Supplementary table 1. Antibodies used in this study

Antibody	Species/type	Dilution	Epitope	Source
AT8	Mouse/monoclonal	1:1,000	Tau phosphorylated at Ser 202	Innogenetics
RD3	Mouse/monoclonal	1:2,000	3-repeat tau-specific anti-tau antibody	Merck Millipore
RD4	Mouse/monoclonal	1:100	4-repeat tau-specific anti-tau antibody	Merck Millipore
Anti-4R tau	Rabbit/polyclonal	1:2,000	4-repeat tau-specific anti-tau antibody	Cosmo Bio
12B2	Mouse/monoclonal	1:100	Aβ(11–28)	IBL
psyn#64	Mouse/monoclonal	1:5,000	Phosphorylated α-synuclein	Wako
pS409/410-2	Rabbit/polyclonal	1:5,000	Phosphorylated TDP-43	Cosmo Bio
HPA008784	Rabbit/polyclonal	1:200	FUS	Sigma-Aldrich
SMI31	Mouse/monoclonal	1:1,000	Phosphorylated neurofilament	Sternberger
p62-N	Guinea pig/polyclonal	1:100	N-terminus of p62 protein	Progen Biotechnik
p62-C	Guinea pig/polyclonal	1:500	C-terminus of p62 protein	Progen Biotechnik

Supplementary table 2. Clinical and pathological features in diffuse form pAGD cases

	Case 1				Case 2				Case 3			
Clinical features												
Age at onset (y)	49				64				44			
Age at death (y)	86				81				60			
Disease duration (y)	38				17				16			
Sex	Female				Male				Male			
Family history	-				-				-			
MAPT mutation	-				-				n.a.			
Apo E genotype	ε3/ε3				ε3/ε3				n.a.			
Clinical diagnosis	bvFTD				Right temporal variant FTD				Manic state			
Onset symptoms	Lavish expenditure				Impairment of face recognition				Breaking into a residence, behavioral stereotypy			
Behavioral stereotypy	+				+				+			
Semantic memory impairment	+				-				n.a.			
Prosopagnosia	-				+				n.a.			
Impairment of eye movement	-				-				n.a.			
Parkinsonism	+ (R>L)				+ (L>R)				n.a.			
Pyramidal sign	-				-				n.a.			
Lower motor neuron sign	-				-				n.a.			
Pathological features												
Brain weight (g)	856				1,188				1,040			
Post-mortem interval (h)	3.0				2.5				2.1			
Braak NFT stage	Stage II				Stage IV				Stage I			
Thal phase	Phase 0				Phase 1				Phase 0			
CERAD neuritic plaque score	0				0				0			
Lewy body disease	-				-				-			
Braak Parkinson's disease	Stage 0				Stage 0				Stage 0			
LATE-NC stage/Josephs stage	Stage 3/6				Stage 2/3				Stage 0/0			
TDP-43 histologic subtype	Type β				Type β				-			
FUS pathology	-				-				-			
Saito AG stage	Stage III (diffuse form)				Stage III (diffuse form)				Stage III (diffuse form)			
Lesions	NL	AG	NFT	GFA	NL	AG	NFT	GFA	NL	AG	NFT	GFA
Motor cortex	+	0.5	++	+++	-	0.5	++	+++	-	0.5	++	+++
Middle frontal gyrus	+	+	++	+++	++	0.5	++	+++	++	0.5	+++	+++
Orbital gyrus	+	++	++	+++	+	0.5	++	+++	++	++	+++	+
Superior temporal gyrus	+	++	+++	+++	+	+	++++	+++	+	++	+	-
Inferior temporal gyrus	+++	+	++	++	++	++	++	+++	++	+++	+++	-
Inferior parietal lobule	+	0.5	++	++	+	0.5	++	+++	+	0.5	++	-
Striate region	+	-	-	-	-	-	-	+	-	-	-	-
Insular cortex	+++	+++	++	+++	+++	++	++	+++	+++	++	+++	+
Caudate nucleus	+++	0.5	++++	+++	++	0.5	++	+++	+++	0.5	++++	-
Putamen	++	0.5	+++	+++	+	0.5	+++	+++	++	0.5	++	-
Globus pallidus, internal segment	+++	-	++	++	+++	-	++	++	+++	-	+	-
Globus pallidus, external segment	++	-	+++	++	++	-	++	+++	+++	-	+	-
Thalamus	++	0.5	++	-	++	0.5	++	++	+++	0.5	++	-
Subthalamic nucleus	-	-	++	-	-	0.5	++	+	-	0.5	++	-
Amygdala	+++	+++	+++	+++	+++	++	++++	+++	+++	+++	++	++
Ambient gyrus	+++	+++	++	+++	+++	++	+++++	+++	+++	++	++	++
Hippocampal CA1	+++	++	++	-	+++	++	++++	-	+++	+++	+++	-
Hippocampal dentate gyrus	-	-	+++	-	-	+	+++++	-	-	-	++	-
Parahippocampal gyrus	+++	0.5	+++	+++	+++	0.5	++++	+++	+++	+	++	-
Oculomotor nucleus	-	-	++	+	+	0.5	++	+++	-	0.5	+	+
Red nucleus	-	0.5	++	-	-	0.5	++	+++	-	0.5	++	++
Substantia nigra	+++	-	+++	-	+++	0.5	++	+	+++	0.5	++	+
Locus coeruleus	-	0.5	+++	-	++	0.5	++	-	++	0.5	++	-
Superior cerebellar peduncle	-	-	NT+	-	-	-	NT+	-	-	-	NT++	-
Pontine nucleus	-	-	++	+	-	0.5	++	+	-	-	++	+
Hypoglossal nucleus	-	0.5	-	+	-	0.5	-	-	-	-	-	-
Dorsal vagal nucleus	-	0.5	++	-	-	-	++	-	-	0.5	++	+
Inferior olivary nucleus	+	0.5	++	+	-	-	+	++	-	0.5	+	++
Frontopontine tract	+	-	NT++	-	-	-	NT+	-	+++	0.5	NT++	-
Corticospinal tract (cerebral peduncle)	-	-	NT+	-	-	-	-	-	-	-	NT+	-
Corticospinal tract (medulla oblongata)	-	-	NT+	-	-	-	NT+	-	-	-	NT+	-
Corticospinal tract (cervical cord)	-	-	-	-	-	-	-	-	n.a.	n.a.	n.a.	n.a.
Anterior horn cells	-	-	+	+	-	-	NT+	+	n.a.	n.a.	n.a.	n.a.
Cerebellar cortex	-	-	-	-	-	-	-	-	-	-	-	-
Dentate nucleus	-	-	+	-	-	-	++	+	-	-	+	-

y: years, MAPT: microtubule associated protein tau, bvFTD: behavioral variant frontotemporal dementia, +: present, -: absent, R>L: right side predominant, L>R: left side predominant, n.a. not

available, h: hours, CERAD: the Consortium to Establish a Registry for Alzheimer's Disease, LATE-NC: limbic-predominant age-related TDP-43 encephalopathy neuropathologic changes, TDP-43: TAR DNA-binding protein of 43 kDa, FUS: fused in sarcoma, AGD: argyrophilic grain disease, NL: neuronal loss, AG: argyrophilic grains, NFT: neurofibrillary tangles and threads, GFA: granular fuzzy astrocytes. The grading system of each lesion is noted in the text.

Supplementary table 3. Correlations between the age at death, Braak NFT stage, Thal phase, Saito AG stage, GFA stage, LATE-NC stage and severity of neuronal loss in pAGD cases

	Age at death		Braak NFT stage		Thal phase		Saito AG stage		GFA stage (frontal cortex)		GFA stage (caudate nucleus)		GFA stage (putamen)		GFA stage (amygdala)		LATE-NC stage	
	ρ	p	ρ	p	ρ	p	ρ	p	ρ	p	ρ	p	ρ	p	ρ	p	ρ	p
Age at death	1.0000	-	0.5469	**0.0018****	0.0437	0.8188	0.3538	0.0551	0.1504	0.4362	0.1477	0.4360	0.1259	0.5075	0.2160	0.2892	0.4751	**0.0080****
Braak NFT stage	0.5469	**0.0018****	1.0000	-	0.2409	0.1997	0.1520	0.4225	0.2105	0.2730	0.2501	0.1826	0.3698	**0.0443***	0.2019	0.3227	0.1925	0.3082
Thal phase	0.0437	0.8188	0.2409	0.1997	1.0000	-	0.2310	0.2194	-0.0911	0.6384	0.2436	0.1946	0.0960	0.6139	0.2544	0.2098	0.2097	0.2661
Saito AG stage	0.3538	0.0551	0.1520	0.4225	0.2310	0.2194	1.0000	-	0.3346	0.0760	0.2360	0.2092	0.2825	0.1304	0.0214	0.9172	0.4009	**0.0281***
GFA stage (frontal cortex)	0.1504	0.4362	0.2105	0.2730	-0.0911	0.6384	0.3346	0.0760	1.0000	-	0.2134	0.2664	0.1423	0.4614	-0.1648	0.4312	-0.0096	0.9607
GFA stage (caudate nucleus)	0.1477	0.4360	0.2501	0.1826	0.2436	0.1946	0.2360	0.2092	0.2134	0.2664	1.0000	-	0.5058	**0.0044****	0.3801	0.0554	0.1818	0.3363
GFA stage (putamen)	0.1259	0.5075	0.3698	**0.0443***	0.0960	0.6139	0.2825	0.1304	0.1423	0.4614	0.5058	**0.0044****	1.0000	-	-0.0011	0.9956	0.1669	0.3781
GFA stage (amygdala)	0.2160	0.2892	0.2019	0.3227	0.2544	0.2098	0.0214	0.9172	-0.1648	0.4312	0.3801	0.0554	-0.0011	0.9956	1.0000	-	0.1683	0.4111
LATE-NC stage	0.4751	**0.0080****	0.1925	0.3082	0.2097	0.2661	0.4009	**0.0281***	-0.0096	0.9607	0.1818	0.3363	0.1669	0.3781	0.1683	0.4111	1.0000	-
Neuronal loss stage																		
Amygdala	0.3079	0.1182	0.0828	0.6812	-0.0636	0.7525	0.5744	**0.0017****	0.4022	**0.0417***	0.0352	0.8616	-0.1084	0.5903	-0.2321	0.2539	0.2505	0.2075
Ambient gyrus	0.3807	0.0501	0.1493	0.4573	-0.0766	0.7040	0.6732	**< 0.001****	0.3022	0.1335	0.1989	0.3198	0.1051	0.6019	-0.1319	0.5205	0.3403	0.0824
Entorhinal gyrus	0.3375	0.0852	0.1090	0.5882	0.0623	0.7574	0.7517	**< 0.001****	0.3709	0.0621	0.1001	0.6192	-0.0299	0.8823	-0.2519	0.2244	0.5380	**0.0038****
Hippocampal CA1	0.1889	0.3265	0.1687	0.3817	0.0826	0.6701	0.5904	**< 0.001****	0.3961	**0.0369***	0.0643	0.7405	0.3209	0.0897	-0.3220	0.1165	0.5052	**0.0052****
Subiculum	0.3653	0.0514	0.3484	0.0640	0.1629	0.3986	0.4927	**0.0066****	0.2608	0.1800	0.1303	0.5006	0.4285	**0.0204***	-0.1532	0.4648	0.6051	**< 0.001****
Insular cortex	0.2241	0.2339	-0.0452	0.8125	0.1092	0.5656	0.6212	**< 0.001****	0.2841	0.1352	0.1434	0.4497	0.0700	0.7132	-0.2243	0.2706	0.4718	**0.0085****
Superior temporal gyrus	0.2117	0.2891	-0.0937	0.6420	0.1655	0.4094	0.7628	**< 0.001****	0.3715	0.0617	0.2684	0.1758	0.0254	0.9001	-0.0006	0.9978	0.3566	0.0679
Middle temporal gyrus	0.3114	0.0939	0.0446	0.8150	0.2022	0.2838	0.7526	**< 0.001****	0.4045	**0.0295***	0.2534	0.1766	0.1181	0.5343	-0.1475	0.4721	0.4736	**0.0082****
Inferior temporal gyrus	0.2317	0.2180	-0.0639	0.7373	0.0814	0.6688	0.7292	**< 0.001****	0.4415	**0.0165***	0.3040	0.1024	0.1566	0.4084	-0.0615	0.7652	0.3853	**0.0355***
Occipitotemporal gyrus	0.2779	0.1370	-0.0030	0.9876	0.1062	0.5766	0.6689	**< 0.001****	0.3979	**0.0325***	0.2095	0.2666	0.0582	0.7600	-0.2198	0.2805	0.4406	**0.0148***
Superior frontal gyrus	0.1933	0.3060	-0.0135	0.9436	0.2800	0.1339	0.6284	**< 0.001****	0.2529	0.1857	0.1470	0.4383	-0.0445	0.8152	-0.1517	0.4595	0.3725	**0.0426***
Middle frontal gyrus	0.1820	0.3356	-0.0509	0.7892	0.2299	0.2216	0.6519	**< 0.001****	0.2873	0.1308	0.1914	0.3110	-0.0445	0.8152	-0.0910	0.6583	0.3225	0.0822
Inferior frontal gyrus	0.1830	0.3920	-0.1047	0.6262	0.3316	0.1134	0.6813	**< 0.001****	0.3439	0.1081	0.0242	0.9106	-0.0815	0.7051	-0.2712	0.2107	0.2601	0.2196
Orbital gyrus	0.0775	0.7126	-0.1286	0.5402	0.1290	0.5388	0.5584	**0.0037****	0.0782	0.7164	0.1690	0.4193	-0.0029	0.9889	-0.2162	0.3103	0.3742	0.0654
Gyrus rectus	0.0723	0.7313	-0.1664	0.4268	0.1968	0.3458	0.6452	**< 0.001****	0.1536	0.4737	0.0950	0.6514	-0.0653	0.7563	-0.1337	0.5335	0.4165	**0.0384***
Caudate nucleus	0.1604	0.3973	0.0420	0.8256	-0.0152	0.9364	0.4846	**0.0066****	0.4281	**0.0205***	-0.0420	0.8258	0.1270	0.5037	-0.3881	0.0501	0.4519	**0.0122***
Putamen	0.0322	0.8660	-0.0787	0.6792	-0.1541	0.4162	0.4969	**0.0052****	0.5608	**0.0016****	0.0454	0.8117	0.2364	0.2085	-0.2825	0.1621	0.3320	0.0731
Globus pallidus	0.0752	0.6931	-0.1114	0.5579	-0.2180	0.2472	0.4851	**0.0066****	0.4286	**0.0204***	0.1433	0.4500	0.1390	0.4637	-0.1855	0.3642	0.4075	**0.0254***
Thalamus	0.0964	0.6125	-0.1223	0.5196	-0.0387	0.8391	0.5080	**0.0042****	0.3836	**0.0399***	0.0560	0.7689	-0.0837	0.6601	-0.1364	0.5065	0.1928	0.3075
Substantia nigra	-0.0603	0.7518	-0.0400	0.8337	0.0105	0.9561	0.3889	**0.0337***	0.3523	0.0609	-0.0878	0.6445	0.2831	0.1295	-0.3714	0.0618	0.2197	0.2433

Correlations between clinical and pathological variables of 30 pAGD cases were assessed with Spearman's rank-order correlation test. Because all diffuse form pAGD cases fit the criteria of Saito AG stage III, the diffuse form was regarded as Saito AG stage III in statistical analyses. NFT: neurofibrillary tangle, AG: argyrophilic grain, LATE-NC: limbic-predominant age-related TDP-43 encephalopathy pathologic change, NL: neuronal loss. *: $p < 0.05$, **: $p < 0.01$.

Supplementary table 4. Additional multivariate analyses of predictors for neuronal loss in the amygdala, frontal cortex, striatum, and substantia nigra in pAGD and PART cases

Multivariate ordered logistic regression analyses			
	Odds ratio	95% CI	p value
Amygdala (n = 63) [a)]			
Age at death	1.0180	0.9792-1.0584	0.3673
Braak NFT stage	0.9438	0.4634-1.9223	0.8734
Saito AG stage	5.2730	2.2509-12.3526	**< 0.001****
GFA stage in the amygdala	0.0499	0.0015-1.6130	0.0909
LATE-NC stage	0.9936	0.4076-2.4225	0.9888
Middle frontal gyrus (n = 63) [a)]			
Age at death	0.9688	0.8756-1.0719	0.5390
Braak NFT stage	0.4938	0.1863-1.3088	0.1559
Saito AG stage	4.2678	1.5875-11.4737	**0.0040****
GFA stage in the middle frontal gyrus	4.9444	0.0323-756.3003	0.5335
LATE-NC stage	1.2979	0.4458-3.7790	0.6325
Binomial logistic regression analysis			
Caudate nucleus (n = 63) [b)]			
Age at death	0.8134	0.6585-1.0049	0.0555
Braak NFT stages III-IV	10.0945	0.1704-597.8869	0.2669
Saito AG stage III [c)]	114.5962	1.4586-9003.1459	**0.0332***
Presence of GFAs in the caudate nucleus [d)]	0.0000	0.0000-15314.8940	0.0941
LATE-NC stage 2 [e)]	738.6657	2.3224-2.3494.E+05	**0.0247***
Putamen (n = 63) [b)]			
Age at death	0.8423	0.6805-1.0426	0.1148
Braak NFT stages III-IV	0.0966	0.0005-18.8232	0.3850
Saito AG stage III [c)]	369.9374	2.2451-60957.1736	**0.0232***
Presence of GFAs in the putamen [d)]	111.2875	0.0000-3.1574.E+28	0.8795
LATE-NC stage 2 [e)]	41.1989	0.0403-42125.7008	0.2930

30 pAGD and 34 PART cases were examined. The GFA status was additionally submitted as an independent variable in each model. CI: confidence interval, NFT: neurofibrillary tangle, AG: argyrophilic grains, LATE-NC: limbic-predominant age-related TDP-43 encephalopathy neuropathologic change (LATE-NC). (a) The dependent variable was a four-point staging system of neuronal loss (none, mild, moderate, and severe. The definitions are noted in the text) on each region. The age at death, Braak NFT stage, Saito AG stage, GFA stage, and LATE-NC stage were submitted as independent variables. (b) The dependent variable was the presence or absence of neuronal loss in each region. c) Because all diffuse-form pAGD cases fit the criteria of Saito AG stage III, the diffuse form was regarded as Saito AG stage III in statistical analyses. d) The presence of GFAs in each region. e) No pAGD or PART case had LATE-NC in stage 3. *: $p < 0.05$, **: $p < 0.01$.

Supplementary table 5. Univariate binomial logistic regression analyses of predictors for dementia in pAGD and PART cases

	OR	95% CI	*p*
Age at death	1.12	1.04-1.20	**0.0032****
Braak NFT stages III-IV	5.71	1.50-21.84	**0.0108***
Thal phase 1 or over	1.05	0.31-3.59	0.9410
Saito AG stage I	2.25	0.51-9.94	0.2829
Saito AG stage II	2.25	0.51-9.94	0.2829
Saito AG stage II or over	9.30	2.29-37.70	**0.0018****
Density of AGs in the amygdala (per x400 visual field)			
One to 49 AGs	2.18	0.49-9.63	0.3032
50 to 99 AGs	12.36	1.25-122.62	**0.0317***
100 or more AGs	8.25	1.38-49.21	**0.0206***
Presence of AGs in the amygdala	21.94	4.07-118.28	**<0.001****
Density of AGs in the CA1 (per x400 visual field)			
One to 49 AGs	2.00	0.39-10.28	0.4067
50 to 99 AGs	2.00	0.39-10.28	0.4067
100 or more AGs	2.46	1.37-4.41	**0.0025****
Presence of AGs in the CA1	16.90	3.22-88.68	**<0.001****
Presence of AGs in the lateral occipitotemporal gyrus	13.95	3.08-63.13	**<0.001****
Presence of AGs in the inferior temporal gyrus	19.83	3.29-119.41	**0.0011****
Presence of AGs in the insular cortex	17.60	3.46-89.51	**<0.001****
Presence of LATE-NC	8.50	1.43-50.66	**0.0188***
LATE-NC stage 2[a)]	12.73	1.28-126.14	**0.0297***
Neuronal loss stages 2-3 in the amygdala	34.02	3.60-321.60	**0.0021****

51 cases (23 pAGD cases and 28 PART cases) that lacked two or more lacunae or larger infarctions in the cortex and/or subcortical regions were included in univariate analyses. Because all diffuse form pAGD cases fit the criteria of Saito AG stage III, the diffuse form was regarded as Saito AG stage III in statistical analyses. OR: odds ratio, CI: confidence interval, NFT: neurofibrillary tangle, AG: argyrophilic grains, LATE-NC: limbic-predominant age-related TDP-43 encephalopathy neuropathologic change. a) No pAGD or PART case had LATE-NC in stage 3. *: $p < 0.05$, **: $p < 0.01$.

Supplementary table 6. Eight previously reported pAGD cases having AGs in the frontal cortex and subcortical nuclei

		1	2	3	4	5	6	7	8
References		Ishihara et al. [20]	Inoue et al. [19]	Hokelekli et al. [16]	Itagaki et al. [21]	Muarage et al. (case 1) [35]	Muarage et al. (case 2) [35]	Tsuchiya et al. [62]	Arakawa A et al. (case 1) [4]
Sex		M	M	M	F	F	F	F	M
Age at onset (y)		49	52	55	61	62	72	74	81
Age at death (y)		54	55	82	68	76	79	89	84
Disease duration (y)		5	3	27	7	6	7	15	3
Initial symptoms		character change, behavioral change	quadri-paresis, bulbar palsy, cognitive decline	personality change	memory loss	obsession, changes of eating habits, apathy	memory impairment	memory impairment	forgetfulness
Parkinsonism		-	+	+	n.d.	-	+	-	+
Braak NFT stage		I	I	III	n.d. (rare)	n.d.	0	II	II
Aβ deposits		n.d.	-	Thal phase 0	-	neocortical, focal	occipital, focal	-	Thal phase 4
Lewy bodies		+[a]	-		n.d.	+[b]	-	n.d.	-
TDP-43		n.d.	-	-	n.d.	n.d.	n.d.	n.d.	LATE-NC stage 2
AGs	Frontal cortex	+	+	+	+	+	+	+	n.d.
	Primary motor cortex	n.d.	+	n.d.	+	+	+	n.d.	n.d.
	Basal ganglia	n.d.	-	+	+	+	+	+	+
	Brain stem	+	+	+	+	-	-	n.d.	+
Neu-ronal loss	CA1	+ (severe)	-	n.d.	-	n.d.	n.d.	+ (prominent)	n.d.
	Substantia nigra	+ (severe)	+ (moderate)	n.d.	+	-	n.d.	+ (obvious)	+

y: years, NFT: neurofibrillary changes. -: absent, +: present, n.d.: not described. a) Lewy bodies in the substantia nigra and locus coeruleus. b) Rare Lewy bodies in the substantia nigra and dorsal vagal nucleus.