Inheritance pattern and molecular causes of familial megalencephalic leukoencephalopathy among clusters of Palestinian villages.

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Abstract :

Megalencephalic leukoencephalopathy with subcortical cysts (MLC) is a rare autosomal recessive neurodegenerative disorder characterized by early onset macrocephaly, developmental delay, and seizures. We investigated the clinical presentation, neuroimaging characteristics, and gene involvement in a group of Palestinian patients with megalencephalic leukoencephalopathy with subcortical cysts.

PATIENTS AND METHODS:

5 patients from three unrelated families living in the south east of Nablus district were involved in our study meeting the inclusion criteria. The inclusion criteria was macrocephaly, developmental delay and diffuse white matter abnormality in both cerebral hemispheres. Direct sequencing of the MLC1 gene in the patients' and their families was performed using BigDye Terminator cycle sequencing.

RESULTS:

There was a wide range of variability in clinical presentations, both Intra- and interfamilial. Developmental delays ranged from
globally severe or moderate to mild delay in achieving walking or speech. Head circumference above the 99th percentile was constant in all patients. Magnetic Resonance Imaging showed diffuse white matter involvement and characteristic subcortical cysts. Two variants were found, the first one was proved to be an MLC1 splicing mutation in intron 5 (c422+1G>A), it was recurrent in two families, and we expect to see the same mutation in the rest of the patients and their families due to a possible founder effect. The second variant was found to be a normal polymorphism in Palestinian population.

CONCLUSIONS:

The presence of the same mutation in two un related families who live in small geographic area is a strong indicator for a possible founder effect in Palestine. This study is first of its kind in Palestine and it will help in establishing a genetic database regarding MLC disease mutations in Palestine and the region. Further studies are needed on possible patients to confirm the founder

effect. This study will assist in extending our knowledge regarding MLC disease in the Palestinian population.