Hello to dear master, Dr.M.Hemmati

I explicated the gangliosidosis and effects or signs that cause

**Gangliosidosis** is a sub-category of **Sphingolipidosis** that contains two different types of **lipid storage disorders** caused by the accumulation of lipids known as **gangliosides**. There are two distinct genetic causes of the disease. Both are autosomal recessive and affect males and females equally.

**For GM2**

GM1 has three forms: early infantile, late infantile, and adult.

**Early infantile GM1**

Symptoms of early infantile GM1 (the most severe subtype, with onset shortly after birth) may include **neurodegeneration**, **seizures**, liver enlargement (**hepatomegaly**), spleen enlargement (**splenomegaly**), coarsening of facial features, skeletal irregularities, joint stiffness, distended abdomen, muscle weakness, exaggerated startle response to sound, and problems with **gait**.

About half of affected patients develop cherry-red spots in the eye.

Children may be **deaf** and **blind** by age 1 and often die by age 3 from **cardiac** complications or **pneumonia**.

- **Autosomal recessive disorder:** beta-galactosidase deficiency; neuronal storage of GM1 ganglioside and visceral storage of galactosyl oligosaccharides and **keratan sulfate**.
- Early psychomotor deterioration: decreased activity and lethargy in the first weeks; never sit; feeding problems - failure to thrive; visual failure (nystagmus noted) by 6 months; initial hypotonia; later spasticity with pyramidal signs; secondary microcephaly develops; decerebrate rigidity by 1 year and death by age 1–2 years (due to pneumonia and respiratory failure); some have hyperacusis.
- Macular cherry-red spots in 50% by 6–10 months; corneal opacities in some
- Facial dysmorphology: frontal bossing, wide nasal bridge, facial edema (puffy eyelids); peripheral edema, epicanthus, long upper lip, microretrognathia, gingival hypertrophy (thick alveolar ridges), macroglossia
- Hepatomegaly by 6 months and splenomegaly later; some have cardiac failure
• Skeletal deformities: flexion contractures noted by 3 months; early subperiosteal bone formation (may be present at birth); diaphyseal widening later; demineralization; thoracolumbar vertebral hypoplasia and beaking at age 3–6 months; kyphoscoliosis. *Dysostosis multiplex (as in the mucopolysaccharidoses)

• 10–80% of peripheral lymphocytes are vacuolated; foamy histiocytes in bone marrow; visceral mucopolysaccharide storage similar to that in Hurler disease; GM1 storage in cerebral gray matter is 10-fold elevated (20–50-fold increased in viscera)

• Galactose-containing oligosacchariduria and moderate keratan sulfaturia

• Morquio disease Type B: Mutations with higher residual beta-galactosidase activity for the GM1 substrate than for keratan sulfate and other galactose-containing oligosaccharides have minimal neurologic involvement but severe dysostosis resembling Morquio disease type A (Mucopolysaccharidosis type 4).

Late infantile GM1

Onset of late infantile GM1 is typically between ages 1 and 3 years.

Neurological symptoms include ataxia, seizures, dementia, and difficulties with speech.

Adult GM1

Onset of adult GM1 is between ages 3 and 30.

Symptoms include muscle atrophy, neurological complications that are less severe and progress at a slower rate than in other forms of the disorder, corneal clouding in some patients, and dystonia (sustained muscle contractions that cause twisting and repetitive movements or abnormal postures). Angiokeratomas may develop on the lower part of the trunk of the body. Most patients have a normal size liver and spleen.

And for GM2

Signs and symptoms

Tay–Sachs disease is typically first noticed in infants around 6 months old displaying an abnormally strong response to sudden noises or other stimulus, known as the "startle response", because they are startled. There may also be listlessness or muscle stiffness (hypertonia). The disease is classified into several forms, which are differentiated based on the onset age of neurological symptoms.
**Infantile Tay–Sachs disease.** Infants with Tay–Sachs disease appear to develop normally for the first six months after birth. Then, as neurons become distended with gangliosides, a relentless deterioration of mental and physical abilities begins. The child may become blind, deaf, unable to swallow, atrophied, and paralytic. Death usually occurs before the age of four.

**Juvenile Tay–Sachs disease.** Juvenile Tay–Sachs disease is rarer than other forms of Tay–Sachs, and usually is initially seen in children between two and ten years old. People with Tay–Sachs disease develop cognitive and motor skill deterioration, dysarthria, dysphagia, ataxia, and spasticity. Death usually occurs between the age of five to fifteen years.

**Adult/Late-Onset Tay–Sachs disease.** A rare form of this disease, known as Adult-Onset or Late-Onset Tay–Sachs disease, usually has its first symptoms during the 30s or 40s. In contrast to the other forms, late-onset Tay–Sachs disease is usually not fatal as the effects can stop progressing. It is frequently misdiagnosed. It is characterized by unsteadiness of gait and progressive neurological deterioration. Symptoms of late-onset Tay–Sachs – which typically begin to be seen in adolescence or early adulthood – include speech and swallowing difficulties, unsteadiness of gait, spasticity, cognitive decline, and psychiatric illness, particularly a schizophrenia-like psychosis. People with late-onset Tay–Sachs may become full-time wheelchair users in adulthood.

Until the 1970s and 1980s, when the disease's molecular genetics became known, the juvenile and adult forms of the disease were not always recognized as variants of Tay–Sachs disease. Post-infantile Tay–Sachs was often misdiagnosed as another neurological disorder, such as Friedreich's ataxia.

Thank you for your attention