Acid sphingomyelinase deficiency (ASMD)

Ex-Niemann-Pick disease A, A/B, B

by François Barde

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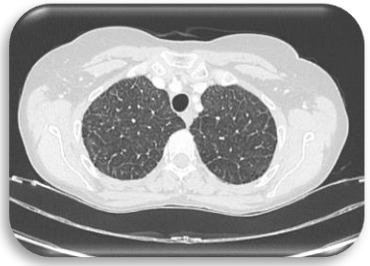
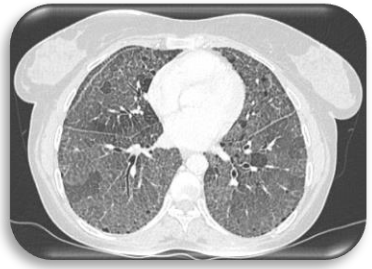
Acid sphingomyelinase deficiency
= ASMD
Ex-Niemann-Pick disease A, A/B, B
Autosomal recessive genetic disorder

Pathogenesis
Lysosomal storage disorder
Accumulation of sphingomyelin in cells of the monocyte-macrophage system
"foam cells"
Substrate-specific toxicity

Diagnosis
Sphingomyelin dosage ↘
Acid sphingomyelinase activity < 10%
SMPD1 gene mutation

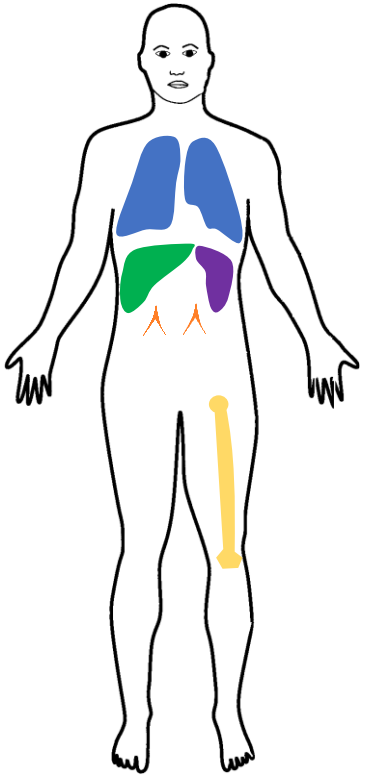
Differencial diagnosis
Gaucher disease ↘ glucocerebrosidase





Clinical manifestations (type B)

Prevalence	1:250 000 (types A and B combined) 1:80 gene mutation frequency in Ashkenazi Jewish community
Onset	Adulthood
Time to diagnosis	5 years



Interstitial lung disease >80%
*Cranio-caudal gradient, bilateral ground-glass opacities, interlobular septal thickening, "crazy paving" pattern , **DLCO** ↘ +++*

Hepatomegaly 70%

Splenomegaly 90%

Adrenal enlargement

Osteopenia, short stature

Biological features

Hepatic cyolysis and cholestasis	75%
Abnormal lipid profile : ↘ **HDL-c**	50-75%
Thrombocytopenia	> 50%
Anemia and leukopenia	30%

Complications
Bleedings, bruise (50%)
Respiratory failure
Hepatic fibrosis
Association with MGUS

Therapeutic management
Enzyme replacement therapy
OLIPUDASE ALFA 3 mg/kg every 2 weeks IV
Non systematic

Niemann-Pick type A
Paediatric onset, acute neuronopathic form,
Death at 2-3 years, no enzymotherapy

Niemann-Pick type A/B
Childhood onset, 1/3 with neurological abnormalities (peripheral neuropathy, intellectual disability)
Enzyme replacement therapy non systematic

Niemann-Pick C ≠ ASMD
NPC1 or *NPC2* gene mutation
Central nervous system involvement : ataxia, vertical supranuclear ophtalmoplegia, cognitive deterioration, schizophrenia