

(PS20) White Matter Disease

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Childhood Leukodystrophies

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Heritable white matter disorders can be classified in two categories for better assessment:

A- classic leukodystrophies, that affect principally the myelin of the brain (sometimes also of the peripheral nerves) and in many cases some involvement of gray nuclei coexists .

B- genetic leukoencephalopathy, in which during clinical course of a systemic neurometabolic disorder, white matter of the nervous system is also affected.

The main inheritance pattern of these disorders is autosomal recessive. The reported incidence of leukodystrophies has a wide range from 1/5000 to 2/100000 among live births. The etiology is not determined in about 50% of patients that are categorized as unclassified leukodystrophies and majority of this last group are belonging to hypomyelinating leukodystrophies.

The main clinical manifestations of leukodystrophies are regression in motor developmental milestones and motor disturbances , especially pyramidal and cerebellar symptoms and signs , with slow mental deterioration .

The leukodystrophies may be classified according to enzymatic defect , pathology , etiology , affected organells and age of onset. Classification of WMDs according to Brain MRI findings seems to be applied and clinically oriented .Major factors in brain MRI that help for better diagnosis are: presence of hypomyelination or dysmyelination in T1 and T2 sequences , main location of involvement (subcortical or periventricular) ; confluent and symmetric lesions versus multifocal and asymmetric ones; tigroid pattern; ; cystic changes and calcification and contrast enhancement. Important clues for diagnostic approach are : age of onset of symptoms; some hints in history and physical examination such as head circumference (macrocephaly or microcephaly) , other organ involvement (skeletal, dental , gastrointestinal and ocular) . The diagnostic strategy rests upon clinical clues and MRI patterns, complemented by appropriately selected electrophysiological and laboratory testing.

Most leukodystrophies are incurable and have a progressive course, leading to premature death. Diagnosis is important as palliative or experimental therapies may offer benefits, for genetic counseling and family screening of currently unaffected individuals. Some beneficial proceedings for improvement of quality of life of patients are: attention to the patient's

swallowing and feeding condition; control of pain and spasm and correction of endocrine abnormalities. More fundamental steps that are considered in recent years to treat these patients are: Enzyme Replacement Therapy (ERT) ,Substrate Reduction Therapy (SRT) , cell-based therapy such as bone marrow transplantation and gene therapy.

In our Neurometabolic registry website that constructed in 2010 about 185 patients have been registered that are belonging to different groups of Neurometabolic disorders. We have registered 80 patients that are categorized into classic and unclassified leukodystrophies. We found that the most common type of leukodystrophy among our patients is Metachromatic leukodystrophy. Other common types were Canavan disease, unclassified leukodystrophies and X-linked Adrenoleukodystrophy.

Key Words : Leukodystrophy , Leukoencephalopathy , Hypomyelination , Dysmyelination