WHEN TO CONSIDER NEURONAL CEROID LIPOFUSCINOSIS (NCL)

*DISORDERS CHARACTERISED BY **MAINLY NEUROLOGICAL DAMAGE, SOMETIMES ASSOCIATED WITH VISUAL IMPAIRMENT.***

*Several forms have been described according to the clinical, electrophysiological and neuropathological criteria, with varying ages of onset: **the early infantile form** (3-18 months, rare congenital form of antenatal onset), **the later infantile form**(18 months-10 years) including CLN2 *, **the juvenile form** (4-9 years) and the adult form.*

Naturally progresses to an aggravation - more or less rapid depending on the form - of multiple disabilities with death in childhood or young adulthood.

Clinical signs

NEUROLOGICAL DAMAGE PROGRESSIVE IN ALL CASES

Earlier or later**psychomotor regression**, sometimes preceded by a delay in psychomotor development

Motor disorders: progressively worsening ataxia, pyramidal syndrome, then spastic quadriparesis and sometimes dystonia

Myoclonic epilepsy which is often drug resistant

Behavioural issues

Microcephaly if onset in young babies

TELLTALE SIGN FOR THE MOST COMMON CLINICAL PICTURES

CLN1:
onset <1 year, little or no psychomotor acquisition, myoclonus, acquired microcephaly

CLN2*:
onset > 18 months, language delay, ataxia, myoclonic epilepsy

CLN3:
onset in older children, behavioural issues, visual damage is often the first manifestation

PROGRESSIVE VISUAL IMPAIRMENT RETINAL DYSTROPHY (RETINITIS PIGMENTOSA)

Sometimes early onset and preceding neurological damage (in some juvenile forms), Inconstant in adult forms

Nyctalopia

Progressive loss of visual acuity leading to blindness

Photophobia

Reduced visual field

Nystagmus

Additional tests

CBC: presence of vacuolated lymphocytes (CLN3 only)

Brain MRI: T2 hyposignal and FLAIR of thalamus and T2 hypersignal and FLAIR of white matter, preceding cerebellar and cerebral atrophy

EEG: vanishing EEG in early forms, phototherapy with intermittent light stimulation (CLN2)

Additional tests

Ophthalmological examination

- Retinal fundus: pallor of the optic papilla; narrowing of blood vessels, changes to retinal pigmentation
- Changes in visual evoked potential and electroretinogram

Specialist workup

Neuronal ceroid lipofuscinosis?

Specialist neuro-paediatric advice

Workup by specialist team

Enzyme assays for CLN1 and CLN2* (palmitoyl protein thioesterase, tri-peptidyl peptidase I)

Genetic analysis for all forms (panel including the 13 NCL genes)

Specialist initial assessment and treatment,
Specific treatments* (indications/initiation) to be coordinated by
Centre of Excellence: Rare Disease Centre of Reference / Competence:
https://www.filiere-g2m.fr/annuaire/

Genetic counselling and family screening in a specialist centre

For more information:
PNDS: pnds_ceroide-lipofuscinoses_neuronales_novembre_2022.pdf (has-sante.fr)
and website:
Centre of Reference for Lysosomal Diseases - CETL: http://www.cetl.net/

Specialist medical opinion and reference laboratory

*** There is a specific treatment for CLN2: thus it is important to rapidly diagnosis and screen siblings to initiate treatment as soon as possible**