

Gastrointestinal Symptoms in Lysosomal Disease

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Mucopolysaccharidoses

The mucopolysaccharidoses (MPS) are lysosomal storage disorders caused by the deficiency of enzymes required for the stepwise breakdown of glycosaminoglycans (GAGs), previously known as mucopolysaccharides (1-5). Fragments of partially degraded GAGs accumulate in the lysosomes, resulting in cellular dysfunction and clinical abnormalities. These are rare conditions, with an estimated total incidence of all types of MPS of approximately 1 in 20,000 live births. Mucopolysaccharidoses are hereditary, progressive disease caused by mutations of genes coding for lysosomal enzymes needed to degrade glycosaminoglycans. Mucopolysaccharidoses are autosomal recessive disorders, with the exception of hunter disease which is x-linked recessive. Their overall frequency is between 3.5/100000 and 4.5/100000. The most common subtype is MPS-III (Sanfilippo), followed by MPS-I (Hurler) and MPS-II (Hunter).

Hurler disease: Presenting symptoms included joint stiffness, corneal clouding, and recurrent ear, nose, and throat complaints. The patient appears normal at birth, but inguinal hernias are often present. Inguinal and umbilical hernias resulting from connective tissue abnormalities are common, especially in MPS I, II, VI, and VII (2,6-7). They may occur early, as part of the initial presentation, and can become quite large (8). Hernias can also occur at the incision site following abdominal surgery. Hepatosplenomegaly between 6-24 month may contribute to increased intra-abdominal pressure and lead to hernia formation.

Surgical repair of inguinal hernias often fails and needs to be repeated. Hepatosplenomegaly and the weak connective tissues may contribute to poor results. Thus, in some patients, management with trusses may be preferable to the risk of anesthesia and a surgical repair that is likely to be temporary. Large umbilical hernias that occur in MPS I should be repaired when possible, as their size can lead to breakdown of the overlying skin.

Diarrhea — MPS II and III patients may develop recurrent or chronic diarrhea. The mechanism is thought to be MPS storage in the neurons of the myenteric plexus, leading to abnormal motility (9). Although motility has not been directly studied, storage in these cells has been demonstrated in biopsies of the intestinal wall (10). Diarrhea can be improved with medications that decrease bowel motility(10).

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Hunter disease: gastrointestinal storage may produce chronic diarrhea.

Sanfilippo disease and MPS-IV: Physical findings are milder than in Hurler syndrome and include typical coarse facial features, dysostosis multiplex, hepatosplenomegaly, and hernias.

Gaucher disease

Gaucher disease (GD) is an inborn error of metabolism that affects the recycling of cellular glycolipids. Glucocerebroside (also called glucosylceramide) and several related compounds that are ordinarily degraded to glucose and lipid components accumulate within the lysosomes of cells.

GD is one of the few inherited metabolic disorders that can be treated by replacement of the deficient enzyme (enzyme replacement therapy). Because early treatment can prevent development of irreversible complications, early identification is crucial to improving ultimate outcome (1).

This disease is a multisystemic lipidosis characterized by hematologic problems, organomegaly, and skeletal involvement. Gaucher disease results from the deficient activity of the lysosomal hydrolase, acid β -glucosidase.

Gastrointestinal manifestation including: progressive massive hepatomegaly (all types; moderate to severe 63% at presentation) with or without elevated liver function results, cholestasis, Splenomegaly (all types; moderate to severe 85% at presentation), ascites, FTT. Liver cirrhosis, portal hypertension, esophageal varices, upper gastrointestinal bleeding and acute liver failure has been reported. Hepatosplenomegaly may be asymptomatic or may be associated with early satiety, abdominal complaints (distension, discomfort, pain), and/or anemia and thrombocytopenia.

Neimann pick disease

Hepatic and gastrointestinal manifestation of NPD characterized by prolonged neonatal jaundice, cholestasis, hepatomegaly, splenomegaly, liver cirrhosis, ascites, portal hypertension, esophageal varices and upper gastrointestinal bleeding, progressive dysphagia makes oral feeding impossible.

Keywords: Gastrointestinal Tract; Symptoms; Diagnosis; Child

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