Congenital Stationary Night Blindness Plus syndrome

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The complete form of congenital stationary night blindness (cCSNB) represents a non-progressive retinal disorder characterized by night vision problems and often congenital nystagmus, reduced vision, high myopia, strabismus and normal fundus appearance (Zeitz, Robson et al. 2015). Clinically this form of CSNB can be diagnosed by full field electroretinogram with specific electronegative waveform and changes in the fotopic ERG (Audo, Robson et al. 2008). Patients with CSNB do not present other systemic problems and have normal mental development. Mutations in *NYX* (MIM: 300278) (Bech-Hansen, Naylor et al. 2000), *GRM6* (MIM: 604096) (Dryja, McGee et al. 2005) , *GPR179* (MIM: 614515) (Audo, Bujakowska et al. 2012), *LRIT3* (MIM: 615004) (Zeitz, Jacobson et al. 2013) and *TRPM1* (MIM: 603576; NM_001252020.1)(Audo, Kohl et al. 2009) lead to this condition.

The patient was a girl referred for ophthalmological evaluation at 1 year of age, because of nystagmus. She also presented systemic abnormalities and mild developmental delay.

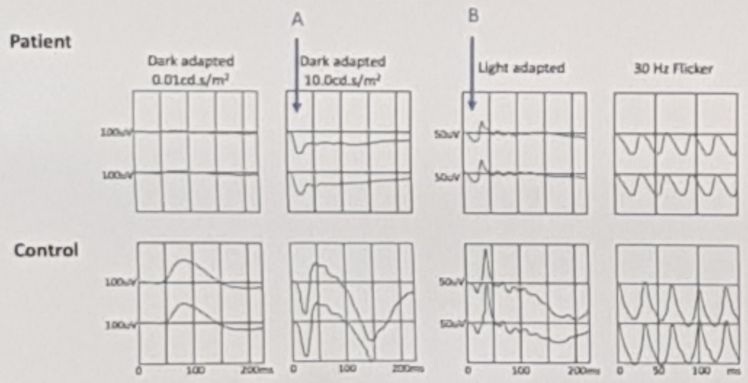
Ocular findings:

- Congenital nystagmus
- Right eye esotropia
- Myopia RE: -5 (-1/170°) LE: -5(-1/20°)
- BCVA at 4y RE: 0,5 LE: 0,4
- Normal anterior segment
- Normal retina and optic nerve

Systemic findings:

- Mild Developmental delay
- Microcephaly
- Torticollis
- Congenital hip luxation

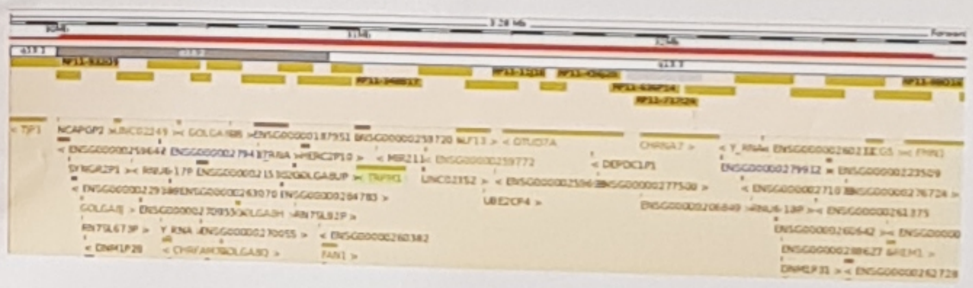
Severely reduced scotopic response, present maximal response with reduced A/B ratio **(A)** indicating electronegativity, photopic response, with broadened through and a sharply arising b-wave **(B)**, square shaped flicker response.



TRPM1 hemizygous variant in ex24: c.3262G>A p.(Ala1088Thr). Heterozygous **deletion chr15q13.2 - q13.3**.

Segregation analysis in the parents showed that the mother carries the deletion and the father carries the *TRPM1* mutation in a heterozygous state. Both parents were asymptomatic.

Ensembl view of the deleted region and location of *TRPM1:*



We present Congenital Stationary Night Blindness in a patient with mild learning disability due to a compound heterozygous microdeletion of chromosome 15q13 and a missense mutation in *TRPM1* gene. Both the *TRPM1* variant and the microdeletion have been previously described and shown to be pathogenic (Hassfurther, Komini et al. 2016; Zhou L et al. 2016). We show for the first time, the combination of both genetic abnormalities leading to a syndromic CSNB – **CSNB plus syndrome**. With this report we would like to raise awareness to this type of complex genetic defects leading to atypical phenotypes. We also show the importance of testing for chromosomal deletions, duplications and inversions in patients with unexplained retinal dystrophies.