Case Report

Late Infantile Metachromatic Leucodystrophy

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ABSRACT

Metachromatic leucodystrophy (MLD) is a genetically heterogenous disorder and comprises of atleast five distinct autosomal recessive disorders . Demyelination in central and peripheral nervous systems is the hall mark in all of them .There is accumulation of galactosyl sulphatide in the schwann cells, macrophages and glia ; due to deficiency of arylsulphatase A (ASA) . This deposited material stains metachromatically with aniline dyes (toludine blue) and is hence named MLD .The patients of late infantile MLD manifest in the first two or three years of life and die at about the age of 6 years. The diagnosis is usually established by assay of ASA in leucocytes, cultured fibroblast or urine but nerve biopsy can provide extremely rapid and accurate diagnosis. Prenatal diagnosis by amniocentesis is possible in the first trimester of pregnancy. We report a case of late infantile metachromatic leucodystrophy which was admitted with developmental regression and myoclonic seizures. Neurological examination revealed muscle wasting, hypotonia, sluggish deep tendon reflexes and weakness in all four limbs. MRI showed restricted diffusion of white matter and deficiency of aryl sulphatase A in the leucocytes which confirmed the diagnosis of metachromatic leucodystrophy.

KEYWORDS: Metachromatic leucodystrophy; developmental regression; aryl sulphatase A .

CASE REPORT

A five year old male child born to second degree consanginous parents presented with developmental milestones regression and convulsions. This child acquired all the developmental milestones appropriate to the age upto 3 years. After that child had progressive to sit, later became bed ridden indicating progressive loss all the acquired milestones. Since one and half months child was having myoclonic seizures.

On examination, child is alert and normocephalic. All the vital parameters were within normal limits. Anthropometric measurements indicate grade 2 PEM.

On neurological examination, child was conscious, aphasic with emotional instability. All cranial nerves were normal. Reduced muscle bulk, hypotonia, weakness present in all the four

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limbs. Deep tendon reflexes were sluggish in all the four limbs. Plantar response was extensor. Cerebellar signs were absent and autonomic dysfunction was present.

Lab diagnosis indicates normal haemogram, increased CSF protein. MRI brain revealed restricted deffusion noted in genu of corpus callosum corona radiata. Bilateral symmetric diffuse white matter T2 and T2 flair hyperintensity (fig.1&2). For conduction study, facilities are not available. The diagnosis was confirmed by aryl sulphatase A assay, which indicate deficient aryl sulphatase A activity in leucocytes. This patient's aryl sulphatase A level was 20nmol/hour/mg , normal reference value is 62nmol / hour/mg .[10]

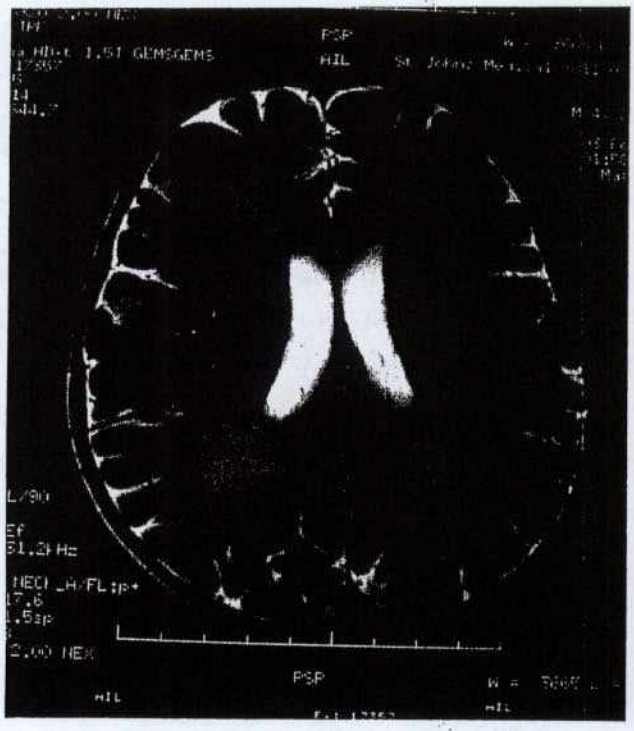

Fig. 1: T2 axial and flair sequences at the level of lateral ventricles.

may lead to progressive psychomotor retardation, morbidity and death of the children. The most distinct members of the category are the so called lysosomal storage diseases. There is a genetic deficiency of the enzyme , that are necessary for the degradation of glycoprotein, glycolipids and mucopolysaccharides within the cells.[1,2] It is the type of enzyme deficiency and accumulated metabolite, as well as the tissue distribution of the undergradable substrate, that impart a distinctive biochemical and clinical character to the disease.[3] This disease can be diagnosed prenatally and prevented. Detection of carrier state is also possible.[4] Leucodystrophies constitute a significant proportion of the inherited metabolic disorders.

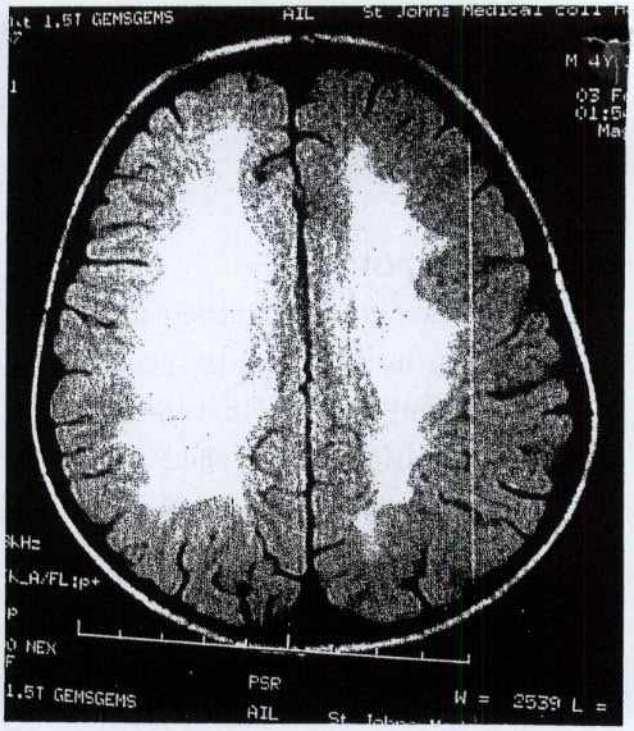

Fig. 2: Showing hyperintense signals in the bilateral periventricular deep white matter.

DISCUSSION

Inherited metabolic disorders of nervous system

They manifest as Psychomotor retardation, optic atrophy and spasticity with abolished tendon

reflexes (peripheral neuropathy). MLD is easy to differentiate from the other leucodystrophies by detection of metachromatic bodies in urine and nerve biopsy.[5] There are at least five distinct disorders of MLD depending on age of presentation and clinical features. Late infantile MLD begins between 1 and 4 years, usually between 15 and 18 months with normal antecedent development. The siblings reported here fit into this category of MLD. Hagberg[2] divided the course of the disease into 4 stages. Walking difficulties, unsteady gait, inability to stand, weakness of feet, hypotonia in lower limbs and retardation of mental development are seen in the first phase. In the second phase ataxia, more pronounced hypotonia with weakness of legs, inability to sit support, hyporeflexia, spasticity and seizures are seen .Central nervous symptoms like speech impairment, apathy, vision loss predominate in the third stage. In the fourth stage, decebrate rigidity, bulbar symptoms, deafness, blindness and hypertonic seizures are seen .

A rapid and accurate diagnosis of MLD is possible by pathological study of the nerves.[6,7] Extensive segmental demylination with metachromatically staining material within Schwann cells and macrophages and abnormally thin myelin are seen in the peripheral nerves in all types of MLD.[8] and provides rapid and accurate diagnosis. The treatment is mainly supportive. Presymptomatic late infantile MLD patient, as well as those with juvenile or adult MLD that are either symptomatic 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 disease , or stop its progression in the central nervous system. However, results in the peripheral nervous system have been less dramatic, and the long-term results of these therapies have been mixed. Several treatment options for the future are currently being investigated.[9] These include gene therapy and enzyme replacement therapy (ERT), substrate reduction therapy (SRT), and potentially enzyme enhancement therapy (EET).[10]

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