Supplementary Table 6. Pathogenic and Likely Pathogenic variants in this cohort with detailed phenotypes and ACMG classification and criteria.

Patient ID	Variant ID	Age	Sex	Clinical Diagnosis	Beighton score	Villefranche Criteria Major Minor	Aortic & Other Vascular involvement	Auto. Dom Family History	Skin Biopsy	Gene NM	Protein	Rs ID ClinVar ID (classification)	gnomAD allele frequency	CADD DANN	ACMG classification (See footnote) ACMG criteria
33	1	40-49	F	HDCT	9	A, C, E, H, I, J a, d, f, n, s, u, w, x, y	MVR Carotid dissection	+	normal	TGFB3 NM_003239.4 c.463C>T	p.Arg155Trp	rs868258653 543955 (LP/VUS)	0	33 0.999	LP PM2, PP5 PP3 (Supp)
34	2	30-39	F	HDCT	3	A, C, E, H, I d,j	Carotid artery dissection	+	normal	COL5A1 NM_000093.4 c.4068G>A	Splice	– 1000751 (VUS)	0	14.8 0.808	LP PM2, PP5 PP3 (Supp)
34	3	30-39	F	HDCT	3	A, C, E, H, I d,j	Carotid artery dissection	+	normal	ITGB3 NM_000212.3 c.565C>T	p.Pro189Ser	rs958609406 812735 (P)	0.0000119	28.9 0.999	P PP1, PS3 PS4, PP5 PP3 (S) PM2, PP2
402	4	30-39	M	hEDS Marfanoid	6	A, C, H, I d, i, u	–	+	normal	COL12A1 NM_004370.6 c.5097+1G>A	Splice	–	0.0000119	25.2 0.992	LP PVS1, PM2
479	8	20-29	F	HDCT	6	A, C, H, I, J, K e, f, g, t, w	–	+	normal	SMAD2 NM_001003652.3 c.842A>T	p.Glu281Val	– –	0	33 0.994	LP PM2, PP2 PP3 (S)
564	9	20-29	M	HDCT	8	A, C, H, I a, d, g, u	Aortic dilatation	Biparental	abnormal packing	TGFB2 NM_001135599.3 c.989G>A	p.Arg330His	rs1553303213 440982 (LP)	0	34 0.999	P PM2, PM5 PM1, PP5
755	10	40-49	F	hEDS	4	A, C, H, I, J, K d, e	–	+	normal	COL12A1 NM_004370.6 c.8321G>A	p.Gly2774Glu	–	0	25.7 0.997	P PM2, PP3 (S)
814	14	30-39	F	HDCT	8	B, C, D, H, J d, n, r, s, t, u, v	–	Biparental	abnormal packing	TGFBR2 NM_001024847.2 c.1613T>C	p.Val538Ala	– –	0	26.3 0.998	LP PM1, PM2 PP2 PS3 (ref 16)
1420	17	0-9	M	HDCT	–	C, H d, s, t	–	–	–	ALPL NM_000478.6 c.394G>A	p.Ala132Thr	rs757771793 –	0.000004	33 0.999	P PM1, PP2 PM2, PM5 PP3 (Sup) PP5
1484	18	50-59	F	hEDS	4	C, H d, h, s, t, u			–	COMP NM_000095.3 c.2048G>T	p.Arg683Leu	rs565459602	0.0000239	34 0.999	LP PM2, PP2 PP3 (S)
1528	19	30-39	M	cEDS	–	A, C, H, I d, f, g, k q, s, u	–	–	–	COL5A1 NM_001278074.1 c.3397C>T	p.Arg1133Ter	rs886042045 280931 (P)	0	41 0.998	P PVS1, PP5 PM2

Supplemental Table 6, 7 Keys:
Clinical Diagnosis: expert clinical diagnosis based on history and examination, prior to any diagnostic genetic testing.
Vascular involvement: as stated: – = no known vascular aneurysm/ dissection or aortic root dilatation.
Autosomal Dominant Family History: + = one or more affected individual on either side of the family, biparental = family history of GJH or related phenotypes in both sides of the family.
Skin Biopsy: 3mm punch biopsies were taken from the upper inner arm, with expert review of light microscopy (H&E and elastin van Geisen) and ultrastructural analysis (FMP and Prof. David Ferguson, Univ. of Oxford).

EDS Diagnostic Criteria as per list in Supplementary Table 1.

ACMG criteria as per Richards *et al.* (9): P = pathogenic, LP = likely pathogenic, VUS/LP = variant of uncertain significance close to criteria for LP classification, VUS = variant of uncertain significance, LB = likely benign, B = benign. Individual criteria ((9), Table 3)

VUS* are defined here as including VUS that according to ACGS criteria are "hot", "warm" or "tepid" Variants of Uncertain Significance (Figure 6 of https://www.acgs.uk.com/media/11631/uk-practice-guidelines-for-variant-classification-v4-01-2020.pdf).
Segregation analysis, re-evaluation for specific phenotypic features and/or further functional analysis may enable variant reclassification, using ACMG criteria.