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!