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Argentinian clinical genomics in a leukodystrophies and genetic leukoencephalopathies cohort: Diagnostic yield in our first 9 years

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Abstract

Introduction and objectives: Leukodystrophies and genetic leukoencephalopathies constitute a vast group of pathologies of the cerebral white matter. The large number of etiopathogenic genes and the frequent unspecificity on the clinical-radiological presentation generate remarkable difficulties in the diagnosis approach. Despite recent and significant developments, molecular diagnostic yield is still less than 50%. Our objective was to develop and explore the usefulness of a new diagnostic procedure using standardized molecular diagnostic tools, and next-generation sequencing techniques.

Materials and methods: A prospective, observational, analytical study was conducted in a cohort of 46 patients, evaluated between May 2008 and December 2016, with a suspected genetic leukoencephalopathy or leukodystrophy. A diagnostic procedure was set up using classical monogenic tools in patients with characteristic phenotypes, and next-generation techniques in nonspecific ones.

Results: Global diagnostic procedure yield was 57.9%, identifying the etiological pathogenesis in 22 of the 38 studied subjects. Analysis by subgroups, Sanger method, and next-generation sequencing showed a yield of 64%, and 46.1% respectively. The most common pathologies were adrenoleukodystrophy, cerebral autosomal-dominant arteriopathy with subcortical infarcts (CADASIL), and vanishing white matter disease.

Conclusions: Our results confirm the usefulness of the proposed diagnostic procedure expressed in a high diagnostic yield and suggest a more optimal cost-effectiveness in an etiological analysis phase.

Keywords: diagnostic procedure; genetic leukoencephalopathies; leukodystrophies; next-generation sequencing.

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