Cystic leukoencephalopathy

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Cystic changes in the white matter can be caused by heterogeneous neurologic disorders. They are classified in two main categories: a) cystic finding in association with known classic leukodystrophy and b) white matter cystic abnormalities that are not seen in the background of a classic leukodystrophy.

The main disorders in group (a) are including: Megalencephalic leukoencephalopathy with subcortical cyst(MLC) or vanderknaap disease, RNAase T2 deficiency, congenital CMV infection, cerebroretinal microangiopathy with calcificationand cysts (coat's plus syndrome or CRMCC) and less commonly Aicardi-Goutieres syndrome and Alexander's disease.

Group (b) consists of various disorders. Autistic spectrum disorders, mucopolysaccharidosis, structural chromosomal abnormalities, migraine headache, mitochondrial leukoencephalopathy (complex I, complex II and complex IV deficiency) and COL4A1 associated disorder are main diseases that can be classified in this group. For some of these disorders, such asautistic spectrum disorders and mucopolysaccharidosisCystic changes are thought to be due to dilated Virchow-robin or perivascular spaces. It is not cleared that cystic findings of white matter in these disorders are functional effects or are specific for diagnosis.

Megalencephalicleukoencephalopathy with subcortical cyst (MLC) or van der Knaap's disease is characterized by a mild course and macrocephaly that is a cardinal feature for diagnosis and differentiates MLC from RNAase T2 deficient leukoencephalopathy, AGS and CMV infection. In the initial stages of disease, Patients show mild motor and cognitive delay. Later in life spastic ataxia, epilepsy, dysarthric speech and cognitive deterioration are seen. Important brain MRI features are including: diffuse white matter signal abnormality with relative sparing of central structures and cystic changes in temporal or frontoparietal regions. Genetic study and searching for MLC1 gene mutation confirms the diagnosis of MLC.

RNAase T2 deficient leukoencephalopathy that was described for the first time by henneke in 2009 is characterized by psychomotor delay, spasticity and epilepsy. Its radiologic findings in brain MRI resemble congenital CMV infection and MLC, but in contrast to MLC the patient has normo- or microcephaly in association with intracranial calcifications. In another hand there is no evidence of CMV infection. It must to be mentioned that human RNAase T2 is a catalytic enzyme with some new known function about tumor suppression. Its role in this type of leukoencephalopathy is still unclear.

Cerebroretinal microangiopathy with calcification and cysts (CRMCC)or labrunedisease is an obliterativevasculopathy with unidentified genetic etiology that involves multiple organs mainly brain, eyes, liver, intestine and bones. Therefore progressive neurologic symptoms, bone fracture and osteopenia, bilateral retinal

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telangectasia and portal hypertension are main clinical symptoms in this disease, although not all organs are involved in each patient. Neuroimaging findings are a distinct pattern of calcification in white matter of brain and cerebellum, basal ganglia and thalamus with parenchymal cysts and leukoencephalopathy.

Aicardi-Goutieres syndrome (AGS) is a calcifying leukoencephalopathy that can present in both neonatal period or in older infants. Symptoms in neonatal period resemble a TORCH-like disorder such as congenital CMV, but in older infants the disease is characterized by progressive microcephaly, dystonia, seizures and progressive cerebral atrophy and calcification. One of important diagnostic criteria in AGS is CSF findings of leukocytes, pterins and interferon-alpha.

Naidu described in 2005 a specific type of cystic leukoencephalopathy as named progressive cavitatingleukoencephalopathy, but it seems there is no consensus on this term and many things can cause cavitating degeneration of white matter. For example in recent years it has been found that some mitochondrial diseases such as complex I deficiency can present with progressive cavitating leukoencephalopathy.

Some infectious agents such as CMV, HIV, and papoavirus that cause progressive cystic leukoencephalopathyare mentioned as a group of etiologic factors in association with cystic changes in white matter in the literature.

Therefore, as mentioned before this, cystic leukoencephalopathy can be caused by heterogeneous factors that may be heritable or acquired.

Keywords: Leukoencephalopathy; Cystic;
Leukodystrophy