

NA, not available, AAO, age at onset, AAE, age at examination, EEG, electroencephalography, * initially
Supplementary Table 1. Clinical and genetic features of patients with cerebrotendinous xanthomatosis in

Reference	Origin	No. of cases	Mutation of CYP27A1	Mean AAO years	Mean AAE years	Xanthoma	Cerebellar ataxia	Pyramidal signs	Peripheral neuropathy	Impaired cognition/cognitive impairment	Cataracts	Chronic diarrhea	Seizure	Parkinsonism	EEG abnormality	Abnormal brain MRI	Additional information
Kuriyama et al., 1991	Japan	8	NA	18.5	39.1	7/8	4/8	8/8	2/8	6/8	6/8	NA	0/8	1/8	6/8	NA	
Leitersdorf et al., 1993	Morocco, Jews	5	819delT, 866-1g→a, 852G→A	NA	31	4/5	5/5	5/5	NA	5/5	5/5	NA	4/5	NA	5/5	5/5	
Leitersdorf et al., 1994	Israeli Druze	10	355delC	NA	23	5/10	8/10	8/10	NA	8/10	10/10	NA	8/10	NA	9/10	6/10	
Kim et al., 1994	Japan	0	1421G>A, 1420C>T	Patients were reported in Kuriyama et al., 1991				-	-	-	-	-	-	-	-	-	
Nakashima et al., 1994	Japan	2	409C>T, 366A>C	30	60	2/2	0/2	1/2	1/2	2/2	0/2	NA	NA	NA	1/2	NA	
Meiner et al., 1994	Africa, Netherland	2	850A>T	NA	43	2/2	2/2	2/2	0/2	2/2	2/2	NA	0/2	0/2	1/2, NA (1/2)	1/2, NA (1/2)	Convulsion (1/2)
Reshef et al., 1994	Sephardic Jews,	3	1016C→T	NA	28	2/3	2/3	3/3	NA	3/3	2/3	NA	1/3	NA	3/3	3/3	
Segev et al., 1995	France	3	5-6insC	NA	19	2/3	0/3	0/3	NA	3/3	3/3	NA	1/3	NA	1/3	0/3	
Chen et al., 1996	Japan	1	1184G→A	17	24	1/1	0/1	0/1	NA	1/1	NA	NA	0/1	0/1	1/1	0/1	

Garuti et al., 1996a	Italy	1	Del 1.9 kb	6	27	1/1	NA	NA	NA	1/1	1/1	NA	NA	NA	1/1	1/1	Psychiatric disturbances
Garuti et al., 1996b	Italy, Tunisia	2	646G→C,1263+1G→A1421G→A,1202C→G	16.5	41	2/2	1/2	2/2	NA	0/2	2/2	NA	0/2	NA	NA	2/2	
Okuyama et al., 1996	Japan	3		NA	NA	2/3	2/3	NA	NA	2/3	2/3	NA	2/3	NA	NA	NA	
Watts et al., 1996	UK	2	380G→A	NA	41	2/2	1/2	1/2	1/2	2/2	2/2	NA	1/2	NA	2/2	0/2	
Verrips et al., 1996	Netherlands, Suriname Creole	2	475C→T,525/526delG	NA	44.5	1/2	NA	1/2	NA	2/2	2/2	NA	1/2	NA	NA	NA	
Verrips et al., 1997	Netherlands Pakistan,	3	844+1g→a	NA	41	3/3	2/3	3/3	3/3	3/3	3/3	1/3	3/3	NA	NA	NA	
Ahmed et al., 1997	Netherlands	4	808C→T	NA	NA	4/4	4/4	4/4	NA	4/4	4/4	4/4	4/4	NA	4/4	4/4	
Chen et al., 1997	Japan	1	1214G>A	NA	NA	1/1	NA	NA	NA	NA	1/1	NA	NA	NA	NA	NA	
Garuti et al., 1997	Italy	5	691C→T,1184+1g→a,Del 1.9 kb 1263+1g→a,1263+5g→t,1264-1g→a	13.5	39	5/5	1/5	4/5	NA	5/5	5/5	NA	NA	NA	NA	NA	
Chen et al., 1998a	Japan	1	1183C>A	NA	57	1/1	1/1	1/1	NA	1/1	1/1	NA	NA	NA	NA	NA	

Chen et al., 1998b	Japan	3	435G>T	25	44.7	3/3	2/3	2/3	NA	0/3	1/3	NA	NA	NA	NA	NA
Chen et al., 1998c	Japan	1	1184G>A	NA	17	1/1	0/1	0/1	NA	1/1	0/1	NA	0/1	0/1	NA	NA
Verrips et al., 1999	Netherlands, Belgium	7	379C→T	30	37	1/7	2/7	7/7	2/7	1/7	7/7	4/7	1/7	NA	NA	5/7
Aad Verrips et al., 2000a	Netherlands, UK, Belgium, Spain, Tunisia, Germany and China	54	446+1g→a/467+1g→a;745C→T/766C→T;776A→G/797A→G;779G→A/800G→A;1061A→G/1082A→G;1151C→T/1172C→T;1213C→T/1234C→T;1415G→C/1436G→C;	12	35	27/54	35/54	39/54	15/54	33/54	52/54	19/54	14/54	NA	21/54	33/54

Author(s)	Country	n	Genotype	Age (yr)	Survival (%)	13/32	18/32	26/32	10/32	21/32	31/32	16/32	5/32	1/32	NA	NA
Aad Verrips et al., 2000b	Netherlands	32	26/27insC, 400C>T, 496C>T, 546/547delG, 829C>T, 865+1g>a, 871A>T, 1037C>T, 1204C>T, 1234C>T, 1284+1g>a	18	35	13/32	18/32	26/32	10/32	21/32	31/32	16/32	5/32	1/32	NA	NA
Bel et al., 2001	Netherlands	1	NA	1	55	1/1	1/1	1/1	1/1	1/1	1/1	0/1	1/1	NA	1/1	1/1
Verrips et al., 2001	Netherlands	2	NA	NA	18.5	2/2	NA	NA	NA	NA	2/2	NA	0/2	NA	NA	NA
Lee et al., 2001	America	19	Trp100Stop, Pro408Ser, Gln428Stop, a 10-base pair deletion in exon 1, and a 2-bp deletion in exon 6	NA	42	19/19	17/19	17/19	NA	17/19	14/19	NA	NA	NA	NA	NA

Burnett et al. 2001	Australia	1	G>A transition in the splice donor site of intron 4	0	34	1/1	NA	NA	0/1	1/1	1/1	0/1	1/1	0/1	1/1	1/1	
Heller et al., 2002	Germany	2	1016C>T, 1183C>A	25	44	2/2	2/2	2/2	2/2	2/2	2/2	1/2	0/2	0/2	2/2	2/2	
Rystedt et al., 2002	Scandinav ia	2	1441C>T	NA	35	2/2	NA	1/2	0/2	1/2	2/2	0/2	0/2	0/2	2/2	NA	
Grandas et al., 2002	France	1	NA	26	39	1/1	1/1	1/1	1/1	1/1	1/1	0/1	0/1	1/1	NA	1/1	
Campdelacr eu et al., 2002	Spain	2	NA	Childho od	NA	0/2	NA	2/2	NA	NA	2/2	NA	2/2	NA	NA	2/2	
H Toba et al., 2002	Japan	1	1235G>A, 1441C>T	Juvenile	33	1/1	1/1	NA	0/1	1/1	1/1	0/1	0/1	0/1	NA	NA	
Lamon-Fava et al., 2002	America	1	455G>A(G112E),a five- nucleotide deletion in exon 5 (from nucleotide 965 to 969)	Early adolesce nce	31	1/1	0/1	0/1	0/1	1/1	0/1	0/1	0/1	0/1	1/1	1/1	
Lee et al., 2002	China	1	379C>T,1 263+1G> A		16	34	1/1	1/1	1/1	1/1	NA	1/1	NA	0/1	0/1	NA	1/1

Castelnovo et al. 2003	France	1	1183C>T, 1209C>G	NA	37	1/1	1/1	1/1	1/1	1/1	0/1	0/1	1/1	0/1	1/1	1/1	Oromandibular dyskinesia	
Bordia et al., 2003	India	1	Glu162T>G,Arg441T>C	33	58	1/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	NA		0/1
KATO et al., 2003	Japan	1	89A>C	NA	45	1/1	1/1	1/1	0/1	1/1	0/1	0/1	0/1	0/1	0/1	NA		1/1
Gaikwad et al., 2003	India	2	NA	5	23	1/2	2/2	0/2	0/2	2/2	2/2	0/2	0/2	0/2	0/2	NA	2/2	Gallbladder cancer
Lange et la., 2004	Brazil	2	1187C>T	20, Childhood	43.5	2/2	2/2	2/2	2/2	2/2	1/2	2/2	0/2	0/2	2/2	2/2	2/2	
Valdivielso et al., 2004	Spain	3	441G>A(Kim et al.,Garuti et al.)	Childhood	26	2/3	0/3	0/3	0/3	1/3	3/3	0/3	1/3	0/3	NA	NA	NA	
Bartholdi et al., 2004	Switzerland	2	646G>C,1213C>T	Childhood,25	51.5	0/2	0/2	2/2	0/2	1/2	1/2	1/2	0/2	0/2	0/2	NA	2/2	Coronary heart disease
Mak et al., 2004	China	1	1185-1G>T,p.R372Q	NA	48	1/1	1/1	1/1	NA	1/1	1/1	0/1	0/1	0/1	0/1	NA	1/1	Spinal xanthomatosis
Lorincz et al., 2005	German-English	2	1384C>T	Childhood	54	1/2	2/2	2/2	NA	2/2	2/2	1/2	1/2	1/2	1/2	NA	2/2	Fronto-temporal dementia Pediatric hepatology
Guyant-Marchal L et al., 2005	France	1	1016C>T, 1435C>G	Adolescence	44	1/1	0/1	0/1	0/1	1/1	0/1	0/1	0/1	0/1	0/1	NA	1/1	
Vonbahr et al., 2005	Bangladesh	1	1234G>T	Birth	6 weeks	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	NA	NA	
Schols et al., 2006	German	1	NA	Infancy	42	0/1	1/1	1/1	NA	1/1	1/1	1/1	1/1	1/1	0/1	NA	1/1	

Brodsky et al., 2006	America	1	NA	25	31	1/1	1/1	NA	NA	0/1	0/1	0/1	0/1	0/1	NA	NA
Siman-Tov et al., 2006	Ashkenazi /Jewish	1	NA	4	29	0/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1
Srinivas et al., 2006	India	1	NA	Birth	26	1/1	0/1	1/1	NA	1/1	1/1	0/1	0/1	0/1	NA	NA
Wang et al., 2006	China	3	326delC	3/3	3/3	3/3	3/3	3/3	3/3	NA	0/3	0/3	0/3	NA	NA	NA
Geraldes et al., 2007	France	1	Negative	27	47	1/1	1/1	1/1	1/1	1/1	1/1	0/1	0/1	0/1	NA	0/1
Hansson et al., 2007	Sweden	1	1434C>A, 1435C>A	18-20	26	1/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	NA	0/1
Okuma et al., 2007	Japan	1	Negative	Childhood	46	1/1	1/1	0/1	0/1	1/1	1/1	1/1	0/1	0/1	NA	1/1
Smithard et al., 2007	UK	2	NA	NA	36	2/2	0/2	0/2	0/2	1/2	0/2	0/2	0/2	0/2	NA	2/2
Gonzalez-Cuyar et al., 2007	America	1	NA	NA	49	1/1	NA	1/1	1/1	1/1	1/1	NA	1/1	NA	NA	NA
Wang et al., 2007	China	1	379C>T,1420C>T	6	42	1/1	1/1	1/1	1/1	1/1	1/1	NA	0/1	0/1	NA	1/1
M. Szlago et al., 2008	Argentina	2	11_12insT GGGCTG CGC,1183 C>T(R395C)	Infancy	15	0/2	0/2	0/2	NA	2/2	2/2	2/2	2/2	1/2	2/2	1/2

Mutations
c.1016C>
T and
c.1183
C>T in the
CYP21A2
gene.

Pilo de la Fuente et al., 2008	Spain	1	845-1 G>A		18	52	0/1	0/1	1/1	0/1	0/1	1/1	0/1	0/1	1/1	0/1	1/1	Personalit y changes
Germaine Pierre et al., 2008	Asia	2	1184+1G>A	Infancy	1		0/2	0/2	0/2	0/2	2/2	0/2	0/2	0/2	0/2	0/2	0/2	Chronic active hepatitis
Alcalay et al., 2009	America	1	exon 5: T306M and exon 6: E359A	Infancy	33		1/1	1/1	1/1	1/1	1/1	1/1	1/1	0/1	0/1	NA	1/1	Oromandi bular dystonia
Karandikar et al., 2009	America	1	NA	Childho od	36		1/1	1/1	0/1	0/1	1/1	1/1	1/1	0/1	0/1	NA	1/1	
Bonnot et al., 2010	France	2	Arg 395 Cys,Arg 479 Cys		6	11	0/2	0/2	1/2	2/2	2/2	1/2	1/2	0/2	0/2	NA	1/2	Behavioral disturbanc es
Bourkiza et al., 2010	Banglades h	6	1184+1G>A (homozygo us)		3	childre n	0/6	1/6	1/6	0/6	6/6	3/6	3/6	0/6	0/6	NA	NA	
Gallus et al., 2010	Italy	7	752C>A,1263 + 5 G>T,433 G>A,647-1 G>T, 1183C>T, 863 del A 1330-1333delTT CC,1381C > T	Infancy	26		5/7	5/7	6/7	5/7	4/7	6/7	4/7	0/7	0/7	5/7	5/7	Psychiatri c manifestat ions, osteopenia
Schneider et al., 2010	German	1	1333delTT CC,1381C > T	Infancy	35		1/1	1/1	1/1	1/1	1/1	1/1	1/1	0/1	0/1	1/1	0/1	

Kamate et al., 2010	India	2	NA	11.5	15.5	2/2	2/2	2/2	NA	2/2	2/2	2/2	0/2	0/2	NA	NA	Oromandibular dyskinesia
Nozue et al., 2010	Japan	2	p.R104Q*, p.R441Q,p .R441W 1333C>T,I	33.5	66	2/2	2/2	2/2	NA	2/2	0/2	0/2	0/2	0/2	NA	1/2	
Su et al., 2010	China	2	VS7+1G> A	NA	23.5	2/2	2/2	2/2	2/2	2/2	2/2	1/1	1/1	0/1	NA	2/2	
Wallon et al., 2010	France	1	1435C>T, 1017G>C	51	64	1/1	1/1	1/1	NA	1/1	0/1	0/1	1/1	0/1	NA	1/1	
Chen et al., 2011	China	1	205- 206delC,3 10C>T	NA	42	1/1	0/1	0/1	0/1	0/1	0/1	NA	0/1	0/1	NA	NA	
Seidel et al., 2011	Australia	1	1263+1G> A,p.446C> T	Juvenile	34	0/1	1/1	0/1	1/1	1/1	1/1	1/1	0/1	0/1	NA	1/1	Presenile osteoporosis
Androdias et al., 2011	France	1	1183C>T, 1184+1G> A	50	59	0/1	1/1	1/1	1/1	1/1	1/1	1/1	0/1	1/1	0/1	1/1	
Bhojwani et al., 2011	India	1	NA	Infancy	32	1/1	0/1	1/1	0/1	1/1	1/1	0/1	1/1	0/1	1/1	1/1	
Chen et al., 2011	China	4	305delC,1 333C>T/I VS7+1G> A	NA	29	4/4	4/4	4/4	4/4	4/4	4/4	0/4	0/4	2/4	NA	NA	Osteoporosis with multiple fractures (2/4)

Pilo et al., 2011	Spain	13	688C>T,804G>T,845-1G>A,1213C>T,1183C>T,1043-1054delTGTACCACTCT,1414-1421delGGGTCCG,1016C>T,1473C>T,1184+1G>A	15.8	39	6/13	10/13	12/13	13/13	8/13	12/13	NA	2/13	4/13	NA	NA	Muscular atrophy (9/13), hypoaesthesia (1/13), psychiatric disorders (8/13)
Huijgen et al., 2011	Netherlands, Chile	2	p.Leu142Pro/p.Arg395Cys,p.Arg395Cys/p.Arg405Trp	NA	24.5	2/2	0/2	0/2	0/2	0/2	0/2	NA	0/2	0/2	NA	0/2	Extreme xanthomatosis, hypercholesterolemia
Matysik et al., 2011	German	1	646G>C,1184+1G>A	Childhood	27	1/1	1/1	1/1	1/1	1/1	1/1	1/1	0/1	NA	NA	NA	
Monson et al., 2011	NA	2	NA	Early childhood	10	0/2	0/2	0/2	0/2	2/2	2/2	2/2	1/2	0/2	NA	NA	
Ostrowska et al., 2011	NA	1	NA	Childhood	34	1/1	1/1	1/1	1/1	1/1	1/1	0/1	1/1	0/1	1/1	1/1	

B. Pilo de la Fuente et al., 2011	Spain	14	399G > A,688C > T, 1183C > T,804G > T,844 + 1G > T,845-1G > A,1016C > T,1209C > G,1043-1054 delTGTA CCACCT CT,1213C > G,1184 + 1G > A	20	39	7/14	14/14	13/14	9/12	9/14	13/14	NA	4/14	3/14	NA	NA	
Rafiq et al., 2011	UK	3	NA	Childhood, 41	39	1/3	1/3	2/3	1/3	1/3	3/3	2/3	1/3	0/3	NA	NA	
Tian et al., 2011	China	1	73delG,369-375delGT ACCCA	7	36	1/1	1/1	1/1	1/1	1/1	1/1	NA	0/1	0/1	NA	1/1	
Posada et al., 2011	Spain	1	1184+1G>A	NA	36	1/1	1/1	NA	1/1	1/1	1/1	NA	0/1	1/1	NA	1/1	Botulinum toxin-responsive oromandibular dystonia

Agrawal et al., 2012	India	1	NA	3	38	1/1	NA	NA	NA	1/1	1/1	1/1	NA	NA	NA	1/1	Repeated pathological fractures
Chen et al., 2012	China	1	NA	37	39	1/1	0/1	1/1	0/1	1/1	0/1	NA	0/1	NA	1/1	1/1	Spontaneous clonus, depression
Kauffman et al., 2012	Argentina	1	1213C>T	Infancy	16	0/1	1/1	1/1	NA	NA	1/1	1/1	1/1	0/1	1/1	1/1	Drug-resistant epilepsy, learning difficulties, attention deficit and marked hyperactivity
Kottahachchi et al., 2012	Sri Lanka	2	NA	8	28.5	1/2	2/2	2/2	NA	NA	2/2	NA	1/2	NA	NA	2/2	
Koyama et al., 2012	Japan	1	1238T>A	12	18	1/1	0/1	0/1	0/1	1/1	0/1	0/1	1/1	0/1	1/1	1/1	
Lagarde et al., 2012	Turkey	6	1476 2 T>C,644 G>C,1183 C>T,1213 C>T,1435 C>T	12	23	1/6	6/6	3/6	5/5	6/6	4/6	4/6	2/4	0/6	NA	6/6	Distal myoclonus with mild dystonia of the upper limbs
Mao et al., 2012	China	1	1016C>T	NA	36	1/1	1/1	1/1	1/1	1/1	NA	NA	0/1	0/1	NA	1/1	

Martini et al., 2012	Italy	11	646G>C,688C>T,776A>G,1183C>T,752C>A,1263+5G>T,863 delA	NA	26.4	9/11	NA	NA	NA	NA	10/11	NA	NA	NA	NA	NA	Osteoporosis and multiple bone fractures Non-ST elevation myocardial infarction in 50 years Dystonia, dysphagia Corticobasal syndrome (CBS)
Mignarri et al., 2012a	Italy	1	808c>T,1435C>G	50	67	1/1	0/1	0/1	NA	1/1	1/1	NA	0/1	1/1	NA	1/1	
Mignarri et al., 2012b	Italy	1	752C>A	30	33	0/1	1/1	NA	NA	1/1	1/1	1/1	NA	NA	NA	1/1	
Passaseo et al., 2012	Italy	1	NA	12	25	1/1	NA	NA	NA	NA	1/1	1/1	NA	NA	NA	NA	
Pedroso et al., 2012	Brazil	1	NA	5	35	1/1	0/1	0/1	0/1	0/1	1/1	NA	1/1	0/1	0/1	1/1	
Rohani et al., 2012	Iran	1	NA	2	40	1/1	1/1	1/1	NA	1/1	1/1	NA	0/1	1/1	NA	1/1	
Rubio-Agusti et al., 2012	India	4	NA	15.3	39.3	2/3	1/3	1/3	NA	3/3	3/3	NA	0/3	2/3	2/3	3/3	
Schotsmans et al., 2012	Belgium	1	1263+1g>a	NA	44	0/1	1/1	1/1	1/1	1/1	1/1	NA	NA	1/1	NA	1/1	

Suh et al., 2012	Korea	3	1146_1151 delins,121 4G>A	NA	43.3	3/3	3/3	3/3	3/3	3/3	3/3	NA	NA	NA	NA	3/3	Osteopenia (3/3)
Bajaj et al., 2013	India	2	1151C>T/2T>C	NA	39	2/2	NA	2/2	1/2	2/2	1/2	1/2	1/2	0/2	NA	2/2	
Caroppo et al., 2013	Italy	1	1016C>T 646G>C,752C>A,776A>G,863delA,1183C>T,1263+1G>A,1263+5G>T,1263+81_1596+?del,1183C>T,1184+1G>A,1435C>T,647-1G>T	Childhood	48	0/1	1/1	1/1	NA	1/1	1/1	NA	NA	NA	NA	1/1	
Ginanneschi et al., 2013	Italy	35	63+5G>T,1263+81_1596+?del,1183C>T,1184+1G>A,1435C>T,647-1G>T	NA	43.1	30/35	18/35	24/33	26/33	NA	NA	NA	NA	NA	NA	NA	Learning difficulties (3/6)
Fraidakis, 2013	France(4), France-Spain (2)	6	p.R395C/p.R479C,IVS4-1G>A,	NA	adolescence	1/6	4/6	3/6	2/6	6/6	1/6	1/6	2/6	0/6	NA	4/6	
Pudhiavan et al., 2013	India	1	NA	Childhood	30	1/1	1/1	NA	NA	1/1	1/1	1/1	NA	NA	NA	1/1	
V adapalli et al., 2013	India	1	NA	10	20	1/1	1/1	1/1	0/1	1/1	1/1	NA	1/1	0/1	1/1	1/1	

Jain et al., 2013	India	1	NA	12	25	1/1	1/1	1/1	0/1	1/1	1/1	1/1	0/1	0/1	NA	1/1	'Hot cross bun' (HCB) appearance in the pons Blepharospasm (BSP), postural irregular myoclonic jerks of the upper limbs with distal dystonia
Lagarde et al., 2013	France	1	1213C>T	Childhood	30	1/1	1/1	1/1	NA	NA	1/1	NA	NA	NA	NA	1/1	
Mirzanli et al., 2013	Turkey	1	NA	15	21	0/1	0/1	0/1	0/1	1/1	1/1	NA	0/1	0/1	NA	0/1	
Yahalom et al., 2013	Jewish	18	delT1253, 1037C>T, IVS4-1G>A	NA	22.6	15/18	13/18	16/18	NA	12/18	17/18	13/18	10/18	6/18	NA	NA	
Kulkarni et al., 2014	India	1	NA	Childhood	17	1/1	0/1	0/1	0/1	0/1	1/1	0/1	0/1	0/1	NA	1/1	Altered Welch's angle

Lionnet et al., 2014	France	12	IVS4-1g>a,646G>C,1184+1g>a,1183C>T,1198G>T,1263+1g>a,1016C>T,IVS7+1g>a	5 months-45 years	39	2/12	11/12	10/12	6/12	9/12	3/12	2/18	8/12	NA	NA	12/12	
Luyckx et al., 2014	Belgium	2	1037C>T	Childhood	13	0/2	2/2	0/2	2/2	2/2	2/2	2/2	0/2	0/2	NA	0/2	Bilateral undescended testes
Mandrile et al., 2014	Sardinia	3	1435C>T	20	45.5	3/3	1/3	3/3	2/3	3/3	2/3	0/3	0/3	0/3	1/3,NA2/3	2/3	Gallbladder stones (1/3)
Sastri et al., 2014	India	1	NA	Childhood	19	1/1	0/1	0/1	NA	1/1	1/1	1/1	0/1	0/1	NA	NA	
Yoshinaga et al., 2014	Japan	1	1004C>T* (p.A335V),1214G>A	25	47	1/1	1/1	1/1	NA	1/1	1/1	NA	0/1	1/1	1/1	1/1	Dystonia of the jaw, tongue and right upper limb
Kapás et al., 2014	Hungary	2	379C>T	Childhood	44.5	2/2	1/2	2/2	1/2	2/2	2/2	2/2	1/2	0/2	NA	1/1	Hepatomegaly (2/2), osteoporosis (1/2)

Zhong et al., 2014	China	1	1016C>T, 446+1G>T *	14	21	1/1	1/1	0/1	NA	1/1	1/1	NA	0/1	0/1	NA	1/1	Palatal myoclonus (1/2), infertility (1/2)
Dutta et al., 2015	India	2	526delG,4 46+1G>A	5.5	29.5	2/2	2/2	2/2	2/2	2/2	2/2	2/2	1/2	NA	NA	2/2	
Giraldo-Chica et al., 2015	Colombia	3	1183_1184 insT	14.7	NA	3/3	1/3	2/3	0/3	3/3	1/3	2/3	2/3	3/3	0/3	3/3	
Nicholls et al., 2015	UK	1	1183C>T	Childhood	27	0/1	0/1	1/1	1/1	0/1	0/1	1/1	0/1	1/1	NA	1/1	Spontaneous clonus, depression
Ragno et al., 2015	Italy	1	380G>A	1	32	1/1	0/1	1/1	0/1	0/1	1/1	1/1	1/1	0/1	1/1	1/1	
Smalley et al., 2015	Chile	2	256- 1G>T/118 3C>T,118 5-1G>A	NA	28.5	1/2	1/2	2/2	1/2	0/2	2/2	2/2	0/2	0/2	0/2	2/2	Spinal cord MRI showed long hyperintense lesions
Muniaswamy et al., 2016	India	1	NA	4	27	1/1	NA	NA	NA	1/1	1/1	NA	NA	NA	NA	1/1	
Abe et al., 2016	Japan	1	1214G>A	39	46	0/1	0/1	1/1	NA	NA	0/1	NA	0/1	0/1	NA	1/1	

Degos et al., 2016	Caucasian, Turkey	13	667G>C/808C>T,1184+1G>A,845-1G>A,256-2del,1183C>T/1213C>T,646G>C,1435C>T,1476+2T>C1263+5G>T,1435C>G43_44delGG	4.2	30	3/13	7/13	1/13	10/13	13/13	11/13	10/13	1/13	NA	NA	13/13	School difficulties (11/13), psychiatric symptoms (6/13), myoclonic dystonia (7/13)
Di Taranto et al., 2016	Italy	2	T,1435C>G	NA	30.5	2/2	1/2	0/2	0/2	1/2	1/2	NA	NA	0/2	NA	0/2	
Höflinger et al., 2016	Japan	1	G43_44delGG	23	35	0/1	0/1	1/1	0/1	1/1	0/1	0/1	1/1	0/1	1/1	1/1	
Kulkarni et al., 2016	India	1	525delG	1 month	10	0/1	1/1	NA	1/1	1/1	1/1	1/1	0/1	NA	NA	1/1	Dystonia
Larson et al., 2016	Caucasian	1	1016C>T	4 months	12	0/1	1/1	1/1	NA	1/1	1/1	0/1	0/1	0/1	1/1	1/1	Infantile spasms Spinal xanthomatosis
Parente et al., 2016	Canada	1	32440 G/A-> A/A	1.5	35	1/1	1/1	1/1	0/1	0/1	1/1	1/1	1/1	0/1	NA	1/1	
Razi et al., 2016	India	1	NA	23	25	1/1	0/1	0/1	0/1	0/1	1/1	0/1	0/1	0/1	NA	1/1	
Rosafio et al., 2016	Italy	2	1263G>A	20	48	1/2	1/2	1/2	1/2,N A(1/2)	2/2	2/2	NA	1/2	NA	1/2,N A(1/2)	1/2,N A(1/2)	
Saxena et al., 2016	India	3	NA	NA	14.3	1/3	1/3	3/3	1/3	3/3	2/3	2/3	0/3	0/3	NA	1/3	
Varman et al., 2016	America	1	1183C > T	NA	70	1/1	NA	NA	NA	1/1	1/1	NA	NA	NA	NA	NA	Osteoporosis

Yanagihashi et al., 2016	Japan	1	p.Q85R,p.R405Q	40	77	1/1	1/1	1/1	NA	0/1	0/1	NA	0/1	0/1	NA	1/1	Late-onset spinal CTX
Za'dori et al., 2016	Hungary	2	819delT 379C>	Childhood, NA	40	0/2	1/2	1/2	NA	2/2	1/2	1/2	0/2	2/2	NA	2/2	
Zhang et al., 2016	China	1	T,1174G>A	NA	27	1/1	1/1	1/1	NA	1/1	1/1	NA	0/1	0/1	NA	1/1	
Roy et al., 2017	India	1	NA	NA	11	1/1	1/1	NA	NA	NA	1/1	1/1	NA	NA	NA	NA	Psychiatric symptoms
Abdel-Hamid et al., 2017	Egypt	1	1169delT	9	35	1/1	1/1	1/1	0/1	1/1	0/1	NA	1/1	0/1	1/1	1/1	
Alhariri et al., 2017	Han ethnicity	1	446+1G>T,808C>T	19	36	1/1	1/1	1/1	NA	1/1	1/1	0/1	0/1	0/1	NA	1/1	
Jung et al., 2017	Korea	1	435G>T,435G>T	20	39	1/1	0/1	1/1	1/1	1/1	0/1	1/1	0/1	0/1	NA	1/1	
Chen et al., 2017	China	5	1537C>T,1477-2A>C,562C>T,	30-40	40	5/5	2/5	3/5	0/5	2/5	0/5	NA	0/5	0/5	NA	4/5	

Mignarri et al., 2017	Italy	37	688C>T,1 183C>T,6 46G>C,12 63+5G>T, 397C>T,7 52C>A,12 63+1G>A, 808C>T,1 435C>T,7 76A>G,11 84+1G>A, 863delA,6 47- 1G>T,126 3+81_159 6+?del,143 5C>T,380 G>A,1538 G>A,1264 - 1G>A,101 6C>T	NA	39.1	31/37	15/37	27/37	NA	29/37	34/37	NA	9/37	4/37	NA	37/37	Psychiatric symptoms (26/27)
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Souza et al., 2017	NA	1	NA	NA	40	1/1	NA	NA	1/1	1/1	1/1	NA	NA	NA	NA	1/1	Early-onset dementia, Tc-99m brain SPECT scan shows hypoperfusion involving the frontal and temporal lobes and basal ganglia.
Tibrewal et al., 2017	America	1	379C>T,1420C>T	Infancy	8	0/1	NA	NA	NA	NA	1/1	1/1	NA	NA	NA	NA	Bilateral femoral Neck Fractures Psychiatric symptoms (3/6)
Wejjakul et al., 2017	Thailand	1	1072C>T	10	46	1/1	1/1	0/1	NA	1/1	1/1	NA	0/1	0/1	NA	NA	Spinal root hypertrophy on MRI
Zubarioglu et al., 2017	Turkey	6	NA	3.2	11.1	0/6	6/6	0/6	5/6	5/6	3/6	2/6	0/6	NA	NA	5/6	
Hashimoto et al., 2018	Japan	1	1421G>A	4	39	NA	1/1	1/1	NA	1/1	1/1	NA	NA	NA	NA	1/1	

Mukaino et al., 2018	Japan	1	1421G>A	Infancy	47	1/1	1/1	1/1	NA	1/1	1/1	1/1	NA	NA	1/1	1/1	Extensive cerebral cortex symptoms (ECCS)
Nambirajan et al., 2018	NA	2	NA	Childhood	24	2/2	NA	NA	NA	2/2	2/2	2/2	NA	NA	NA	1/2	
Rossi et al., 2018	NA	1	1183C>T, 1184+1G>A	Childhood	31	0/1	1/1	1/1	1/1	NA	0/1	1/1	NA	NA	NA	1/1	Palatal tremor, depression
Sasamura et al., 2018	Japan	1	1421G>A, 1342_1343 insCACC	7	50	1/1	0/1	1/1	NA	0/1	1/1	0/1	1/1	0/1	NA	1/1	Osteoporosis
Tada et al., 2018	Japan	1	410G>A	NA	63	1/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	NA	1/1	Abdominal aortic aneurysm
Wong et al., 2018	NA	5	380G>A, p.R395C, 296A>G, 1420C>T	NA	34.2	4/5	4/5	3/5	3/5	4/5	4/5	3/5	1/5	1/5	1/5	4/5	
Weissfeld et al., 2018	NA	1	379C>T, 1016C>T	NA	45	0/1	1/1	1/1	NA	1/1	1/1	NA	0/1	0/1	NA	1/1	Psychiatric symptoms
Shaji et al., 2019	India	1	p.Arg127Gly	Childhood	35	1/1	1/1	0/1	1/1	1/1	1/1	NA	0/1	0/1	1/1	1/1	Myoclonic jerks

Freedman et al., 2019	White, Black, Asian	3	p.R127W: c.379C>T/ c.1180_1181delCT,p. Q358X:c.1072C>T/p. G472V:c.1415G>T,p. R231X:c.691C>T/p. Q85Q:c.255G>A 368_374del 1CCAGTAC*, 389 T>A*,571 C>T*,379 C>T, 435G>T,1016C>T,1 214G>A, 1263+1G>A,1420C>T,1435C>T 850_854delinsCTC	NA	16	NA	2/3	NA	NA	2/3	3/3	1/3	2/3	NA	2/3	NA	Frequent fractures (2/3)
Tao et al., 2019	China	6	435G>T,1016C>T,1 214G>A, 1263+1G>A,1420C>T,1435C>T 850_854delinsCTC	NA	31.8	3/6	4/6	6/6	NA	2/6	1/6	1/6	1/6	NA	5/6,1/6(NA)	3/6,1/6(NA)	
Gelzo et al., 2019	Caucasian	1	850_854delinsCTC	5	28	0/1	1/1	1/1	1/1	0/1	1/1	1/1	0/1	0/1	NA	1/1	
Lee et al., 2019	China	2	435G>T,1264A>G 1016C>T, 1263+1G>A	15	38	2/2	2/2	2/2	2/2	2/2	0/2	0/2	0/2	2/2	NA	2/2	
Li et al., 2019	China	1	1263+1G>A	9	40	1/1	0/1	1/1	NA	1/1	1/1	1/1	1/1	1/1	NA	1/1	

Miyamoto et al., 2019	Japan	1	1421G>A	NA	39	1/1	1/1	1/1	NA	NA	1/1	0/1	1/1	NA	NA	1/1	Optic neuritis
Mutlu et al., 2019	Turkey	1	1571T>G	NA	42	0/1	1/1	1/1	NA	NA	NA	NA	0/1	0/1	NA	1/1	
	Japan	1	p.Arg372Gln	31	43	1/1	NA	NA	NA	1/1	NA	NA	NA	NA	NA	NA	Severe coronary artery calcification
Tang et al., 2020	China	2	562C>T*, 435G>T	1	46.5	2/2	2/2	1/2,NA (1/2)	1/2,NA (1/2)	2/2	1/2,NA (1/2)	2/2	0/2	0/2	NA	1/2,NA (1/2)	
Total		520				379/570	345/540	6	78	386/508	535	11	49	44/295	99/175	267/348	
						(66.49%)	(63.89%)	(72.95%)	(52.91%)	(75.98%)	(80.37%)	(47.59%)	(27.39%)	(14.92%)	(56.57%)	(76.72%)	