WHEN TO CONSIDER NIEMANN PICK DISEASE TYPE C

Wide clinical spectrum, continuum of more or less severe forms depending on the age of onset of the neurological impairment

❶ Early childhood forms (onset 2-24 months), ❷ late childhood (onset 2-6 years), ❸ juvenile (onset 6-15 years) and ❹ adolescent form over the age of 15 years/adult

Clinical signs

Internal organ damage ★
(inconstant, frequently precedes neurological impairment)

Organomegaly 80%*
Splenomegaly +/-
Hepatomegaly

Liver damage
Perinatal **liver failure****
Prolonged transient neonatal **cholestatic jaundice**

Lung damage
Interstitial or alveolar interstitial impairmentof varying severity: sometimes severe in infants, and can progress to **respiratory failure****

Progressive neurological impairment ★
(age at onset will impact the progressive neurological prognosis, may be isolated without splenomegaly)

- **Paralysis of the eyes when looking downwards and/or upwards*** ** (supranuclear vertical gaze palsy), **vertical eye jerks** ❶❷❸❹
- **Hypotonia, delayed psychomotor development, language delay** ❶❷
- **Motor disorders linked to cerebellar ataxia** and/or **dystonia: difficulty walking, clumsiness, dysarthria, dysphagia** ❷❸❹
- **Educational problems, psychomotor regression, cognitive decline** ❶❷❸❹
- **Cataplexy +/- narcolepsy** ❷❸
- **Epilepsy** ❷❸
- **Psychological impairment, behavioural issues, dementia** ❹

Other
Perceptive deafness ❷❸❹

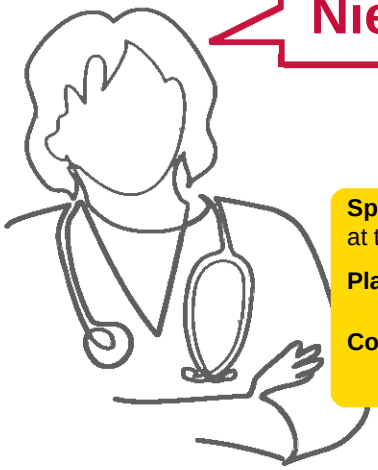
Additional tests

Laboratory tests: moderate cholestasis, liver cytolysis and/or thrombocytopaenia
Abdominal ultrasound: splenomegaly +/- hepatomegaly
Thoracic x-ray or scan: interstitial or alveolar interstitial damage
Myelogram (if performed; non-routine): foamy macrophages or sea-blue histiocytes

Brain MRI: normal ❶❷❸❹ or cerebellar then supratentorial atrophy, discrete atrophy of white matter ❶❷❸❹

Specialist workup

Niemann Pick disease type C?



★ Specialist medical opinion and reference laboratory

Seek specialist neuro-metabolic advice ★

Specialist workup in collaboration with a Centre of Excellence ★
at the same time as looking for other potential differential diagnoses

Plasma biomarker determination: oxysterols and lysosphingolipids

Confirmatory genetic analysis

Initial assessment: specialist treatment coordinated by a specialist centre: Rare Disease Centre of Reference / Competence: : https://www.filiere-g2m.fr/annuaire/

There is a specific treatment for neurological forms

Genetic counselling, family screening in a specialist centre

For more information:
French National Diagnosis and Treatment Protocol: PNDS Niemann Pick disease type C
and CETL website (Lysosomal disease treatment assessment committee): www.cetl.net

* Persistent from the neonatal stage, once jaundice has subsided or reappeared later on, at varying ages. May then regress in adults
** Rare fulminant visceral perinatal form in neonates / small babies, with early death
*** This should be sought specifically during the examination, as it is rarely complained of. Fairly specific of the disease

Maladies rares Héréditaires du Métabolisme
Filière nationale de santé