International Niemann-Pick Disease Registry (INPDR)

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Niemann-Pick Disease Type C (NPC)

Niemann-Pick Type C (NPC) is a progressive and life limiting autosomal recessive disorder caused by mutations in either the NPC1 or NPC2 gene. Mutations are associated with abnormal endosomal-lysosomal trafficking, resulting in the accumulation of multiple tissue specific lipids in the lysosome. The clinical spectrum of NPC ranges from a neonatal rapidly progressive fatal disorder to an adult-onset chronic neurodegenerative disease. The age of onset of the first neurological symptom may predict the severity of the disease and life expectancy. NPC has an estimated incidence of ~ 1: 100,000 and the rarity of the disease translate into misdiagnosis, delayed diagnosis and barriers to quality care.

The consensus clinical management guidelines for NPC have been developed by an group of international experts and are freely available online. A brief summary of key aspects of the guidelines are below.

Signs and Symptoms

- NPC can be classified according to the age of onset of neurological manifestations:
  - Visceral-neurodegenerative form
    Early-infantile (< 2 years)
  - Neurodegenerative form
    Late-infantile (2–6 years)
    -Juvenile (6–15 years)
  - Psychiatric-neurodegenerative form
    Adult (> 15 years)
- Signs and symptoms varies between NPD disease classification (Table 1)

Diagnosis:

- Several plasma metabolites have emerged as sensitive and specific diagnostic biomarkers for NPC and their study, complimented by genetic analyses of NPC1 and NPC2, should be considered for first line laboratory testing

Disease Evaluation, Management and Treatment

- NPC specific disease severity scores are useful in assessing disease burden, response to therapy and determining prognosis
- Optimal disease management employs a multi-disciplinary, multi-professional team based in a specialist centre (Table 2), closely liaising with community care providers
- Miglustat, is the only licensed disease modifying medicine in the European Union for the treatment of neurological manifestations of patients with NPC disease, and has been shown to halt or attenuate disease progression in some patients

To assess the full guidelines, please scan the QR code.

Disease classification	Systemic features	Neurological features
Neonatal systemic fatal	Multiple, including hepatomegaly, foetal ascites and liver failure	Hypotonia
Early infantile neurological onset	Hepato/splenomegaly, prolonged neonatal jaundice	Hypotonia, motor development delay, dysphagia, vertical supranuclear gaze palsy
Late infantile neurological onset	Hepato/splenomegaly, history of prolonged neonatal jaundice	Multiple, including development delay/regression, progressive ataxia, seizures, cataplexy
Juvenile neurological onset	Hepato/splenomegaly	Multiple, including poor academic performance, progressive ataxia, VSGP, seizures
Adolescent & adult neurological onset	Splenomegaly	Cognitive decline, dementia, psychiatric signs, progressive motor symptoms, VSGP

Table 1. NPC Disease features by subtype

Recommended assessment	Frequency
Baseline history	At diagnosis
Interval history	Each visit
NPC Clinical Severity Scale	At diagnosis and then every 6 months
Neuropsychiatric evaluation	At diagnosis then every 6–12 months
Developmental or cognitive assessment	At diagnosis; Children - every 6 months; Adults - every 12 months
Swallowing assessment	At diagnosis; Children - every 6 months. Adults: every 12 months if asymptomatic and disease is stable
Neuroimaging	At baseline if available; Decisions about follow up neuroimaging will depend on local availability and need for general anaesthesia
Ophthalmology evaluation	At diagnosis; at 6 and 12 months; after starting treatment; frequency after 12 months can be determined by clinical response
Audiometry	At diagnosis then every 12 months

Table 2. Recommended assessments for NPC patients

Geberhiwot T, Moro A, Dardis A, Ramaswami U, Sirrs S, Marfa MP, et al. Consensus Clinical Management Guidelines for Niemann-Pick Disease Type C. Orphanet Journal of Rare Diseases. 2018;13(1). doi:10.1186/s13023-018-0785-7