Metachromatic leukodystrophy: Overveiw

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MLD, also called Arylsulfatase A deficiency is a lysosomal storage disease which is commonly listed in the family of leukodystrophies It is caused by the enzyme deficiency arylsulfatase A(ARSA) and is characterized by enzyme activity in leukocytes that is less than 10% of normal controls. However, assay of the ARSA enzyme activity alone is not sufficient for diagnosis; ARSA Pseudodeficiency, which is characterized by enzyme activity that is 5-20% of normal controls does not cause MLD. A recent study indicates sulfatide is not completely responsible for MLD because it is nontoxic, instead lysosulfatide, which has its acyl group removed, plays cytotoxic role in vitro.

In addition there is a 'pseudo'-deficiency that affects 7%-15% of the population. People with the pseudo deficiency do not have any MLD problems unless they have affected status. With the current diagnostic tests, Pseudo-deficiency reports as low enzyme levels but sulfatide is processed normally so MLD symptoms do not exist. The incidence of MLD that has autosomal recessive inheritance pattern. is estimated to occur in 1 in 40, 000 to 1 in 160, 000 individuals worldwide, but much higher in certain genetically isolated populations, in jewish. There are several forms of MLD, which are late infantile, juvenile, and adult. The late infantile form is the most common form in which affected children display walking difficulty after the first year of life, Symptoms include muscle weakness, rigidity, developmental delays, progressive loss of vision leading to convulsions, impaired swallowing, paralysis, and dementia. Untreated, most die by age 5. Children with the juvenile form onset between 3 and 10 years of age usually with impaired school performance, and dementia, then develop symptoms similar to the late infantile form but with slower progression.The adult form that consists of 15 to 25 percent of the cases can appear at any age after puberty. It presents as a psychiatric disorder or progressive dementia. Adult-onset MLD progresses more slowly than the late infantile and juvenile forms, Carriers have low enzyme levels " but adequate to process the body's sulfatide MLD diagnosis is often missed or delayed because it is not the first cause that comes to mind when a patient presents with symptoms. In young children, MLD is often confused with CP or other causes of developmental delay. In older children, it is frequently confused with Batten disease, ADHD or adolescent/puberty-related behavioral changes. In adults, psychological conditions are often suspected. .MRI of the brain may be the first indicative test a patient undergoes. It shows patterns of dysmyelination. Urine and blood samples are required for a formal diagnosis MRI is not definitive for diagnosis since abnormal findings could be seen in other conditions. The blood arylsulfatase A enzyme levels are measured first, followed by urine sulfatide levels and clinical analysis. An increased amount of sulfatide in the urine suggests MLD. While low level of ASA enzyme in the blood is not a

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definitive test for MLD because the low levels of ASA are also found in ASA pseudodeficiency, a condition that results in individuals having only 5% to 15% of ASA enzyme function. However, this deficiency does not pose a health risk and individuals do not develop MLD.
An evoked potential test and a nerve conduction velocity test may also be performed.. These tests can reveal a delayed or impaired response in brain and peripheral Nerves consequently.
Finally, molecular analysis, also called DNA testing, can be done to confirm a diagnosis of MLD. In many cases, this kind of test can even determine which one of the more than 110 MLD-associated alleles is present. This can be useful if the patient has a family history of MLD.

Treatment

Currently there is no treatment or cure for advanced MLD.and treatment is limited to symptom management. Presymptomatic late infantile MLD patients, as well as those with juvenile or adult MLD that are either presymptomatic or displaying mild to moderate symptoms, have the option of bone marrow transplantation (including stem cell transplantation), which is under investigation to see if it may slow down progression of the disease or stop its progression in the central nervous system. However, results in the peripheral nervous system have been less dramatic. Several future treatment options are currently being investigated. These include gene therapy, enzyme replacement therapy (ERT), substrate reduction therapy (SRT), and potentially enzyme enhancement therapy.

Keywords: MLD; Form; Symptoms; Diagnosis; Treatment