***SPHINGOLIPIDOSES***

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*Learning Objective*

*Enlist the disorders with their respective enzyme deficiencies.*

*Discuss pathology of the Sphingolipidoses*

*Explain the presentation and progression*

*Describe principles of management*

*What is Sphingolipid*

***Sphingolipids****are a class of lipids containing a backbone of sphingoid bases, a set of aliphatic amino alcohols that includes sphingosine*

*Sphingolipids*

*Are present in all Human tissues*

*The greatest concentration is found in central nervous system(CNS), particularly the white matter*

*These compounds play important roles in signal transmission and cell recognition*

*Sphingolipidoses*

*“Are inherited genetic disorder referred to as Lipid storage disease, in which there is deficiency of an enzyme that is involved in the normal catabolism of a particular sphingolipid. This results in the intracellular accumulation of that lipid leading to harmful events”.*

*Sphingolipidosis*

*Tay-Sachs disease*

*Enzyme deficiency: hexosaminidase A*

*Metabolite accumulation: GM2 ganglioside*

*Primary seen in Ashkenazi Jews*

*Patients are normal at birth but develop signs of severe mental retardation within 6 months*

*massive hepatosplenomegaly*

*Mental retardation, blindness*

*Cherry-red spot in the macula*

*Muscle weakness and flaccidity*

*Death by 2-3 years*

*Niemann-Pick*

*- Enzyme deficiency: sphingomyelinase*

*Metabolite accumulation: sphingomyelin*

*The accumulation of sphinomyelin is primarily in macrophages (bubbly appearance) and in neurons*

*Severe mental retardation, massive hepatosplenomegaly, and deterioration of psychomotor function.*

*The disease is fatal in early life(death by 2 yrs)*

*Zebra bodies are noted in lysosomes on electron microscopy*

*Gaucher disease*

 *- Enzyme deficiency: glucocerbrosidase*

*Metabolite accumulation: glucocerebroside*

*massive hepatosplenomegaly*

*Bone pain,bone marrow (produces pancytopenia)*

*No CNS involvement*

*Increase in the total acid phosphatase*

*Compatible with life*

Metachromatic leukodystrophy

*Enzyme deficiency: arylsulfatase A*

*Metabolite accumulation: sulfatide*

*The myelin that is synthesized is abnormal, affecting the CNS and peripheral nerves*

*Clinical:*

*Mental retardation, peripheral neuropathy and problems with visceral organs*

*Urine arylsulfatase activity is decreased or absent*

*Krabbe disease*

*Enzyme deficiency: galactosylceramidase*

*Metabolite accumulation: galactocerebroside*

*Similar to metachromatic leukodystrophy with synthesis of abnormal myelin*

*Clinical:*

*Progressive psychomotor retardation*

*Brains at autopsy show multinucleated globoid cells containing the galactocerebroside*

*Fabry disease*

*Enzyme deficiency: alpha galactocerebrosidase A*

*Metabolite accumulation: ceramide trihexoside*

*Clinical:*

*Characterized by angiokeratomas on the skin, hypertension and renal failure*

*Diagnosis: for presence enzyme activity and accumulated lipid*

*1. Enzyme assay activity*

 *Peripheral blood , fibroblast, Plasma or/and amniotic fluid*

*2. Accumulated lipid in tissue biopsies*

*3. DNA analysis*

*Treatment*

* *Enzyme Replacement Therapy*
* *Bone Marrow Transplant*
* *Gene Therapy*

*Take Home Message*

* *Sphingolipids are complex lipids that includes sphingo-phospholipids and glycolipids*
* *Sphingolipids are present mainly in nerve tissue*
* *Sphingolipidosis are rare, genetic diseases due to defective degradation of sphingolipids*

 *Have a Great day!*