# Neuronal Ceroid Lipofuscinosis 3 : from early foveopathy to systemic involvement.

## *Evolution of clinical phenotype in one family.*

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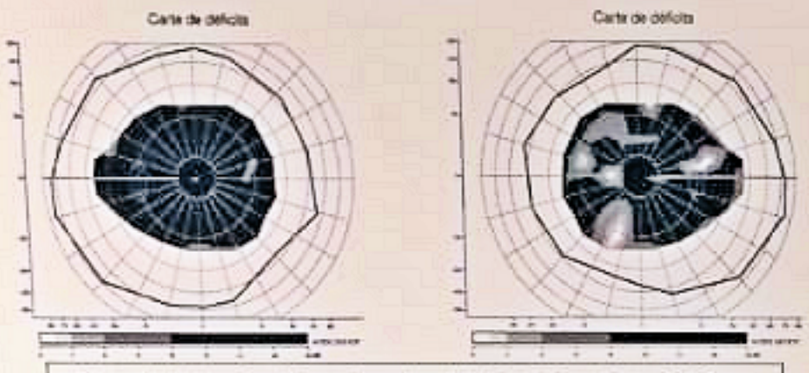
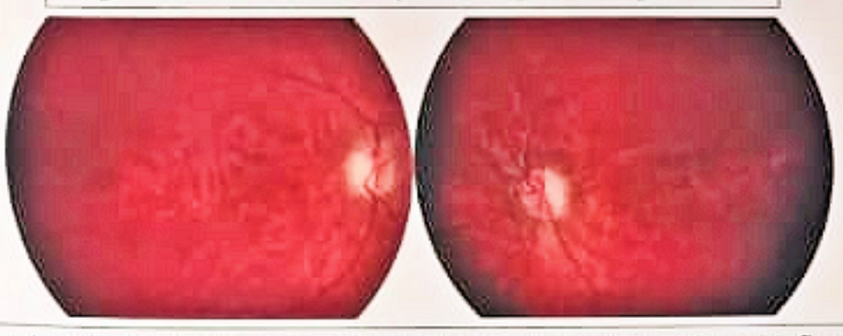
**Introduction.** Neuronal ceroid lipofuscinosis (CLN) is a group of lysosomal storage disorders leading to widespread neuronal degeneration. In juvenile form of CLN or Batten disease (CLN3) visual symptoms are first to be noted. Specific retinal findings and evolution in one family are reported here.

**Patient 1**. Boy, 11 y.o. Progressive visual loss, scolar problems, insomnia Right esotropia.

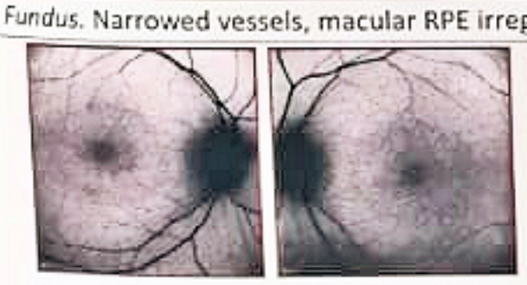
| BCVA | OD | OS |
|---|---|---|
| 7 y.o. | 0,9 | 0,9 |
| 9 y.o. | 0,4 | 1,0 |
| 11 y.o. | 0,05 | 0,05 |



*Mixed stato-cinetic perimetry Metrivision, MonCV One.* Large central scotoma. Peripheral isopter III4e preserved.

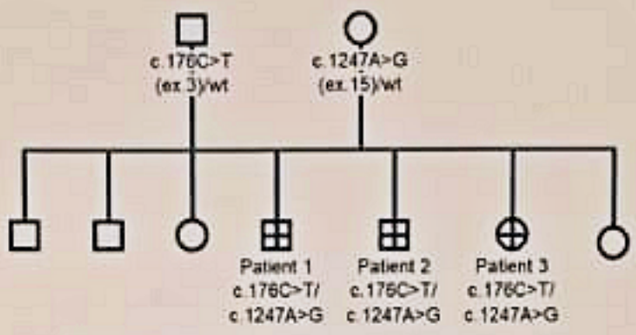


*Fundus.* Narrowed vessels, macular RPE irregularity, loss of foveal reflex.



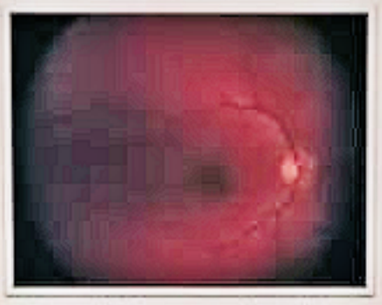
*FAF, Heidelberg Retinal Tomograph.* Enlarged foveal hypoAF zone.

*SD-OCT, Cirrus, Zeiss.* Destruction of outer retinal layers and global retinal thinning




*Pedigree*. Compound heterozygous mutation in *CLN3* gène. Parent are not consanguineous.

**Differential: Stargardt disease**

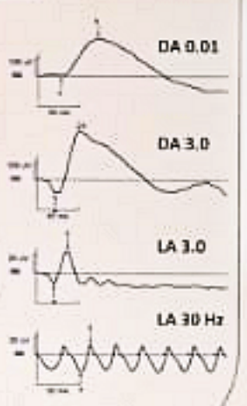


Fundus and OCT are comparable at all stages

But...

FAF is different: Ovoid hypoAF and hyperAF flecks

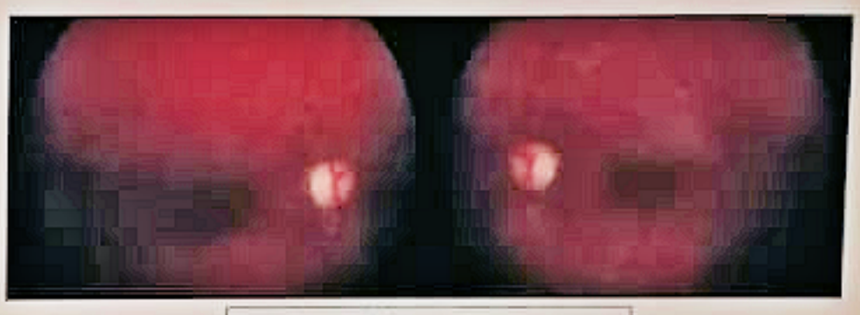
And...



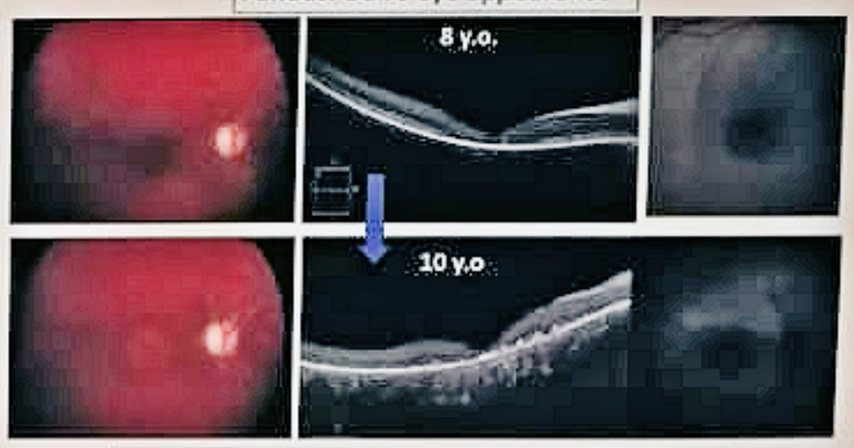

ERG is normal, at least in the beginning

**Patient 2**. Boy, 9 y.o. Scolar difficulties, especially in writing.

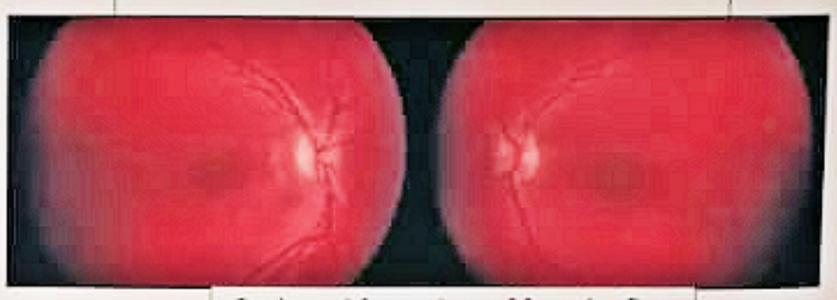
| BCVA | OD | OS |
|---|---|---|
| 8 y.o. | 0,8 | 0,7 |
| 9 y.o. | 0,1 | 0,08 |



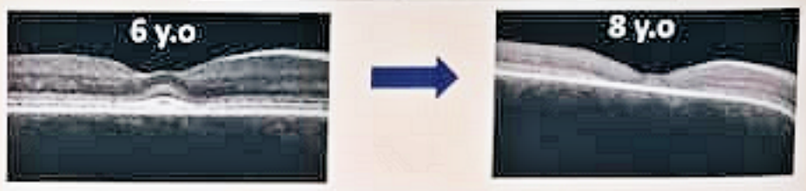
*Fundus.* Bull's eye appearence



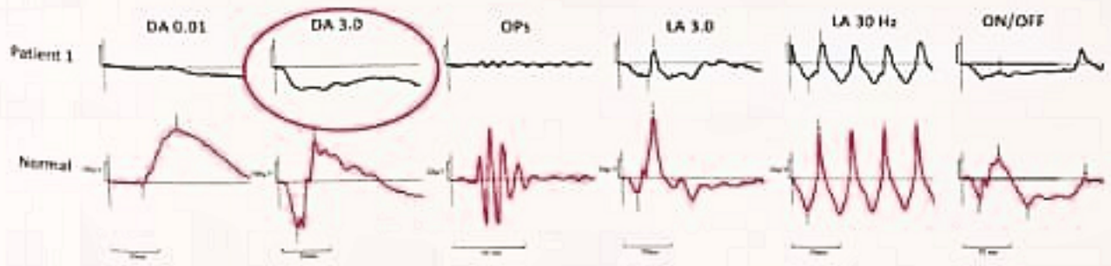

**Patient 3**. Girl, 6 years old, visual loss finally linked with uncorrected hyperopia.



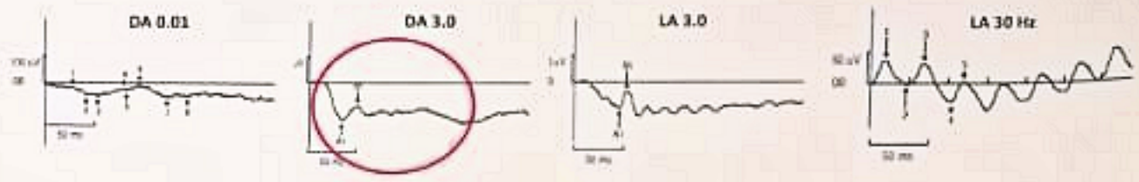
Darkened fovea, loss of foveal reflex.




*SD-OCT, Cirrus, Zeiss.* Foveolopathy (ELM and EZ thickening) evolving in maculopathy with progressive destruction of outer retinal layers.




*ERG, MonColor, Metrovision*. Negative ERG, ON-system is predominantly affected.




*ERG, MonColor, Metrovision*. Negative ERG (b<a).

**Patients.** Patient 1 developped a multiresistant myoclonic epilepsia at 12 y.o. Behaviourl disorders (auto- and hétéro-agressivity) are also part of his neurological picture. Patient 2 presents only mild myoclonic seizures. Patient 3 is 13 y.o. to date ; she presents only a mild cognitive disability without seizures.

**Discussion.** Neurological picture is variable and less specific then ocular findings in the beginning of CLN3. Diagnosis of an evolving **maculopathy**/retinopathy **with negative ERG** waveform in a child should raise the suspicion of **CLN3** and prompt neurological assessement. Diagnosis will be ultimately confirmed by genetic testing (recessive mutations in *CLN3* gene). Unfortunately, there is no specific treatment for this fatal disorder. Early presymtomatic diagnosis coud raise ethical questionning; at the same time it could be useful in the setting of gene therapy trials.

1. Weleber RG. The dystrophic retina in multisystem disorders: the electroretinogram in neuronal ceroid lipofuscinoses. Eye Lond Engl. 1998;12 ( Pt 3b):580–90.
2. Preising MN, Abura M, Jäger M, Wassill K-H, Lorenz B. Ocular morphology and function in juvenile neuronal ceroid lipofuscinosis (CLN3) in the first decade of life. Ophthalmic Genet. 2017 Jun;38(3):252–9.
3. Dulz S, Wagenfeld L, Nickel M, Richard G, Schwartz R, Bartsch U, Kohlschütter A, Schulz A. Novel morphological macular findings in juvenile CLN3 disease. Br J Ophthalmol. 2016;100(6):824–8.