NGLY1 Deficiency

- Global developmental delay
- Intellectual diability
- Hypotonia
- Hypo- or alacrima

Eye Findings

- Hypolacrima (83%)
- Incomplete or abnormal blink (73%)
- Optic disc abnormalities (73%)
    - Peripapillary atrophy, cupping
- Corneal abnormalities typically found with dry eye
    - punctate epithelial erosions
    - pannus and neovascularization
- Conjunctival injection (60%)
- Strabismus (33%)
    - Exotropia > Esotropia
    - Restricted ocular movements
- Iris abnormalities
    - Reduced pupillary reactivity (47%)
    - Irregular iris (27%)
- Nystagmus- rare

Other Findings

- Increased liver transaminases
- Polyneuropathy

Etiology

- Autosomal Recessive
- Loss-of-function variants of the NGLY1 encoding N-glycanase 1
    - an enzyme that removes the sugar moiety from proteins
    - cleaves N-glycans to generate deglycosylated proteins and oligosaccharides containing 1-amino-GlcNac
    - degrades misfolded proteins in the endoplasmic reticulum

Resources

- Frater CH et al. Ocular features of NGLY1 deficiency from a prospective longitudinal

cohort. J AAPOS 2024;28:103925

syndrome