Title: Alexander Disease *GeneReview* Table 2

Authors: Srivastava S, Naidu S

Updated: January 2015

Note: The following information is provided by the authors listed above and has not been reviewed by *GeneReviews* staff.

Table 2. *GFAP* Mutation Screening in Individuals with Alexander Disease [%]

Exon	Nucleotide Change (Amino Acid Change)	Infantile	Juvenile	Adult	Asymptomatic	Total Affected Individuals	References [†]
1	187A>C **Lys63Gln**			1		1	[1A] (Li et al 2005, van der Knaap et al 2005)
1	197G>A **Arg66Gln**			3		3	[1A] Hida et al 2012 [1A] Pedroso et al 2014 [1A] Prust et al 2011 [aa]
1	205G>A **Glu69Lys**		1			1	[1J] Davison et al 2011
1	~ **Arg70Trp**			1		1	[1A] Yoshida et al 2011b
1	208C>T **Arg70Trp**			4		4	[1A] Salvi et al 2005 [1A] Sreedharan et al 2007 [1A] Caroli et al 2007 [1A] (Farina et al 2008, Pareyson et al 2008)
1	209G>A **Arg70Gln**			4		4	[1A] Caroli et al 2007 [1A] Sechi et al 2008 [1A] (Farina et al 2008, Pareyson et al 2008) [1A] Graff-Radford et al 2014
1	214G>A **Glu72Lys**	1				1	[1I] Prust et al 2011 [bb]
1	218T>G **Met73Arg**		1			1	[1J] Gorospe et al 2002
1	218T>C **Met73Thr**	2				2	[1I] Li et al 2005 [1I] Vasquez et al 2008
1	218T>A **Met73Lys**	1				1	[1I] Caroli et al 2007
1	~ **Met74Thr**			3		3	[1A] Yonezu et al 2012 [1A] Yoshida et al 2011b [1A] Yoshida et al 2011a
1	221T>C **Met74Thr**			1		1	[1A] Ohnari et al 2007

Exon	Nucleotide Change (Amino Acid Change)	Infantile	Juvenile	Adult	Asymptomatic	Total Affected Individuals	References [†]
1	226C>T **Leu76Phe**	2				2	[1I] Rodriguez et al 2001 [1I] Li et al 2005
1	226C>G **Leu76Val**	1				1	[1I] Li et al 2005
1	229A>T **Asn77Tyr**	1				1	[1I] Rodriguez et al 2001
1	230A>G **Asn77Ser**	2				2	[1I] Li et al 2005 [1I] Caroli et al 2007
1	232G>A **Asp78Asn**			2	1	3	[2A 1As] Wada et al 2013 [l]
1	234C>A **Asp78Glu**		1	4	1	6	[1J 4A 1As] Stumpf et al 2003 [a]
1	~ **Arg79Cys**	4				4	[4I] Yoshida et al 2011a
1	235C>G **Arg79Gly**	1				1	[1I] Gorospe et al 2002
1	235C>T **Arg79Cys**	14	2			16	[2I] Brenner et al 2001 [1I] Gorospe et al 2002 [2I] Shiroma et al 2003 [b] [1J] Probst et al 2003 [1I] Ma et al 2005 [2I 1J] Li et al 2005 [3I] Caroli et al 2007 [1I] Mignot et al 2009 [1I] Poloni et al 2009 [1I] Biancheri et al 2013
1	~ **Arg79His**		2	1		3	[1J] Yoshida et al 2013 [1J] Yoshida et al 2011a [1A] Yoshida et al 2011b
1	236G>A **Arg79His**	10	2			12	[1I 1J] Brenner et al 2001 [4I] Rodriguez et al 2001 [2I] Gorospe et al 2002 [2I] (Meins et al 2002, Brockmann et al 2003a) [b] [1J] Asahina et al 2006 [1I] Ashrafi et al 2013
1	[236G>A; 667G>C] **[Arg79His; Glu223Gln]**	1				1	[1I] Dotti et al 2009 [w]
1	~ **Arg79Leu**		1			1	[1J] Yoshida et al 2011a

Exon	Nucleotide Change (Amino Acid Change)	Infantile	Juvenile	Adult	Asymptomatic	Total Affected Individuals	References [†]
1	236G>T **Arg79Leu**	1				1	[1I] Shiroma et al 2003
1	236G>C **Arg79Pro**		1			1	[1J] Caroli et al 2007
1	239T>C **Phe80Ser**	1				1	[1I] da Silva Pereira et al 2013
1	247T>C **Tyr83His**	1				1	[1I] Wu et al 2008
1	256A>G **Lys86Glu**	2				2	[1I] Prust et al 2011 [cc] [1I] Barreau et al 2011 [cc]
1	256_259delinsGAGT **Lys86_Val87delinsGluPhe**		1			1	[1J] van der Knaap et al 2006
1	~ **Val87Gly**			2	1	3	[1A] Yoshida et al 2011b [1A 1As] Yoshida et al 2011a
1	260T>G **Val87Gly**			3		3	[3A] Okamoto et al 2002 [c]
1	259G>C **Val87Leu**			1		1	[1A] Suzuki et al 2012 [dd]
1	259G>A **Val87Ile**		1	1		2	[1A] Graff-Radford et al 2014 [1J] Restrepo et al 2011
1	~ **Arg88Cys**	1	1			2	[1I 1J] Yoshida et al 2011a
1	262C>T **Arg88Cys**	4	10			14	[2I] Rodriguez et al 2001 [2J] Gorospe et al 2002 [d] [1J] Nobuhara et al 2004 [e] [1J] Li et al 2005 [1I] Kyllerman et al 2005 [3J] van der Knaap et al 2006 [x] [1I] Caroli et al 2007 [1J] Kmiec et al 2007 [2J] Wu et al 2008
1	262C>A **Arg88Ser**	1				1	[1I] Rodriguez et al 2001
1	269T>C **Leu90Pro**	1				1	[1I] Suzuki et al 2004
1	278A>C **Gln93Pro**		1			1	[1J] Kyllerman et al 2005
1	290T>C **Leu97Pro**	2				2	[1I] Meins et al 2002 [1I] Li et al 2005

Exon	Nucleotide Change (Amino Acid Change)	Infantile	Juvenile	Adult	Asymptomatic	Total Affected Individuals	References [†]
1	~ **Leu101Pro**			1		1	[1A] Yoshida et al 2011a
1	302T>C **Leu101Pro**			1		1	[1A] Kaneko et al 2009
1	365_373dup **Arg124_Leu125insGlnLeuArg**			1		1	[1A] Schmidt et al 2013
1	375_380dupGCGGCT **Arg126_Leu127dup**		1			1	[1J] van der Knaap et al 2006
1	382G>A **Asp128Asn**			1		1	[1A] (Farina et al 2008, Pareyson et al 2008)
3	613G>A **Glu205Lys**			2		2	[2A] (Farina et al 2008, Pareyson et al 2008)
4	619G>A **Glu207Lys**		1			1	[1J] (Li et al 2005, van der Knaap et al 2005, Franzoni et al 2006)
4	619G>C **Glu207Gln**		1			1	[1J] (Li et al 2005, van der Knaap et al 2005)
4	628G>A **Glu210Lys**		2	1		3	[1A] Li et al 2005 [1J] Kyllerman et al 2005 [1J] van der Knaap et al 2006
4	667G>C **Glu223Gln**			2		2	[2A] Brockmann et al 2003b [f]
4	692T>A **Leu231His**			2		2	[2A] Delnooz et al 2008 [g]
4	704T>C **Leu235Pro**		3			3	[3J] (Li et al 2005, van der Knaap et al 2005) [b]
4	707A>C **Lys236Thr**	1				1	[1I] Prust et al 2011 [ee]
4	~ **Arg239Gly**		1			1	[1J] Osorio et al 2012
4	715C>G **Arg239Gly**			1		1	[1A] Graff-Radford et al 2014
4	~ **Arg239Cys**	1	2			3	[1I 2J] Yoshida et al 2011a

Exon	Nucleotide Change (Amino Acid Change)	Infantile	Juvenile	Adult	Asymptomatic	Total Affected Individuals	References [†]
4	715C>T **Arg239Cys**	18	5			23	[4I] Brenner et al 2001 [4I] Rodriguez et al 2001 [1I] Shiroma et al 2001 [1I] Gorospe et al 2002 [1J] Shiihara et al 2002 [1I] (Meins et al 2002, Brockmann et al 2003a) [1I] Shiroma et al 2003 [4I 2J] (Li et al 2005, van der Knaap et al 2005) [1I] Wakabayashi et al 2005 [h] [2I] Li et al 2006 [1J] Barreau et al 2011 [ff]
4	~ **Arg239His**	1				1	[1I] Yoshida et al 2011a
4	716G>A **Arg239His**	10				10	[1I] Brenner et al 2001 [1I] Rodriguez et al 2001 [5I] Li et al 2005 [1I] Caroli et al 2007 [1I] Sakakibara et al 2007 [1I] Ashrafi et al 2013
4	716G>C **Arg239Pro**	2	1			3	[1I] (Meins et al 2002, Brockmann et al 2003a) [1J] (Li et al 2005, van der Knaap et al 2005) [1I] Caroli et al 2007
4	716G>T **Arg239Leu**	2				2	[1I] Lee et al 2006 [1I] Shiihara et al 2011 [gg]
4	724T>G **Tyr242Asp**	1				1	[1I] Gorospe et al 2002
4	~ **Ala244Val**		1	1		2	[1J 1A] Yoshida et al 2011a
4	731C>T **Ala244Val**	1	1			2	[1I] Aoki et al 2001 [1J] (Li et al 2005, van der Knaap et al 2005)
4	739T>C **Ser247Pro**		1	2	2	5	[1J 2A 2As] Messing et al 2012 [n]
4	758C>G **Ala253Gly**	1				1	[1I] (Li et al 2005, van der Knaap et al 2005)
4	770A>G **Tyr257Cys**			1		1	[1A] Howard et al 2008

Exon	Nucleotide Change (Amino Acid Change)	Infantile	Juvenile	Adult	Asymptomatic	Total Affected Individuals	References [†]
4	~ **Arg258Cys**			3		3	[1A] Spritzer et al 2013 [1A] Yoshida et al 2011b [1A] Yoshida et al 2011a
4	772C>T **Arg258Cys**		1			1	[1J] Van Poppel et al 2009
4	773G>C **Arg258Pro**	1				1	[1I] Brenner et al 2001
5	~ **Leu264Pro**			1		1	[1A] Yoshida et al 2011a
5	791T>C **Leu264Pro**			1		1	[1A] Graff-Radford et al 2014 [jj]
5	791_792delinsCT **Leu264Pro**			1		1	[1A] Ayaki et al 2010
5	799G>C **Ala267Pro**		1			1	[1J] Hinttala et al 2007 [e]
5	~ **Ala268Asp**		1			1	[1J] Yoshida et al 2013
5	~ **Arg276Leu**			3	1	4	[3A] Yoshida et al 2011a [1As] Yoshida et al 2011a
5	827G>T **Arg276Leu**		1	2		3	[2A] Namekawa et al 2002 [g] [1J] Namekawa et al 2012
5	835A>G **Lys279Glu**		1			1	[1J] Li et al 2005
5	868C>G **Gln290Glu**	1				1	[1I] Barreau et al 2011
6	934G>T **Glu312Ter**			1		1	[1A] Nam et al 2014
6	[988C>G; 994G>A] **[Arg330Gly; Glu332Lys]**			4		4	[4A] Balbi et al 2008 [i]
6	992T>C **Leu331Pro**	1			2	3	[1I 2As] Shiihara et al 2004 [j]
6	994G>A **Glu332Lys**			1		1	[1A] (Farina et al 2008, Pareyson et al 2008)
6	**Tyr349_Gln350insHisLeu**	1				1	[1I] Li et al 2005
6	1051G>C **Asp351His**			1		1	[1A] Tschampa et al 2011 [q]
6	1055T>C **Leu352Pro**	2				2	[1I] (Bassuk et al 2003, Li et al 2005) [1I] Niinikoski et al 2009

Exon	Nucleotide Change (Amino Acid Change)	Infantile	Juvenile	Adult	Asymptomatic	Total Affected Individuals	References [†]
6	~ **Leu357Pro**			1		1	[1A] Yoshida et al 2011b
6	1073C>T **Ala358Val**	1				1	[1I] Dinopoulos et al 2006
6	1074C>G **Leu359Val**		1			1	[1J] Li et al 2005
6	1075C>G **Leu359Val**	1				1	[1I] Ramesh et al 2013
6	1076T>C **Leu359Pro**			2		2	[1A] (Caroli et al 2007, Romano et al 2007) [1A] (Farina et al 2008, Pareyson et al 2008)
6	~ **Asp360Val**		1			1	[1J] Yoshida et al 2011a
6	~ **Glu362Gly**		1			1	[1J] Yoshida et al 2013
6	1086>C **Glu362Asp**		1			1	[1J] Sawaishi et al 2002
6	~ **Ala364Thr**			2		2	[2A] Yoshida et al 2011a
6	1090G>C **Ala364Pro**	1				1	[1I] Li et al 2005
6	1091C>T **Ala364Val**	1				1	[1I] Hartmann et al 2007
6	1096T>C **Tyr366His**	1				1	[1I] Li et al 2005
6	1097A>G **Tyr366Cys**	1				1	[1I] Hartmann et al 2007
6	1112A>G **Glu371Gly**	1				1	[1I] Kawai et al 2006
6	1111G>C **Glu371Gln**	1				1	[1I] Prust et al 2011 [hh]
6	1112A>T **Glu371Val**	1				1	[1I] Prust et al 2011 [ii]
6	~ **Glu373Asp**		1			1	[1J] Yoshida et al 2011a
6	1117G>A **Glu373Lys**	5				5	[1I] Gorospe et al 2002 [2I] Li et al 2005 [1I] Matej et al 2008 [1I] Larsen et al 2012

Exon	Nucleotide Change (Amino Acid Change)	Infantile	Juvenile	Adult	Asymptomatic	Total Affected Individuals	References [†]
6	1117G>C **Glu373Gln**	1				1	[1I] Li et al 2005
6	1118A>C **Glu373Ala**			2		2	[2A] Graff-Radford et al 2014[z]
6	1121A>G **Glu374Gly**	1				1	[1I] Li et al 2005
6	~ **Arg376Trp**	1		1		2	[1J] Zafeiriou et al 2013 [1A] Yoshida et al 2011a
6	1126C>T **Arg376Trp**		1	1		2	[1J 1A] Hirayama et al 2008[f]
7	1148C>T **Thr383Ile**			1		1	[1A] Schmidt et al 2011
7	1154C>T **Ser385Phe**	1				1	[1I] Torisu et al 2013
7	1154C>G **Ser385Cys**			2		2	[2A] Graff-Radford et al 2014 [k]
7	1157A>T **Asn386Ile**	1				1	[1I] Caceres-Marzal et al 2006
8	~ **Ser393Ile**			1		1	[1A] Yoshida et al 2011a
8	1178G>T **Ser393Ile**		1	2		3	[1J 1A] Salmaggi et al 2007 [f] [1A] (Farina et al 2008, Pareyson et al 2008)
8	~ **Ser398Phe**			2		2	[1A] Yoshida et al 2011a [1A] Sueda et al 2009
8	1193C>A **Ser398Tyr**			1		1	[1A] (Farina et al 2008, Pareyson et al 2008)
8	~ **Met415Ile**		1	1		2	[1J] Rezende et al 2012 [y]
8	~ **Arg416Trp**	1				1	[1I] Nishri et al 2014
8	1246C>T **Arg416Trp**	2	4	5		11	[2I] Brenner et al 2001 [2J] Gorospe et al 2002 [1A] Kinoshita et al 2003 [2A] Thyagarajan et al 2004 [f] [1A] Li et al 2005 [1J] van der Knaap et al 2006 [1J] Caroli et al 2007 [1A] (Farina et al 2008, Pareyson et al 2008)

Exon	Nucleotide Change (Amino Acid Change)	Infantile	Juvenile	Adult	Asymptomatic	Total Affected Individuals	References †
8	1250A>C **Asp417Ala**		1	2	1	4	[1J 2A 1As] Messing et al 2012
8	1249delG **Asp417MetfsTer15**	3				3	[1I] Murakami et al 2008 [u] [1I] Flint et al 2012 [1I] Yoshida et al 2011a
9	1277A>T **Gln426Leu**			1	1	2	[1A] Messing et al 2012 [p, v]
9	1292_1299delinsATC **Val431_Met432delinsAspArgGlnAspProProGlyGlyLeuCysProValSer (Val431AspfsTer14)**	1				1	[1I] Flint et al 2012 [m]
7A[s]	1289G>A **Arg430His**			2		2	[2A] Melchionda et al 2013 [r, t]
Splice site	619-3C>G **Glu207_Lys260del (exon 4 skip)**			1		1	[1A] Flint et al 2012
Splice site	IVS4-24_c812delins (56bp del, 20bp ins) **Phe261_Thr302del (exon 5 skip)**			1		1	[1A] Graff-Radford et al 2014
TOTAL Mutation-confirmed Cases		**124**	**63**	**96**	**10**	**293**	
	No mutations identified	2	2	2		6	[1I] Brenner et al 2001 [1I] Rodriguez et al 2001 [1J] Gorospe et al 2002 [1J 1A] Li et al 2005 [1A] Huttner et al 2007
TOTAL Mutation-screened Cases		**126**	**65**	**98**	**10**	**299**	

[%] A separate list of *GFAP* mutations has been maintained by Dr. Albee Messing and is viewable at www.waisman.wisc.edu/alexander-disease/mutation-table.pdf

†[ ] indicates the number of patients and the form of Alexander disease described in the reference: I=infantile, J=juvenile, A=adult, As=asymptomatic.

References enclosed in ( ) described the same patient(s).

~ indicates the nucleotide change has not been reported.

[a] All six individuals belong to a three-generation family [Stumpf et al 2003].

[b] References describe cases of monozygotic twin pairs.

[c] All three individuals belong to the same pedigree [Okamoto et al 2002].

[d] One patient is the same patient described in Guthrie et al 2003.

[e] A concomitant mitochondrial mutation was identified.

[f] Mother and child pair.

[g] Patients described are siblings.

[h] Infantile-onset patient atypical for being a long-term survivor [Wakabayashi et al 2005].

[I] All four individuals belong to the same family [Balbi et al 2008].

[j] All three patients belong to the same family. The proband showed megalencephaly at 4m with no other abnormalities. MRI at 16m revealed abnormalities in the frontal white matter and basal ganglia. An elder sister (7y) and the mother (34y) showed the same nucleotide change but were asymptomatic and showed only mild abnormalities in the frontal and caudate regions by MRI [Shiihara et al 2004].

[k] Father, child pair

[l] Members of a family in which the affected adults are sisters, and the unaffected individual is the son of one of the sisters

[m] Chimera

[n] Members of a 2-generation pedigree with affected members being the father and his 4 children. The father is being counted as asymptomatic, though this is unclear, as he had multiple chronic health problems, including alcoholism, sleep apnea, and scoliosis which began in young adulthood. His mutation was confirmed with sequencing of DNA isolated from paraffin blocks from a testicular biopsy.

[o] Members of a multi-generation pedigree

[p] Mother, daughter pair

[q] Patient also has a heterozygous variant in intron 3 (c.619-35_-21del) and heterozygous polymorphism in exon 2 (rs59291670)

[r] Half-siblings, sharing the same healthy mother (who is suspected of having germinal mosaicism)

[s] Mutation in alternative exon 7A of transcript NM_001131019.2

[t] One of the patients also has a hemizygous variant in *HDAC6* (c.2566C>T; p.P856S); the mother was heterozygous for this variant.

[u] Mutation reported as “1247-1249GGG>GG (Asp417Met14STOP)”

[v] Individual who is asymptomatic had scoliosis at age 9 years but no neurologic symptoms. She developed bipolar affective disorder and abused alcohol, and she died with elevated blood alcohol level.

[w] The *GFAP* variant c.667G>C (p.Glu223Gln) is felt to be a rare variant rather than disease causing but its exact pathogenicity is unclear.

[x] 2 of the patients are a mother-son pair

[y] Mother, daughter pair. Daughter, but not mother, has a *GFAP* variant p.Asp157Gln; the pathogenicity of this variant is unclear.

[z] Mother-daughter pair, both affected by Alexander disease, though only daughter’s mutation reported.

[aa] Nucleotide change reported as c.211G>A; nucleotide sequence written in table is with respect to the start of the coding sequence

[bb] Nucleotide change reported as c.228G>A; nucleotide sequence written in table is with respect to the start of the coding sequence

[cc] Nucleotide change reported as c.270A>G; nucleotide sequence written in table is with respect to the start of the coding sequence

[dd] Nucleotide change reported as c.273G>C; nucleotide sequence written in table is with respect to the start of the coding sequence

[ee] Nucleotide change reported as c.721A>C; nucleotide sequence written in table is with respect to the start of the coding sequence

[ff] Nucleotide change reported as c.729C>T; nucleotide sequence written in table is with respect to the start of the coding sequence

[gg] Nucleotide change reported as c.730G>T; nucleotide sequence written in table is with respect to the start of the coding sequence

[hh] Nucleotide change reported as c.1125G>C; nucleotide sequence written in table is with respect to the start of the coding sequence

[ii] Nucleotide change reported as c.1126A>T; nucleotide sequence written in table is with respect to the start of the coding sequence

[jj] Nucleotide change reported as c.701T>C; nucleotide sequence written in table is with respect to the start of the coding sequence

References

Aoki Y, Haginoya K, Munakata M, Yokoyama H, Nishio T, Togashi N, Ito T, Suzuki Y, Kure S, Iinuma K, Brenner M, Matsubara Y. A novel mutation in glial fibrillary acidic protein gene in a patient with Alexander disease. Neurosci Lett. 2001;312:71-4.

Asahina N, Okamoto T, Sudo A, Kanazawa N, Tsujino S, Saitoh S. An infantile-juvenile form of Alexander disease caused by a R79H mutation in GFAP. Brain Dev. 2006;28:131-3.

Ashrafi M-R, Tavasoli A, Aryani O, Alizadeh H, Houshmand M. Alexander disease: report of two unrelated infantile form cases, identified by GFAP mutation analysis and review of literature; the first report from Iran. Iran J Pediatr. 2013;23:481–4.

Ayaki T, Shinohara M, Tatsumi S, Namekawa M, Yamamoto T. A case of sporadic adult Alexander disease presenting with acute onset, remission and relapse. J Neurol Neurosurg Psychiatry. 2010;81:1292–3.

Balbi P, Seri M, Ceccherini I, Uggetti C, Casale R, Fundarò C, Caroli F, Santoro L. Adult-onset Alexander disease Report on a family. J Neurol. 2008;255:24–30.

Barreau P, Prust MJ, Crane J, Loewenstein J, Kadom N, Vanderver A. Focal central white matter lesions in Alexander disease. J Child Neurol. 2011;26:1422–4.

Bassuk AG, Joshi A, Burton BK, Larsen MB, Burrowes DM, Stack C. Alexander disease with serial MRS and a new mutation in the glial fibrillary acidic protein gene. Neurology. 2003;61:1014-5.

Biancheri R, Rossi A, Ceccherini I, Pezzella M, Prato G, Striano P, Minetti C. Magnetic resonance imaging “tigroid pattern” in Alexander disease. Neuropediatrics. 2013;44:174–6.

Brenner M, Johnson AB, Boespflug-Tanguy O, Rodriguez D, Goldman JE, Messing A. Mutations in GFAP, encoding glial fibrillary acidic protein, are associated with Alexander disease. Nat Genet 2001;27:117-20.

Brockmann K, Dechent P, Meins M, Haupt M, Sperner J, Stephani U, Frahm J, Hanefeld F. Cerebral proton magnetic resonance spectroscopy in infantile Alexander disease. J Neurol. 2003a;250:300-6.

Brockmann K, Meins M, Taubert A, Trappe R, Grond M, Hanefeld F. A novel GFAP mutation and disseminated white matter lesions: adult Alexander disease? Eur Neurol. 2003b;50:100-5.

Cáceres-Marzal C, Vaquerizo J, Galán E, Fernández S. Early mitochondrial dysfunction in an infant with Alexander disease. Pediatr Neurol. 2006;35:293-6.

Caroli F, Biancheri R, Seri M, Rossi A, Pessagno A, Bugiani M, Corsolini F, Savasta S, Romano S, Antonelli C, Romano A, Pareyson D, Gambero P, Uziel G, Ravazzolo R, Ceccherini I, Filocamo M. GFAP mutations and polymorphisms in 13 unrelated Italian patients affected by Alexander disease. Clin Genet. 2007;72:427–33.

Da Silva Pereira CC, Gattás GS, Lucato LT. Alexander disease: a novel mutation in the glial fibrillary acidic protein gene with initial uncommon clinical and magnetic resonance imaging findings. J Comput Assist Tomogr. 2013;37:698–700.

Davison JE, Davies NP, English MW, Philip S, MacPherson LKR, Gissen P, Peet AC. Magnetic resonance spectroscopy in the diagnostic evaluation of brainstem lesions in Alexander disease. J Child Neurol. 2011;26:356–60.

Delnooz CCS, Schelhaas JH, van de Warrenburg BPC, Jan de Graaf R, Salomons GS. Alexander disease causing hereditary late-onset ataxia with only minimal white matter changes: a report of two sibs. Mov Disord. 2008;23:1113-4.

Dinopoulos A, Gorospe JR, Egelhoff JC, Cecil KM, Nicolaidou P, Morehart P, DeGrauw T. Discrepancy between neuroimaging findings and clinical phenotype in Alexander disease. Am J Neuroradiol. 2006;27:2088-92.

Dotti MT, Buccoliero R, Lee A, Gorospe JR, Flint D, Galluzzi P, Bianchi S, D’Eramo C, Naidu S, Federico A, Brenner M. An infantile case of Alexander disease unusual for its MRI features and a GFAP allele carrying both the p.Arg79His mutation and the p.Glu223Gln coding variant. J Neurol. 2009;256:679–82.

Farina L, Pareyson D, Minati L, Ceccherini I, Chiapparini L, Romano S, Gambaro P, Fancellu R, Savoiardo M Can MR Imaging Diagnose Adult-Onset Alexander Disease? Am J Neuroradiol. 2008;29:1190–96.

Flint D, Li R, Webster LS, Naidu S, Kolodny E, Percy A, van der Knaap M, Powers JM, Mantovani JF, Ekstein J, Goldman JE, Messing A, Brenner M. Splice site, frameshift, and chimeric GFAP mutations in Alexander disease. Hum Mutat. 2012;33:1141–8.

Franzoni E, Van der Knaap MS, Errani A, Colonnelli MC, Bracceschi R, Malaspina E, Moscano FC, Garone C, Sarajlija J, Zimmerman RA, Salomons GS, Bernardi B. Unusual diagnosis in a child suffering from juvenile Alexander disease: clinical and imaging report. J Child Neurol 2006;21:1075-80.

Gorospe JR, Naidu S, Johnson AB, Puri V, Raymond GV, Jenkins SD, Pedersen RC, Lewis D, Knowles P, Fernandez R, De Vivo D, van der Knaap MS, Messing A, Brenner M, Hoffman EP. Molecular findings in symptomatic and pre-symptomatic Alexander disease patients. Neurology, 2002;58:1494-500.

Graff-Radford J, Schwartz K, Gavrilova RH, Lachance DH, Kumar N. Neuroimaging and clinical features in type II (late-onset) Alexander disease. Neurology. 2014;82:49–56.

Guthrie SO, Burton EM, Knowles P, Marshall R. Alexander's disease in a neurologically normal child: a case report. Pediatr Radiol. 2003;33:47-9.

Hartmann H, Herchenbach J, Stephani U, Ledaal P, Donnerstag F, Lücke T, Das AM, Christen HJ, Hagedorn M, Meins M. Novel mutations in exon 6 of the GFAP gene affect a highly conserved if motif in the rod domain 2b and are associated with early onset infantile Alexander disease. Neuropediatrics. 2007;38:143–7.

Hida A, Ishiura H, Arai N, Fukuoka H, Hasuo K, Goto J, Uesaka Y, Tsuji S, Takeuchi S. Adult-onset Alexander disease with an R66Q mutation in GFAP presented with severe vocal cord paralysis during sleep. J Neurol. 2012;259:2234–6.

Hinttala R, Karttunen V, Karttunen A, Herva R, Uusimaa J, Remes AM. Alexander disease with occipital predominance and a novel c.799G>C mutation in the GFAP gene. Acta Neuropathol. 2007;114:543–45.

Hirayama T, Fukae J, Noda K, Fujishima K, Yamamoto T, Mori K, Maeda M, Hattori N, Shiroma N, Tsurui S, Okuma Y. Adult-onset Alexander disease with palatal myoclonus and intraventricular tumour. Eur J Neurol. 2008;15:e16–e17.

Howard KL, Hall DA, Moon M, Agarwal P, Newman E, Brenner M. Adult-onset Alexander disease with progressive ataxia and palatal tremor. Mov Disord. 2008;23:118-22.

Huttner HB, Richter G, Hildebrandt M, Blumcke I, Fritscher T, Bruck W, Gartner J, Seifert F, Staykov D, Hilz MJ, Schwab S, Bardutzky J. Acute onset of fatal vegetative symptoms: unusual presentation of adult Alexander disease. Eur J Neurol. 2007;14:1251–5.

Kaneko H, Hirose M, Katada S, Takahashi T, Naruse S, Tsuchiya M, Yoshida T, Nakagawa M, Onodera O, Nishizawa M, Ikeuchi T. Novel GFAP mutation in patient with adult-onset Alexander disease presenting with spastic ataxia. Mov Disord. 2009;24:1393-5.

Kawai M, Sakai N, Miyake S, Tsukamoto H, Akagi M, Inui K, Mushiake S, Taniike M, Ozono K. Novel mutation of gene coding for glial fibrillary acidic protein in a Japanese patient with Alexander disease. Brain Dev. 2006;28:60-2.

Kinoshita T, Imaizumi T, Miura Y, Fujimoto H, Ayabe M, Shoji H, Okamoto Y, Takashima H, Osame M, Nakagawa M. A case of adult-onset Alexander disease with Arg416Trp human glial fibrillary acidic protein gene mutation. Neurosci Lett. 2003;350:169-72.

Kmieć T, Bilska M, Mierzewska H, Jurkiewicz E, Jóźwiak S. Juvenile form of Alexander's disease - a case confirmed by detection of mutation in GFAP gene. Neurol Neurochir Pol. 2007;41:267-71.

Kyllerman M, Rosengren L, Wiklund LM, Holmberg E. Increased levels of GFAP in the cerebrospinal fluid in three subtypes of genetically confirmed Alexander disease. Neuropediatrics. 2005;36:319-23.

Larsen A, Martin C, Meyer S, Rohrer T, Papanagiotou P, van der Knaap M, Gortner L. A 2-month-old infant with vomiting, seizures, and progressive apathy. Eur J Pediatr. 2012;171:993–5.

Lee JM, Kim AS, Lee SJ, Cho SM, Lee DS, Choi SM, Kim DK, Ki CS, Kim JW. A case of infantile Alexander disease accompanied by infantile spasms diagnosed by DNA analysis. J Korean Med Sci. 2006;21:954-7.

Li R, Johnson AB, Salomons G, Goldman JE, Naidu S, Quinlan R, Cree B, Ruyle SZ, Banwell B, D'Hooghe M, Siebert JR, Rolf CM, Cox H, Reddy A, Gutierrez-Solana LG, Collins A, Weller RO, Messing A, van der Knaap MS, Brenner M. Glial fibrillary acidic protein mutations in infantile, juvenile, and adult forms of Alexander disease. Ann Neurol. 2005;57:310-26.

Ma HW, Lu JF, Jiang J, Chen LY, Niu GH, Wu BM, Kanazawa N, Tsujino S. [Glial fibrillary acidic protein mutation in a Chinese girl with infantile Alexander disease.] Zhonghua Yi Xue Yi Chuan Xue Za Zhi. 2005;22:79-81.

Matej R, Dvoráková L, Mrázová L, Houst'ková H, Elleder M. Early onset Alexander disease: a case report with evidence for manifestation of the disorder in neurohypophyseal pituicytes. Clin Neuropathol. 2008;27:64-71.

Meins M, Brockmann K, Yadav S, Haupt M, Sperner J, Stephani U, Hanefeld F. Infantile Alexander disease: A GFAP mutation in monozygotic twins and novel mutations in two other patients. Neuropediatrics. 2002;33:194-8.

Melchionda L, Fang M, Wang H, Fugnanesi V, Morbin M, Liu X, Li W, Ceccherini I, Farina L, Savoiardo M, D'Adamo P, Zhang J, Costa A, Ravaglia S, Ghezzi D, Zeviani M. Adult-onset Alexander disease, associated with a mutation in an alternative GFAP transcript, may be phenotypically modulated by a non-neutral HDAC6 variant. Orphanet J Rare Dis. 2013;8:66.

Messing A, Li R, Naidu S, Taylor JP, Silverman L, Flint D, van der Knaap MS, Brenner M. Archetypal and new families with Alexander disease and novel mutations in GFAP. Arch Neurol. 2012;69:208–14.

Mignot C, Desguerre I, Burglen L, Hertz-Pannier L, Renaldo F, Gadisseux JF, Gallet S, Pham-Dinh D, Boespflug-Tanguy O, Rodriguez D. Tumor-like enlargement of the optic chiasm in an infant with Alexander disease. Brain Dev. 2009;31:244-7.

Murakami N, Tsuchiya T, Kanazawa N, Tsujino S, Nagai T. Novel deletion mutation in GFAP gene in an infantile form of Alexander disease. Pediatr Neurol. 2008;38:50-2.

Nam T-S, Kim JH, Chang C-H, Yoon W, Jung YS, Kang S-Y, Shin BA, Perng M-D, Choi S-Y, Kim M-K. Identification of a novel nonsense mutation in the rod domain of GFAP that is associated with Alexander disease. Eur J Hum Genet. 2014. Epub ahead of print.

Namekawa M, Takiyama Y, Aoki Y, Takayashiki N, Sakoe K, Shimazaki H, Taguchi T, Tanaka Y, Nishizawa M, Saito K, Matsubara Y, Nakano I. Identification of GFAP gene mutation in hereditary adult-onset Alexander's disease. Ann Neurol. 2002;52:779-85.

Namekawa M, Takiyama Y, Honda J, Sakoe K, Naoi T, Shimazaki H, Yamagata T, Momoi MY, Nakano I. A novel adult case of juvenile-onset Alexander disease: complete remission of neurological symptoms for over 12 years, despite insidiously progressive cervicomedullary atrophy. Neurol Sci Off J Ital Neurol Soc Ital Soc Clin Neurophysiol. 2012;33:1389–92.

Niinikoski H, Haataja L, Brander A, Valanne L, Blaser S. Alexander disease as a cause of nocturnal vomiting in a 7-year-old girl. Pediatr Radiol. 2009;39:872-5.

Nishri D, Edvardson S, Lev D, Leshinsky-Silver E, Ben-Sira L, Henneke M, Lerman-Sagie T, Blumkin L. Diagnosis by whole exome sequencing of atypical infantile onset Alexander disease masquerading as a mitochondrial disorder. Eur J Paediatr Neurol. 2014;18:495–501.

Nobuhara Y, Nakahara K, Higuchi I, Yoshida T, Fushiki S, Osame M, Arimura K, Nakagawa M. Juvenile form of Alexander disease with GFAP mutation and mitochondrial abnormality. Neurology. 2004;63:1302-4.

Ohnari K, Yamano M, Uozumi T, Hashimoto T, Tsuji S, Nakagawa M. An adult form of Alexander disease: a novel mutation in glial fibrillary acidic protein. J Neurol. 2007;254:1390-4.

Okamoto Y, Mitsuyama H, Jonosono M, Hirata K, Arimura K, Osame M, Nakagawa M. Autosomal dominant palatal myoclonus and spinal cord atrophy. J Neurol Sci. 2002;195:71-6.

Osorio MJ, Risen S, Alper G. An unusual presentation of juvenile Alexander disease. J Child Neurol. 2012;27:507–10.

Pareyson D, Fancellu R, Mariotti C, Romano S, Salmaggi A, Carella F, Girotti F, Gattellaro G, Carriero MR, Farina L, Ceccherini I, Savoiardo M. Adult-onset Alexander disease: a series of eleven unrelated cases with review of the literature. Brain. 2008;131:2321-31.

Pedroso JL, Raskin S, Barsottini OGP, Oliveira ASB. Adult onset Alexander disease presenting with progressive spastic paraplegia. Parkinsonism Relat Disord. 2014;20:241-2.

Poloni CB, Ferey S, Haenggeli CA, Delavelle J, Bottani A, Salomons GS, Van Der Knaap MS, Korff CM. Alexander disease: early presence of cerebral MRI criteria. Eur J Paediatr Neurol. 2009;13:556-8.

Probst EN, Hagel C, Weisz V, Nagel S, Wittkugel O, Zeumer H, Kohlschutter A. Atypical focal MRI lesions in a case of juvenile Alexander's disease. Ann Neurol. 2003;53:118-20.

Prust M, Wang J, Morizono H, Messing A, Brenner M, Gordon E, Hartka T, Sokohl A, Schiffmann R, Gordish-Dressman H, Albin R, Amartino H, Brockman K, Dinopoulos A, Dotti MT, Fain D, Fernandez R, Ferreira J, Fleming J, Gill D, Griebel M, Heilstedt H, Kaplan P, Lewis D, Nakagawa M, Pedersen R, Reddy A, Sawaishi Y, Schneider M, Sherr E, Takiyama Y, Wakabayashi K, Gorospe JR, Vanderver A. GFAP mutations, age at onset, and clinical subtypes in Alexander disease. Neurology. 2011;77:1287–94.

Ramesh K, Sharma S, Kumar A, Salomons GS, van der Knaap MS, Gulati S. Infantile-onset Alexander disease: a genetically proven case with mild clinical course in a 6-year-old Indian boy. J Child Neurol. 2013;28:396–8.

Restrepo J, Bernardin L, Hammeke T. Neurocognitive decline in Alexander disease. Clin Neuropsychol 2011;25:1266–77.

Rezende SA de S, Fernandes M, Munhoz RP, Raskin S, Schelp AO, Knaap MS van der, Teive HAG. Cerebellar ataxia as the first manifestation of Alexander's disease. Arq Neuropsiquiatr. 2012;70:309–10.

Rodriguez D, Gauthier F, Bertini E, Bugiani M, Brenner M, N'guyen S, Goizet C, Gelot A, Surtees R, Pedespan JM, Hernandorena X, Troncoso M, Uziel G, Messing A, Ponsot G, Pham-Dinh D, Dautigny A, Boespflug-Tanguy O. Infantile Alexander disease: spectrum of GFAP mutations and genotype-phenotype correlation. Am J Hum Genet. 2001;69:1134-40.

Romano S, Salvetti M, Ceccherini I, De Simone T, Savoiardo M. Brainstem signs with progressing atrophy of medulla oblongata and upper cervical spinal cord. Lancet Neurol. 2007;6:562–70.

Sakakibara T, Takahashi Y, Fukuda K, Inoue T, Kurosawa T, Nishikubo T, Shima M, Taoka T, Aida N, Tsujino S, Kanazawa N, Yoshioka A. A case of infantile Alexander disease diagnosed by magnetic resonance imaging and genetic analysis. Brain Dev. 2007;29:525-8.

Salmaggi A, Botturi A, Lamperti E, Grisoli M, Fischetto R, Ceccherini I, Caroli F, Boiardi A. A novel mutation in the GFAP gene in a familial adult onset Alexander disease. J Neurol. 2007;254:1278-80.

Salvi F, Aoki Y, Della Nave R, Vella A, Pastorelli F, Scaglione C, Matsubara Y, Mascalchi M. Adult Alexander's disease without leukoencephalopathy. Ann Neurol. 2005;58:813-4.

Sawaishi Y, Yano T, Takaku I, Takada G. Juvenile Alexander disease with a novel mutation in glial fibrillary acidic protein gene. Neurology. 2002;58:1541-3.

Schmidt H, Kretzschmar B, Lingor P, Pauli S, Schramm P, Otto M, Ohlenbusch A, Brockmann K. Acute onset of adult Alexander disease. J Neurol Sci. 2013;331:152–4.

Schmidt S, Wattjes MP, Gerding WM, van der Knaap M. Late onset Alexander's disease presenting as cerebellar ataxia associated with a novel mutation in the GFAP gene. J Neurol. 2011;258:938–40.

Sechi GP, Conti M, Sau GF, Cocco GA. Valproate-induced parkinsonism, glial cells and Alexander's disease. Prog Neuropsychopharmacol Biol Psychiatry. 2008;32:1351-2.

Shiihara T, Kato M, Honma T, Ohtaki S, Sawaishi Y, Hayasaka K. Fluctuation of computed tomographic findings in white matter in Alexander's disease. J Child Neurol. 2002;17:227-30.

Shiihara T, Sawaishi Y, Adachi M, Kato M, Hayasaka K. Asymptomatic hereditary Alexander's disease caused by a novel mutation in GFAP. J Neurol Sci. 2004;225:125-7.

Shiihara T, Yoneda T, Mizuta I, Yoshida T, Nakagawa M, Shimizu N. Serial MRI changes in a patient with infantile Alexander disease and prolonged survival. Brain Dev. 2011;33:604–7.

Shiroma N, Kanazawa N, Kato Z, Shimozawa N, Imamura A, Ito M, Ohtani K, Oka A, Wakabayashi K, Iai M, Sugai K, Sasaki M, Kaga M, Ohta T, Tsujino S. Molecular genetic study in Japanese patients with Alexander disease: a novel mutation, R79L. Brain Dev. 2003;25:116-21.

Spritzer SD, Zarkou S, Ireland SP, Carter JL, Goodman BP. Autonomic dysfunction in adult-onset alexander disease: a case report and review of the literature. Clin Auton Res. 2013;23:333–8.

Sreedharan J, Shaw CE, Jarosz J, Samuel M. Alexander disease with hypothermia, microcoria, and psychiatric and endocrine disturbances. Neurology. 2007;68:1322-3.

Stumpf E, Masson H, Duquette A, Berthelet F, McNabb J, Lortie A, Lesage J, Montplaisir J, Brais B, Cossette P. Adult Alexander disease with autosomal dominant transmission: a distinct entity caused by mutation in the glial fibrillary acid protein gene. Arch Neurol. 2003;60:1307-12.

Sueda Y, Takahashi T, Ochi K, Ohtsuki T, Namekawa M, Kohriyama T, Takiyama Y, Matsumoto M. Adult onset Alexander disease with a novel variant (S398F) in the glial fibrillary acidic protein gene. Rinsho Shinkeigaku. 2009;49:358-63.

Suzuki H, Yoshida T, Kitada M, Ichihashi J, Sasayama H, Nishikawa Y, Mistui Y, Nakagawa M, Kusunoki S. Late-onset Alexander disease with a V87L mutation in glial fibrillary acidic protein (GFAP) and calcifying lesions in the sub-cortex and cortex. J Neurol. 2012;259:457–61.

Suzuki Y, Kanazawa N, Takenaka J, Okumura A, Negoro T, Tsujino S. A case of infantile Alexander disease with a milder phenotype and a novel GFAP mutation, L90P. Brain Dev. 2004;26:206-8.

Thyagarajan D, Chataway T, Li R, Gai WP, Brenner M. Dominantly-inherited adult-onset leukodystrophy with palatal tremor caused by a mutation in the glial fibrillary acidic protein gene. Mov Disord. 2004;19:1244-8.

Torisu H, Yoshikawa Y, Yamaguchi-Takada Y, Yano T, Sanefuji M, Ishizaki Y, Sawaishi Y, Hara T. Alexander disease with mild dorsal brainstem atrophy and infantile spasms. Brain Dev. 2013;35:441–4.

Tschampa HJ, Greschus S, Vinahl M, Urbach H, Mueller MM, Gerding WM. MS-like presentation of Alexander disease with multifocal lesions and oligoclonal bands. J Neurol. 2011;258:935–7.

van der Knaap MS, Ramesh V, Schiffmann R, Blaser S, Kyllerman M, Gholkar A, Ellison DW, van der Voorn JP, van Dooren SJ, Jakobs C, Barkhof F, Salomons GS. Alexander disease: ventricular garlands and abnormalities of the medulla and spinal cord. Neurology. 2006;66:494-8.

van der Knaap MS, Salomons GS, Li R, Franzoni E, Gutierrez-Solana LG, Smit LM, Robinson R, Ferrie CD, Cree B, Reddy A, Thomas N, Banwell B, Barkhof F, Jakobs C, Johnson A, Messing A, Brenner M. Unusual variants of Alexander's disease. Ann Neurol. 2005;57:327-38.

Van Poppel K, Broniscer A, Patay Z, Morris EB. Alexander Disease: An important mimicker of focal brainstem glioma. Pediatr Blood Cancer. 2009;53:1355–6.

Vazquez E, Macaya A, Mayolas N, Arevalo S, Poca MA, Enrıquez G. Neonatal Alexander Disease: MR Imaging Prenatal Diagnosis. Am J Neuroradiol. 2008;29:1973–5.

Wada Y, Yanagihara C, Nishimura Y, Namekawa M. Familial adult-onset Alexander disease with a novel mutation (D78N) in the glial fibrillary acidic protein gene with unusual bilateral basal ganglia involvement. J Neurol Sci. 2013;331:161–4.

Wakabayashi K, Lai M, Masuko K, Yamashita S, Yamada M, Iwamoto H, Aida N, Shiroma N, Kanazawa N, Tsujino S. A case of long-term survival of a patient with infantile Alexander disease diagnosed by DNA analysis. No To Hattatsu. 2005;37:55-9.

Wu Y, Gu Q, Wang J, Yang Y, Wu X, Jiang Y. Clinical and genetic study in Chinese patients With Alexander disease. J Child Neurol. 2008;23:173-7.

Yonezu T, Ito S, Kanai K, Masuda S, Shibuya K, Kuwabara S. A case of adult-onset alexander disease featuring severe atrophy of the medulla oblongata and upper cervical cord on magnetic resonance imaging. Case Rep Neurol. 2012;4:202–6.

Yoshida T, Mizuta I, Saito K, Ohara R, Kurisaki H, Ohnari K, Riku Y, Hayashi Y, Suzuki H, Shii H, Fujiwara Y, Yonezu T, Nagaishi A, Nakagawa M. Effects of a polymorphism in the GFAP promoter on the age of onset and ambulatory disability in late-onset Alexander disease. J Hum Genet. 2013;58:635–8.

Yoshida T, Sasaki M, Yoshida M, Namekawa M, Okamoto Y, Tsujino S, Sasayama H, Mizuta I, Nakagawa M, Alexander Disease Study Group in Japan. Nationwide survey of Alexander disease in Japan and proposed new guidelines for diagnosis. J Neurol. 2011a;258:1998–2008.

Yoshida T, Sasayama H, Mizuta I, Okamoto Y, Yoshida M, Riku Y, Hayashi Y, Yonezu T, Takata Y, Ohnari K, Okuda S, Aiba I, Nakagawa M. Glial fibrillary acidic protein mutations in adult-onset Alexander disease: clinical features observed in 12 Japanese patients. Acta Neurol Scand. 2011b;124:104–8.

Zafeiriou DI, Dragoumi P, Vargiami E. Alexander disease. J Pediatr. 2013;162:648.