Table S1. Timeline of the disease progression in Patient 1

|  |  |  |
| --- | --- | --- |
| **Date** | **Relevant past medical history** | |
|  | **Patient 1 had low vision in the right eye(RE) since early childhood, presumed to be due to amblyopia, and did not notice any change in visual function in that eye. As a 6 years old child, he had been first seen at the Eye hospital due to low vision in one eye (RE: 0.1c.c, LE:0.7c.c). Hypermetropic glasses (+7Dsph and+6.5Dsph) were prescribed and VA improved on both eyes to RE: 0.3 c.c. and LE: 1.0 c.c. Amblyopia treatment with the occlusion of the LE was started, but the vision of the RE did not further improve despite occlusion therapy** | |
|  | **Summaries from initial and follow-up visits** | **Interventions and therapy** |
| August 2015 | VA loss on the left eye (LE) | Glasses prescription from the local ophthalmologist. |
| December 2015 (5 months after the onset of the right eye) | Hospitalization at Clinic due to VA loss on the previously healthy left eye. VA RE counting fingers on 2 meters, LE: counting fingers at 1 m Color vision RE 0/15, LE 1/15, central scotoma bilaterally. On fundoscopy reddish optic discs with initial pallor temporally. Thinning of the pRNFL, thinning of the inner retina in the macular region. FA: no leakage, EF: P 50 amplitude normal, lower on amblyopic eye, decreased N95 wave more on the amblyopic eye, N95/P50 ratio RE 0.71 LE:0.78, delayed and decreased VEP P100 with lower amplitude and shorter latency on amblyopic eye. | Systemic corticosteroid therapy for 3 days Solumedrol i.v. (1g/day), no improvement.  MRI of the head and brain, no signs of demyelination, aqp4 negative, antiMOG negative, excluded all other possible signs of theoptic atrophy (infectious, paraneoplastic, compressive etc)  Blood taken for genetic testing. |
| July 2016 (one year after the onset) | VA RE counting fingers on 1,5 meters, LE counting fingers at 1 m Color vision RE 0/15, LE 1/15, central scotoma bilaterally. On fundoscopy both optic discs pale, thinning of the inner retina on OCT bilaterally, further progression of the pRNFL thinning | Genetic testing for 3 common mutations negative, mtDNK ngs performed revealed previously published rare mutation, mother and sister tested for the same mutation. Patient started with Idebenone |
| November 2017 (14 months after the onset on the left eye) | VA RE counting fingers on 1,5 meters, LE counting fingers at 1 m Color vision RE 0/15, LE 1/15, central scotoma bilaterally. On fundoscopy both optic discs pale, thinning of the inner retina on OCT bilaterally, further progression of the pRNFL thinning. EF: P 50 amplitude decreased, more on the amblyopic eye, although still within normal limits, decreased N95 wave on the amblyopic eye, normal on LHON, N95/P50 RE 0.77 LE 1.02, and delayed and decreased VEP P100. | Mutation confirmed in both mother and sister who are asymptomatic carriers |
| January 2018 (3.5 years after the onset) | VA RE counting fingers on 2,5 meters, LE counting fingers at 2,5 m Color vision RE 0/15, LE 1/15, central scotoma bilaterally. On fundoscopy both optic discs pale, thinning of the inner retina on OCT bilaterally, further progression of the pRNFL thinning. EF: SFERG P50 amplitude improved, more on the amblyopic eye, borderline reduced N95 amplitude improved but the wave was in the level of the baseline, again more on the amblyopic eye N95/P50 RE 0.81 LE 0,92 and delayed and decreased VEP P100. |  |
| January 2022  (5.5 years after the onset) | VA RE counting fingers on 1 meter, LE counting fingers at 0.75 m Color vision RE 0/15, LE 1/15, central scotoma bilaterally. On fundoscopy both optic discs pale, thinning of the inner retina on OCT bilaterally, further progression of the pRNFL thinning, with still preserved nasal segment on both eyes |  |