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Clinical, neuroimaging and genetic characteristics of megalencephalic leukoencephalopathy with subcortical cysts in Egyptian patients

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Background: Megalencephalic leukoencephalopathy with subcortical cysts (MLC) is a rare and genetically heterogeneous cerebral white matter disease. Clinically, it is characterized by macrocephaly, developmental delay, and seizures. We explore the clinical spectrum, neuroimaging characteristics, and gene involvement in the first patients with megalencephalic leukoencephalopathy with subcortical cysts described from Egypt.

Patients: Six patients were enrolled from three unrelated families. Patient inclusion criteria were macrocephaly, developmental delay, normal urinary organic acids, and brain imaging of diffuse cerebral white matter involvement. Direct sequencing of the MLC1 gene in patients' families and gliaCAM in one questionable case was performed using BigDye Terminator cycle sequencing.

Results: Clinical heterogeneity, both intra- and interfamilial, was clearly evident. Developmental delays ranged from globally severe or moderate to mild delay in achieving walking or speech. Head circumference above the ninety-seven percentile was a constant feature. Neuroimaging featured variability in white matter involvement and subcortical cysts. However, findings of posterior fossa changes and brain stem atrophy were frequently (66.6%) identified in these Egyptian patients. Discrepancy between severe brain involvement and normal mental functions was evident, particularly in patients from the third family. MLC1 mutations were confirmed in all patients. Deletion/insertion mutation in exon 11 (c.908-918delinsGCA, pVal303 Gly fsX96) was recurrent in two families, whereas a missense mutation in exon 10 (c.880 C>T, p.Pro294Ser) was identified in the third family.

Conclusions: This report extends our knowledge of the clinical and neuroimaging features of megalencephalic leukoencephalopathy with subcortical cysts. It confirms the apparent lack of selective disadvantage of MLC1 mutations on gamete conception and transmission as supported by the presence of multiple affected siblings in Egyptian families.

Biography

Alice K Abdel Aleem has her expertise in the field of Human Clinical and Molecular Genetics with interest in Neurogenetics disorders. Her primary area of interest is to provide reliable and high-quality research results to health care Physicians to improve diagnostics in human genetic disorders. Her current Extramural Funded Research is focusing on genes identification in monogenetic disorders. She is mainly concerned with building clinical and genomic databases for patients, encountered in Qatar, with spastic paraplegias, heritable muscle diseases, brain malformation, and interesting unrecognized Mendelian disorders. Results of her research is functionally investigated in her lab and in collaboration with investigators of international academic institutes to be able to provide confirmed information to the health care Physicians to use in counseling and managing their patients.

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