

Supplementary Table S1. Patient characteristics at baseline (with or without a central nervous system biopsy)

	Biopsy obtained (n=100)	Biopsy not obtained (n=100)	p-value
Mean (SD) age (years)	48 (15)	48 (13)	0.96
Female sex (n, %)	41 (41)	42 (42)	0.89
<i>Symptoms (n, %)</i>			
Seizure	30 (30)	10 (10)	< 0.001
Cognitive impairment	67 (67)	35 (35)	< 0.001
Headache	61 (61)	62 (62)	0.88
<i>Cerebrospinal fluid</i>			
White blood cells (per mm ³ , median, IQR)	14 (3-52)	15 (5-57)	0.66
Protein level (g/L, median, IQR)	0.64 (0.44-0.97)	0.68 (0.45-0.92)	0.92
White blood cells > 10/mm ³ or proteins > 0.70 g/L (n, %)	62 (64)	68 (68)	0.55
<i>Imaging (n, %)</i>			
≥ 1 acute brain infarct	52 (52)	90 (90)	< 0.001
Parenchymal enhancement	51 (55)	13 (16)	< 0.001
Leptomeningeal enhancement	23 (25)	7 (9)	< 0.01
Parenchymal or leptomeningeal enhancement	54 (59)	17 (22)	< 0.001
≥ 1 cerebral microbleed	38 (40)	16 (17)	< 0.001
≥ 1 intracerebral hemorrhage	10 (10)	3 (3)	0.04
Acute subarachnoid hemorrhage	13 (13)	8 (8)	0.24
Tumor-like lesion	24 (24)	1 (1)	< 0.001

Missing values: white blood cells (3), protein level (3), white blood cells > 10/mm³ or proteins > 0.70 g/L (3), parenchymal enhancement (29), leptomeningeal enhancement (29), ≥ 1 cerebral microbleed (11)

Supplementary Table S2. Comparison at baseline of biopsy positive and negative primary angiitis of the central nervous system (excluding amyloid-beta related angiitis)

	Biopsy positive (n=52)	Biopsy negative (n=39)	Odds ratio (95% CI)	p-value
Mean (SD) age (years)	44 (15)	49 (13)	0.97 (0.94-1.002)	0.07
Female sex (n, %)	26 (50)	10 (26)	2.81 (1.18-7.03)	0.02
<i>Symptoms (n, %)</i>				
Seizure	25 (48)	3 (8)	9.67 (3.17-38.92)	< 0.001
Cognitive impairment	38 (73)	21 (54)	2.28 (0.97-5.52)	0.06
Headache	29 (56)	25 (64)	0.71 (0.30-1.65)	0.43
<i>Cerebrospinal fluid</i>				
White blood cells > 10/mm ³ or proteins > 0.70 g/L (n, %)	32 (64)	23 (59)	1.23 (0.53-2.90)	0.63
<i>Imaging (n, %)</i>				
≥ 1 acute brain infarct	10 (19)	37 (95)	0.02 (0.003-0.06)	< 0.001
Parenchymal enhancement	44 (88)	3 (9)	59.66 (16.85-278.21)	< 0.001
Leptomeningeal enhancement	14 (28)	2 (6)	5.01 (1.39-26.83)	0.01
Parenchymal or leptomeningeal enhancement	44 (88)	3 (9)	59.66 (16.85-278.21)	< 0.001
≥ 1 cerebral microbleed	26 (54)	5 (14)	6.96 (2.54-22.03)	< 0.001
≥ 1 intracerebral hemorrhage	6 (12)	2 (5)	2.10 (0.50-11.94)	0.32
Acute subarachnoid hemorrhage	4 (8)	4 (10)	0.73 (0.18-3.02)	0.66

p-value for univariable Firth's bias-reduced logistic regression

Missing: white blood cells > 10/mm³ or proteins > 0.70 g/L (2), parenchymal enhancement (8), leptomeningeal enhancement (8), ≥ 1 cerebral microbleed (6)

Supplementary Table S3. Comparison at baseline of biopsy positive and negative primary angiitis of the central nervous system (restricting biopsy negative patients to cases with inflammatory cerebrospinal fluid)

	Biopsy positive (n=61)	Biopsy negative (n=23)	Odds ratio (95% CI)	p-value
Mean (SD) age (years)	47 (16)	45 (13)	1.01 (0.98-1.04)	0.65
Female sex (n, %)	31 (51)	0 (0)	48.54 (6.22-6262.87)	< 0.001
<i>Symptoms (n, %)</i>				
Seizure	27 (44)	2 (9)	6.86 (1.96-36.23)	<0.00
Cognitive impairment	46 (75)	13 (57)	2.33 (0.86-6.33)	0.10
Headache	36 (59)	16 (70)	0.65 (0.23-1.73)	0.39
<i>Imaging (n, %)</i>				
≥ 1 acute brain infarct	15 (25)	21 (91)	0.04 (0.007-0.14)	< 0.001
Parenchymal enhancement	48 (81)	2 (11)	29.52 (7.83-164.77)	< 0.001
Leptomeningeal enhancement	21 (36)	2 (11)	3.91 (1.08-20.99)	0.04
Parenchymal or leptomeningeal enhancement	51 (86)	2 (11)	42.41 (10.83-244.41)	< 0.001
≥ 1 cerebral microbleed	33 (58)	3 (14)	7.62 (2.41-31.34)	< 0.001
≥ 1 intracerebral hemorrhage	8 (13)	1 (4)	2.38 (0.49-23.32)	0.31
Acute subarachnoid hemorrhage	9 (15)	3 (13)	1.06 (0.30-4.59)	0.93

Inflammatory cerebrospinal fluid : > 10 white blood cells/mm³ or proteins > 0.70 g/L

p-value for univariable Firth's bias-reduced logistic regression

Missing values: parenchymal enhancement (6), leptomeningeal enhancement (6), ≥ 1 cerebral microbleed (5)

Supplementary Table S4. Comparison at baseline of biopsy positive and negative primary angiitis of the central nervous system (after multiple imputation with chained equations)

	Odds ratio (95% CI)	p-value	Adjusted odds ratio (95% CI)	p-value
Age (per 10 years)	0.92 (0.73-1.17)	0.50		
Female sex	2.25 (1.04-4.86)	0.04	3.54 (0.69-18.25)	0.14
<i>Symptoms</i>				
Seizure	14.33 (4.45-46.15)	< 0.001	6.60 (1.17-37.15)	0.04
Cognitive impairment	5.73 (2.72-12.06)	< 0.001	7.46 (1.54-36.19)	0.02
Headache	0.75 (0.37-1.50)	0.42		
<i>Cerebrospinal fluid</i>				
White blood cells > 10/mm ³ or proteins > 0.70 g/L	1.31 (0.67-2.56)	0.43		
<i>Imaging</i>				
≥ 1 acute brain infarct	0.04 (0.01-0.11)	< 0.001	0.17 (0.04-0.81)	0.03
Parenchymal enhancement	37.24 (8.92-155.51)	< 0.001		
Leptomeningeal enhancement	4.63 (1.71-12.56)	< 0.01		
Parenchymal or leptomeningeal enhancement	28.21 (8.63-92.20)	< 0.001	14.89 (2.71-81.67)	< 0.01
≥ 1 cerebral microbleed	6.55 (2.94-14.61)	< 0.001	2.18 (0.55-8.66)	0.27
≥ 1 intracerebral hemorrhage	2.41 (0.71-8.16)	0.16		
Acute subarachnoid hemorrhage	2.06 (0.71-5.93)	0.18		

p-value for uni- and multivariable logistic regression

Supplementary Table S5. Comparison at baseline of granulomatous and purely lymphocytic primary angiitis of the central nervous system (excluding amyloid-beta related angiitis)

	Granulomatous (n=17)	Purely lymphocytic (n=35)	Odds ratio (95% CI)	p-value
Mean (SD) age (years)	44 (15)	44 (15)	1.001 (0.96-1.04)	0.95
Female sex (n, %)	9 (53)	17 (49)	1.18 (0.38-3.73)	0.77
<i>Symptoms (n, %)</i>				
Seizure	8 (47)	17 (49)	0.95 (0.30-2.95)	0.92
Cognitive impairment	12 (71)	26 (74)	0.81 (0.24-2.97)	0.75
Headache	13 (76)	16 (46)	3.55 (1.07-13.63)	0.04
<i>Cerebrospinal fluid</i>				
White blood cells > 10/mm ³ or proteins > 0.70 g/L (n, %)	13 (81)	19 (56)	3.07 (0.85-13.60)	0.08
<i>Imaging (n, %)</i>				
≥ 1 acute brain infarct	4 (24)	6 (17)	1.51 (0.36-5.90)	0.56
Parenchymal enhancement	16 (94)	28 (85)	2.12 (0.38-22.01)	0.41
Leptomeningeal enhancement	6 (35)	8 (24)	1.70 (0.48-5.88)	0.40
Parenchymal or leptomeningeal enhancement	16 (94)	28 (85)	2.12 (0.38-22.01)	0.41
≥ 1 cerebral microbleed	11 (73)	15 (45)	3.05 (0.89-12.01)	0.08
≥ 1 intracerebral hemorrhage	3 (18)	3 (9)	2.24 (0.43-11.84)	0.33
Acute subarachnoid hemorrhage	3 (18)	1 (3)	5.55 (0.83-61.10)	0.08
Tumor-like lesion	5 (29)	15 (43)	0.58 (0.16-1.88)	0.37
Stenosis (any imaging)	1 (6)	2 (6)	1.22 (0.11-9.93)	0.86
Stenosis (digital subtraction angiogram)	1 (13)	1 (5)	2.73 (0.20-37.92)	0.42
<i>Biopsy positive for vasculitis (n, %)</i>				
Leptomeninges	4/8 (50)	4/11 (36)	1.67 (0.29-10.17)	0.57
Parenchyma	15/16 (94)	34/35 (97)	0.45 (0.03-5.86)	0.51

p-value for univariable Firth's bias-reduced logistic regression

Missing values: white blood cells (2), protein level (2), parenchymal enhancement (2), leptomeningeal enhancement (2), ≥ 1 cerebral microbleed (4), stenosis (digital subtraction angiogram) (23)