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Genetic leukoencephalopathies with unknown metabolic pathogenesis

Abstract The authors describe the principal forms of genetic leucodystrophies with unknown metabolic pathogenesis, indicating their main clinical signs and the new findings concerning the molecular genetic that are useful for the laboratory confirmation of the clinical suspicion.

Key words Leukodystrophies • White matter disorders • Neurodegenerative diseases

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Introduction

The recent advances in neuroimaging have actually improved the diagnosis of nervous system diseases leading to the discovery of their underlying pathogenetic mechanisms. These techniques even allow the diagnosis of diseases involving specific areas of the brain associated with progressive neurologic decline and multisystem involvement. The main diagnostic advances have been done in the white matter diseases, previously defined leukodystrophies on the basis of their pathology involving central myelin, and now better defined as leukoencephalopathies. They are characterized by central myelin degeneration and diffuse central myelin loss sparing, in some cases, U fibers.

Clinical aspects

The early infantile clinical onset leads to dysmyelination (structural alteration of myelin) or to hypomyelination (production of myelin that is biochemically normal, but with a developmental delay). The late infantile, juvenile or adult onset form is usually associated with milder symptoms, linked to slow myelin degeneration due to different pathogenetic mechanisms. Clinical findings are characterized by various degrees of behavioral changes, motor (cerebellar and pyramidal) involvement, seizures and inconstant myoclonus. Sometimes the demyelination can involve the peripheral nerves, with reduction of conduction velocities and various degrees of peripheral neuropathy.

Neuroimaging techniques are useful for the diagnosis, and show white matter hypodensity on computed tomography (CT). On magnetic resonance imaging (MRI), there are areas with low signal intensity on T1-weighted sequences because of myelin loss, or hyperintense areas on T2-weighted sequences because of water increase or gliosis.