Supplementary Materials

Characteristics of autosomal dominant *WFS1*-associated optic neuropathy and its comparability to *OPA1*-associated autosomal dominant optic atrophy

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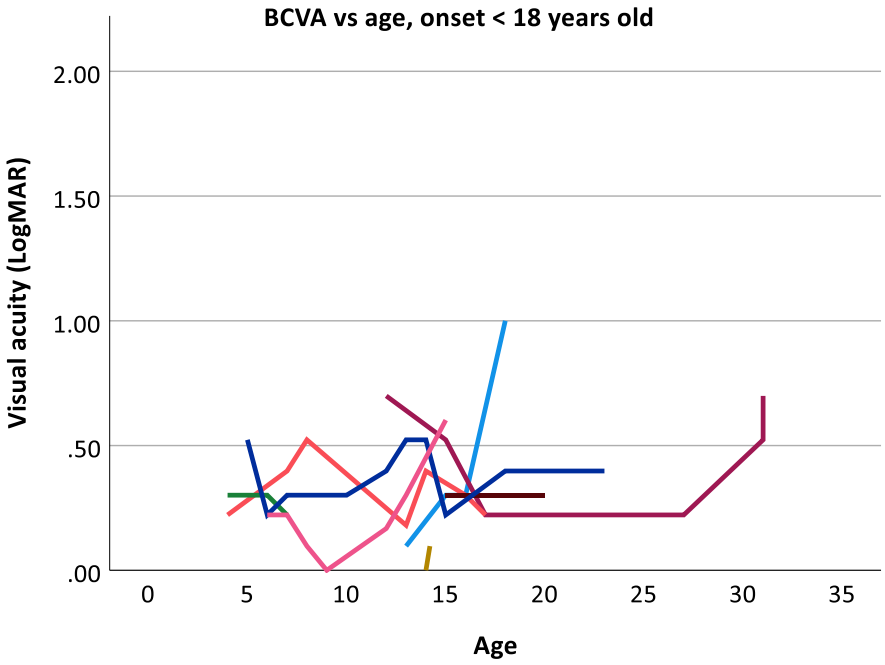
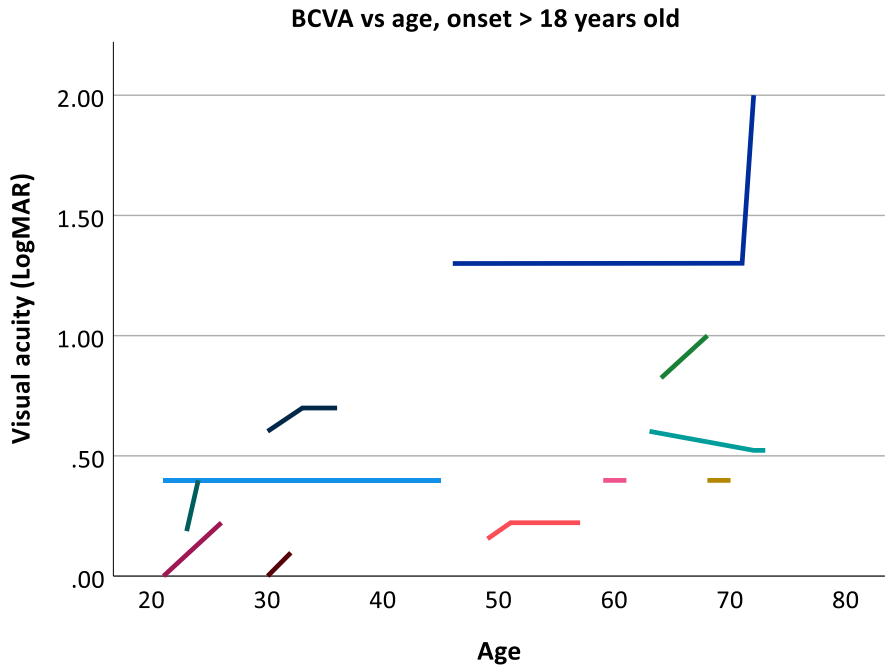
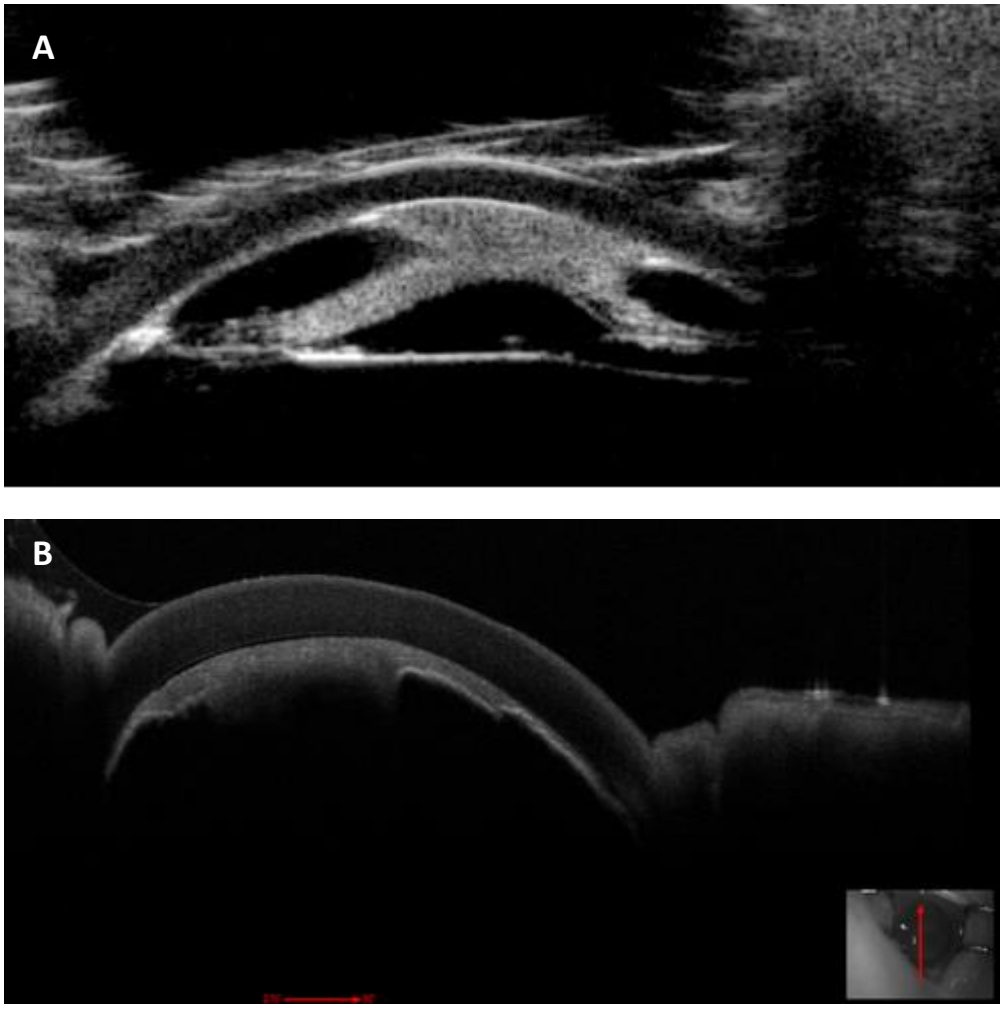
Supp Figure 1. Development of visual acuity over the years. Patients who were diagnosed with optic atrophy under the age of 18 showed fluctuations in the visual acuity, most probably due to the counteracting effects of the maturing visual system versus progressive optic atrophy. Adult onset optic atrophy patients showed on the other hand, relatively a stable visual acuity over the years. One adult patient with visual acuity of 2.0 LogMAR (dark blue line) had, in addition to optic atrophy, corneal band keratopathy in the left eye and vitreomacular traction in both eyes but was not treated operatively because potential visual gain was expected to be insignificant.





Supp Figure 2. Ultrasound (A) and the optical coherence tomography (B) images of the anterior segment showing cystoid iridocorneal membrane obliterating the anterior chamber space



Supplementary Table 1. Summary of the pathogenicity assessment of the disease associated *WFS1* variants in this cohort. ¶ harboured by the same individual.

Variant	ACMG classification	Classification
c.683G>A¶ p.(Arg228His)	BS1, BP2	Likely benign (class 2)
c.937C>T p.(His313Tyr);	PS2_Very Strong, PS3, PM2_Supporting, PP3, PP4	Pathogenic (class 5)
c.[991_993del;1597C>T] p.[(Phe331del);(Pro533Ser)], de novo	PS2, PM2_Supporting, PM4, PP4	Likely Pathogenic (class 4)
c.1672C>T p.(Arg558Cys)	PM3_Very Strong, PM5, PP3, PP4	Pathogenic (class 5)
c.2002C>T p.(Gln668*)	PVS1, PM3_Strong, PM2_Supporting, PP1, PP4	Pathogenic (class 5)
c.2044A>G p.(Asn682Asp)	PM2_Supporting, PP1, PP3, PP4	Variant of unknown significance (class 3)
c.2051C>T p.(Ala684Val)	PS2_Very Strong, PS3, PM2_Supporting, PM5, PP3, PP4	Pathogenic (class 5)
c.2213C>A p.(Ala738Asp)	PM2_Supporting, PM3, PP1_Strong, PP4	Likely pathogenic (class 4)
c.2389G>A p.(Asp797Asn)	PS2, PM2_Supporting, PM5, PP3, PP4	Likely pathogenic (class 4)
c.2389G>T p.(Asp797Tyr)	PM2_Supporting, PM5_Strong, PP3, PP4	Likely pathogenic (class 4)
c.2425G>A p.(Glu809Lys)	PS2_Very Strong, PM2_Supporting, PP3, PP4	Pathogenic (class 5)
c.2430C>A¶ p.(Phe810Leu), de novo	PS2, PM2_Supporting, PP3, PP4	Likely pathogenic (class 4)
c.2541C>G p.(Cys847Trp)	PM2_Supporting, PP3	Variant of unknown significance (class 3)
c.2590G>A p.(Glu864Lys)	PS2, PM2_Supporting, PP1_Strong, PP3, PP4	Pathogenic (class 5)

Supplementary table 2. Details of the retinal nerve fiber layer measurements of the optic nerve head OCT. Normal = healthy controls; DOA = dominant optic atrophy patients; *WFS1* = autosomal dominant *WFS1* associated optic neuropathy patients.

RNFL (µm)	**Type**	**N**	**Mean**	**Std. Deviation**	**Std. Error**	**95% Confidence Interval for Mean**		**Minimum**	**Maximum**
						Lower Bound	Upper Bound		
Temporal	Normal	32	73.59	15.339	2.712	68.06	79.12	53	122
	DOA	36	39.08	12.348	2.058	34.91	43.26	17	77
	AD *WFS1*	30	37.00	14.205	2.594	31.70	42.30	17	64
Superior	Normal	32	135.16	22.760	4.023	126.95	143.36	95	192
	DOA	36	99.22	19.982	3.330	92.46	105.98	66	130
	AD *WFS1*	29	65.41	15.665	2.909	59.46	71.37	23	96
Nasal	Normal	32	75.19	15.890	2.809	69.46	80.92	51	110
	DOA	36	61.28	15.178	2.530	56.14	66.41	39	91
	AD *WFS1*	30	44.77	15.395	2.811	39.02	50.52	6	72
Inferior	Normal	32	139.16	22.558	3.988	131.02	147.29	109	211
	DOA	36	83.53	19.725	3.287	76.85	90.20	57	150
	AD *WFS1*	30	65.83	21.241	3.878	57.90	73.76	30	131