (figure 1). The affected white matter showed hypointensity on T1-weighted images (figure 1a) and hyperintensity on T2-weighted (figure 1b) and FLAIR sequences (figure 1c), involving the subcortical white matter, centrum semiovale, and periventricular regions. There was no diffusion restriction on DWI (figure 1e) and no enhancement after gadolinium administration (figure 1f).

Multiple well-defined subcortical cystic lesions were identified in the bilateral temporo-parietal regions (figure 2). These cysts were oval in shape, hypointense on T1-weighted (figure 2 a, b) and FLAIR images (figure 2 e, f), and hyperintense on T2-weighted images (figure 2 c, d), without diffusion restriction (figure 2 g, h) or contrast enhancement (figure 2 i, j). The largest cyst was in the left temporal lobe. Additional findings included diffuse enlargement of the subarachnoid spaces, more

pronounced in the fronto-parietal regions (figure 2d arrow head), cavum septum pellucidum (figure 1b arrow head).

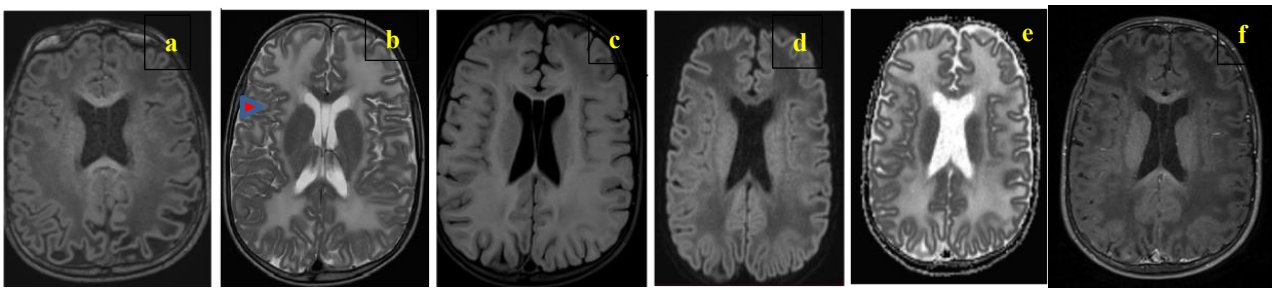

Figure 1: Diffuse, bilateral, and symmetrical abnormalities of the supratentorial white matter, with a swollen appearance of the cerebral parenchyma showed in hypointensity on T1-weighted images (a) and hyperintensity on T2-weighted (b) and FLAIR sequences (c) with no diffusion restriction on DWI (e) and no enhancement after gadolinium administration (f). Cavum septum pellucidum («b» Arrowhead)

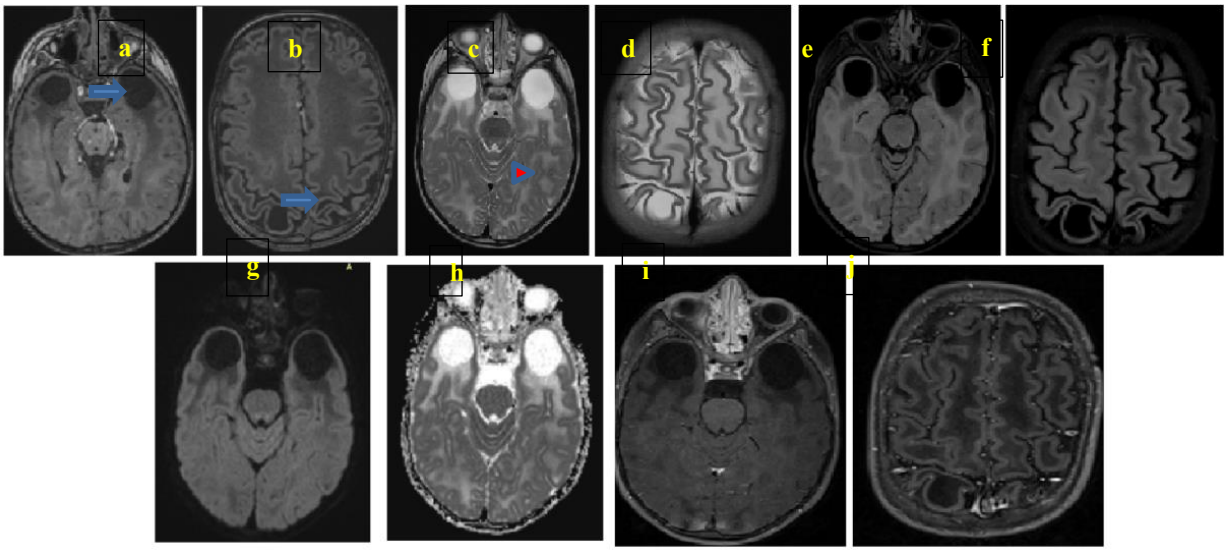

Figure 2: Multiple cystic lesions in the bilateral temporo-parietal regions (arrow), hypointense on T1-weighted (a, b) and FLAIR images (e, f), and hyperintense on T2-weighted images (c, d), without diffusion restriction (g, h) or contrast enhancement (i, j).
Diffuse enlargement of the subarachnoid spaces (« d» arrow head)

DISCUSSION

MLC is an autosomal recessive leukodystrophy mainly caused by mutations in the *MLC1* or *HEPACAM* (*GLIALCAM*) genes, which are involved in ion and water homeostasis of astrocytes [2,7]. Clinically, macrocephaly is usually the earliest manifestation, often preceding neurological deterioration by several years [3]. Seizures are common and may be generalized or focal [5].

From a radiological perspective, MRI is the cornerstone of diagnosis. Typical features include diffuse and symmetrical supratentorial white matter involvement with a swollen appearance, relative preservation of the basal ganglia and brainstem, and the presence of subcortical cysts, especially in the anterior temporal regions [4,6,8]. The absence of diffusion restriction and contrast enhancement helps distinguish MLC from inflammatory, infectious, or metabolic leukodystrophies [9].

Recent literature has reported an expanded mutational spectrum with significant genotype–phenotype variability, reinforcing the diagnostic value of MRI pattern recognition in selecting appropriate genetic testing strategies [10]. Differential diagnoses include metachromatic leukodystrophy, X-linked adrenoleukodystrophy, and hypomyelinating disorders, which typically lack subcortical cysts [4,9].

CONCLUSION

Megalencephalic leukoencephalopathy with subcortical cysts is a rare but distinctive leukodystrophy. MRI provides characteristic imaging findings that allow early and accurate diagnosis, guide genetic confirmation, and prevent unnecessary investigations. Awareness of this entity is essential for radiologists involved in pediatric neuroimaging.

Conflict of Interest: The authors declare no conflict of interest.

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