Acid Sphingomyelinase Deficiency and Niemann-Pick Disease

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NATIONAL NIEMANN-PICK DISEASE FOUNDATION, INC.

Disclosure Slide

- Financial - I have no relevant financial relationships to disclose.

Objectives

- Provide a brief overview of Niemann-Pick Disease
- Define Acid Sphingomyelinase Deficiency (ASMD) and explain why it is the preferred name for the diseases currently identified as Niemann-Pick type A and Niemann-Pick type B
- Describe the intermediate phenotype in ASMD and discuss the importance of its formal recognition in ICD-10-CM

Niemann-Pick Disease: a Lysosomal Storage Disease

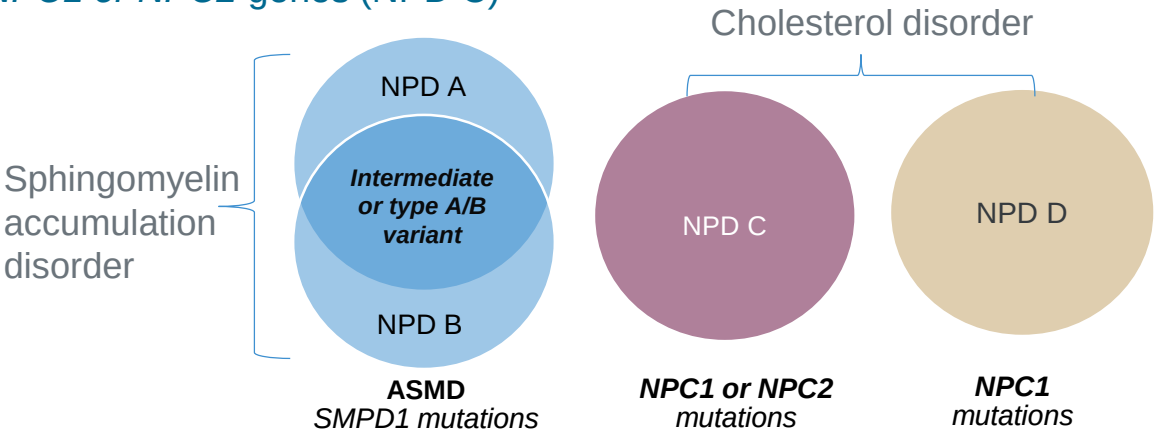
- Lysosomal storage diseases
  - Inherited metabolic disorders
  - Caused by enzyme deficiencies in the lysosome resulting in accumulation of a substrate
  - Multi-systemic, progressive with a significant impact on health
  - Neurodegenerative conditions that usually present in childhood

Overview of ASMD

- Acid Sphingomyelinase Deficiency
- ASMD is a rare autosomal recessive single gene disease with an estimated incidence of 0.4 to 0.6 in 100,000 newborns[1]
- The mutations in the *SMPD1* gene cause sphingomyelin to accumulate in various tissues in the body and cause substantial damage:
  - Commonly in the liver, spleen, bone marrow and lung
  - Brain/central nervous system in more severe cases

How does ASMD relate to the other Niemann-Pick Diseases?

- Niemann-Pick Disease is actually a group of ***different disorders***
  - different genes causing different cholesterol problems resulting in different disease manifestations
- Acid Sphingomyelinase Deficiency (ASMD) is associated with what has historically been called NPD A and NPD B and is caused by mutations in the *sphingomyelin phosphodiesterase 1* (*SMPD1*) gene[1,2]
- NPD C and D are a disorders of cholesterol esterification, and are caused by mutations in *NPC1 (NPD D)* or *NPC1 or NPC2* genes (NPD C)[1,3]



Classification and Spectrum of ASMD Disease

Clinical spectrum

Nomenclature	Severe phenotype	Intermediate Phenotype	Attenuated phenotype
Recommended Revised Nomenclature	Infantile neurovisceral ASMD Type A	Chronic neurovisceral ASMD Type A/B	Chronic visceral ASMD Type B
Onset	Early infancy	Infancy to childhood	Infancy to adulthood
Phenotype	Rapidly progressive, severe visceral disease and neurodegeneration	Slowly progressive, variable visceral disease and neurodegeneration that includes developmental delay, intellectual disability, ataxia, and peripheral neuropathy	Slowly progressive, variable visceral disease with little or no neurologic involvement
Life expectancy	Death by age 3	Death from childhood to mid-adulthood	Death from childhood to late adulthood

Update 1# New ICD-10-CM Code

Chronic Neurovisceral ASMD type A/B

Providers need assistance in diagnosing rare diseases

- Providers need tools including ICD-10-CM to establish the correct diagnosis

Establishing correct treatment plans and providing a prognosis require an accurate diagnosis

- Prognosis, supportive care and outcomes differ between ASMD type A, A/B and B
- Incorrect diagnosis can have a significant impact on patients and families

The ASMD community needs accurate data

- Research is guided by understanding of prevalence
- Clinical trial enrollment (and eventually therapeutic options) will depend on accurate diagnosis

Update #2 Secondary descriptors

- *1) ASMD: Acid sphingomyelinase deficiency*
  - Current nomenclature is outdated and doesn't accurately reflect the ASMD *spectrum* of disease
  - Newer term *ASMD* accurately describes the disease
  - Align with researchers, clinicians, organizations, patients
- *2) Infantile neurovisceral, chronic neurovisceral and chronic visceral*
  - Using terms that describe the manifestations of the disease will improve diagnostic accuracy
  - Common nomenclature already in use the LSD community
  - Establish accurate prognosis to assist and support patients and families
  - Support research and development

Conclusion

- **ICD-10-CM guides clinicians and researchers, especially in rare disease**
- **Modification of these codes will:**
  - Shorten the diagnostic journey
  - Improve patient care
  - Facilitate research
- **INPDA, NNPDF, ASH, AAP, ACMG have reviewed and support this proposal**

thank you