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Primary central nervous system vasculitis mimicking brain tumor: Comprehensive analysis of 13 cases from a single institutional cohort of 191 cases

Carlo Salvarani[a,e,*], Robert D. Brown Jr.[a], Teresa J.H. Christianson[b], John Huston III[c], Jonathan M. Morris[c], Caterina Giannini[d], Gene G. Hunder[f]

[a] The Department of Neurology, Mayo Clinic, Rochester, MN, USA
[b] The Department of Biomedical Statistics and Informatics, Mayo Clinic, Rochester, MN, USA
[c] The Department of Radiology, Mayo Clinic, Rochester, MN, USA
[d] The Department of Anatomic Pathology, Mayo Clinic, Rochester, MN, USA
[e] Rheumatology Division, Azienda USL-IRCCS di Reggio Emilia e Università di Modena e Reggio Emilia, Reggio Emilia, Italy
[f] Division of Rheumatology, Mayo Clinic, Rochester, MN, USA

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ABSTRACT

Objective: To describe the clinical, laboratory, and imaging features and course of patients with primary central nervous system vasculitis (PCNSV) presenting with an intracranial tumor-like mass (TLM).
Methods: We retrospectively studied a cohort of 191 consecutive patients with PCNSV seen at the Mayo Clinic, Rochester, MN over a 35-year period (1982–2017). 13/191 patients presented with a TLM. We compared the findings in these 13 patients with those from the 178 without this presentation.
Results: In 13 of 191 (6.8%) patients with TLM the diagnosis of PCNSV was established by cerebral biopsy. Granulomatous vasculitis was found in 11/13 patients, accompanied by vascular deposits of β-amyloid peptide in 7. Compared to the 178 patients without TLM, the patients with TLM were more likely to be male ($p = 0.04$), and less likely to have a transient ischemic attack ($p = 0.023$), bilateral cerebral infarcts ($p = 0.018$), or vasculitic lesions on angiography ($p = 0.045$). They were more likely to have seizures ($p = 0.022$), gadolinium-enhanced lesions ($p = 0.007$), and amyloid angiopathy ($p = 0.046$). All 13 patients responded to therapy and 8/13 (61.5%) had a Rankin disability score of 0 at last visit. Overall, high disability scores (Rankin scores 4–6) at last follow-up were associated with increasing age (odds ratio, OR, 1.49) and cerebral infarction (OR, 3.47), but were less likely in patients with gadolinium-enhanced lesions (OR, 0.36) and amyloid angiopathy (OR, 0.21).
Conclusion: In PCNSV a TLM at presentation represents a definable subgroup of patients with a favourable treatment response.

1. Introduction

Primary central nervous system vasculitis (PCNSV) is an infrequent and poorly understood form of vasculitis which is limited to the brain and spinal cord [1–5]. Primary CNS vasculitis is a heterogeneous condition and different subsets have been identified. A small proportion of patients may present with a tumor-like mass lesion (TLM) mimicking a cerebral tumor [6–23]. Many of the previously reported cases were derived from small series or individual case reports and follow-up information was limited.

We reviewed all cases of PCNSV evaluated at the Mayo Clinic from 1983 to 2017 to identify patients presenting with TLM. We evaluated the clinical findings, imaging, response to therapy, and clinical course of this subgroup. We also compared PCNSV patients with and without ML.

2. Patients and methods

2.1. Identification of the patients

In this study we extended our earlier PCNSV cohort of 168 consecutive patients seen at Mayo Clinic, Rochester, MN over a 29-year period to 35 years, from 1983 to 2017. We use the same predefined inclusion and exclusion criteria that were previously used to diagnose

* Corresponding author. Rheumatology Division, Azienda USL-IRCCS di Reggio Emilia, V.le Risorgimento N80, 42100, Reggio Emilia, Italy.
E-mail address: salvarani.carlo@ausl.re.it (C. Salvarani).

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the patients with PCNSV [3,4,24,25]. During the more recent period, 25 additional patients were identified. However, 2 patients refused to give the consent to be included in the study, therefore 191 patients with PCNSV seen at the Mayo Clinic from 1983 to 2017 were included in this retrospective study. The study was approved by the Mayo Clinic Institutional Review Board.

Patients with vasculitis in organs other than the CNS and those with evidence of other diseases that could explain the findings were excluded. None of the patients reported a history of exposure to vasoactive substances, were in the postpartum state, or had migraine headaches, thunderclap headaches, or other manifestations typical of reversible cerebral vasoconstriction syndrome.

2.2. Review of biopsy specimen, angiograms, and magnetic resonance imaging (MRI)

Cerebral biopsy specimens were reviewed by one pathologist (CG) without knowledge of clinical information. Angiograms and MRI were reviewed by a neuroradiologist. Conventional digital subtraction angiograms and brain MRI were performed and interpreted according to a clinical protocol used by the Division of Neuroradiology at the Mayo Clinic.

For the present study, we specifically identified those patients with a diagnosis of tumor on brain MRI in the neuroradiological report at disease presentation. The MRI of these patients was characterized by the presence of single or multiple contrast enhanced mass(es) or infiltrative lesion(s), with perilesional edema and mass effect in the absence of ischemic lesions on diffusion-weighted imaging [26].

2.3. Clinical data collection

The data collection form used in our earlier PCNSV studies was completed for all cases [3,4,24]. It included comprehensive information about manifestations at presentation and follow-up, other medical conditions, laboratory investigations, radiological imaging, results of CNS biopsy or autopsy, treatment, relapses, follow-up functional status and cause of death. To determine the effect of treatment, we used the treating physician's opinion about the response to therapy. A neurologist examined all patients at the time of diagnosis and on subsequent visits including the last visit or death.

Relapse of PCNSV was diagnosed if a recrudescence or worsening of symptoms, or of existing lesions occurred and/or new lesions appeared on subsequent MRI examinations while the patient was receiving no medication or was on a stable dosage. Patients with relapse required an increase in therapy. The degree of disability at presentation and at the last visit was defined by a review of the detailed clinical data in the medical record and was categorized by using the modified Rankin scale [27].

2.4. Statistical analysis

We used a two-sided two-sample *t*-test to compare numerical parameters or a Wilcoxon rank-sum test when the distributions were skewed. The chi square or Fischer's exact test were used for comparisons of categorical variables when cell counts were small.

Logistic regression models were used to identify characteristics at diagnosis, including the presence/absence of TLMs that influenced the odds of a poor outcome. Univariate and age-adjusted odds ratios (ORs) and 95% confidence intervals were reported. The Cox proportional hazards model was used to assess the relation between demographic, clinical, laboratory, radiological, pathological and therapeutic parameters at diagnosis, including the presence/absence of TLMs and survival. We reported univariate and age-adjusted hazard ratios (HRs) and 95% confidence intervals. Results were reported as age-adjusted when age was significantly associated with the outcome.

Survival was estimated with the Kaplan–Meier method. Cox proportional hazards modelling was performed for age-adjusted survival comparison. All p values were two-sided; significance was defined at $p < 0.05$. The statistical analysis was performed using SAS version 9.

Table 1
Findings in PCNSV with and without tumor-like mass lesion at diagnosis.[a]

	Tumor-like presentation (n = 13)	Other presentations (n = 178)	P value
Male, sex	10 (76.9)	79 (44.4)	0.040
Age at diagnosis, median (range) years	66 (25–84)	48.5 (17–85)	0.470
Months from symptom onset to diagnosis, median (range)	1.3 (0.2–56.2)	1.6 (0.0–120.6)	0.761
Clinical manifestations at presentation			
Headache	4 (30.8)	107 (60.1)	0.046
Cognitive dysfunction	9 (69.2)	95 (53.4)	0.389
Persistent neurologic deficit or stroke	4 (30.8)	78 (43.8)	0.402
Hemiparesis	4 (30.8)	76 (42.7)	0.563
Aphasia	3 (23.1)	42 (23.6)	1.000
Transient ischemic attack	0	49 (27.5)	0.023
Ataxia	1 (7.7)	34 (19.1)	0.469
Seizures	6 (46.2)	31 (17.4)	0.022
Visual symptoms (any kind)	2 (15.4)	67 (37.6)	0.140
Visual field defect	1 (7.7)	31 (17.4)	0.699
Blurred vision or decreased visual acuity	1 (7.7)	20 (11.2)	1.000
Intracranial hemorrhage	1 (7.7)	15 (8.4)	1.000
Paraparesis or quadriparesis	0	9 (5.1)	1.000
Systemic manifestations[b]	0	18 (10.1)	0.616
Fever	0	17 (9.6)	0.611
ESR, median (range) mm/hour[c]	10 [1–24]	8 (0–124)	0.801
Modified Rankin Score at last follow-up			
0-3	12 (92.3)	132 (74.2)	0.192
4-6	1 (7.7)	46 (25.8)	
Treatment response	13/13	132/162 (81.5)	0.128
No relapse during follow-up	8/13 (61.5)	117/164 (71.3)	0.529
No immunosuppressive therapy required at last follow-up	2/13 (15.4)	43/171 (25.1)	0.738

[a] Continuous data are presented as median and range. Categorical data are presented as number and percentage of patients. PCNSV = primary central nervous system vasculitis. CSF = cerebrospinal fluid. WBC = white blood cell. ESR = erythrocyte sedimentation rate.

[b] Defined as the presence of at least 1 of the following: fatigue, anorexia, weight loss, or fever.

[c] ESR was available for 11 of the 13 patients with tumor-like presentation and for 152 of the 178 patients without tumor-like presentation.

3. Results

Of 191 patients with PCNSV we identified 13 patients (6.8%) who presented with TLM. Cerebral biopsy was used to establish PCNSV diagnosis in all 13 patients.

3.1. Demographic and clinical features

Demographic characteristics, clinical manifestations, and other findings of the 13 patients with TLM lesion at presentation, compared to the 178 without TLM lesion, are summarized in Table 1.

Ten of the 13 (77%) patients were male. The median age at diagnosis was 66 years (range 25–84 years). The median time from onset of symptoms to diagnosis was 1.3 months (range 0.2–56.2 months). Constitutional symptoms such as fever were absent. The most common manifestation at presentation was altered cognition, followed by seizures. One patient had symptoms related to spinal cord involvement. Other medical disorders were noted in 6 patients, including hypertension, diabetes mellitus, and hypothyroidism. Two patients had

Table 2
CSF and MRI results in PCNSV with and without tumor-like mass lesion at diagnosis.[a]

	Tumor-like presentation (n = 13)	Other presentations (n = 178)	P value
CSF			
Protein > 45 mg/dl[b]	8/9 (88.9)	105/137 (76.6)	0.684
WBC count > 5 cells/mm^3	4/9 (44.4)	74/137 (54.0)	0.734
Protein > 45 mg/dl or WBC count > 5 cells/mm^3	8/9 (88.9)	112/139 (80.6)	1.000
Protein > 70 mg/dl or WBC count > 10 cells/mm^3	6/9 (66.7)	87/137 (63.5)	1.000
Initial MRI findings[c]			
Presence of infarct	4/13 (30.8)	91/163 (55.8)	0.092
Single infarct	1/13 (7.7)	8/163 (4.9)	0.507
Multiple infarcts, in the same hemisphere	2/13 (15.4)	17/163 (10.4)	0.441
Multiple infarcts bilateral	1/13 (7.7)	66/163 (40.5)	0.018
Gadolinium-enhancing lesions (intracerebral or meningeal)	10/13 (76.9)	61/163 (37.4)	0.007
Intracerebral gadolinium-enhanced lesions	6/13 (46.2)	34/163 (20.9)	0.077
Meningeal gadolinium-enhanced lesions	4/13 (30.8)	33/163 (20.2)	0.477
Intracerebral hemorrhage	1/13 (7.7)	11/163 (6.7)	1.000
Subarachnoid hemorrhage	0	4/163 (2.5)	1.000
Angiogram showing vasculitis	1/3 (33.3)	128/146 (87.7)	0.047

[a] Categorical data are presented as number and percentage of patients. PCNSV = primary central nervous system vasculitis.
[b] The normal range of protein is 14–45 mg/dl.
[c] Magnetic resonance imaging (MRI) was performed initially in 163 of the 178 patients without tumor-like presentation.

Hodgkin's lymphoma (HL): in one, HL and PCNSV occurred simultaneously, in the second HL was diagnosed 26 years before PCNSV diagnosis.

3.2. Laboratory investigations

Cerebrospinal fluid (CSF) examination results at the time of diagnosis are listed in Table 2. Results were abnormal in 8 of the 9 patients with TLM who had spinal tap. Six had CSF protein levels > 70 mg/dl or white blood cell count of at least 10 cells/mm^3. Morphologic evaluation and/or immunocytochemical studies and/or flow cytometric immunophenotyping were negative in all 13 patients.

Erythrocyte sedimentation rate (ESR) was normal in all 13 patients (median value 10 mm/h; range 1–24 mm/h).

3.3. Radiological imaging

The neuroimaging findings at presentation are also shown in Table 2. For patients with TLM, gadolinium-enhancing lesions were the most common abnormalities, noted in 10/13 (77%), while multiple bilateral infarcts were observed in only 1/13 (8%) of the patients. MRI of the spinal cord in one patient revealed abnormal enhancement of the distal conus medullaris and multiple nerve roots of the cauda equina. Table 3 shows the mass localization and the initial suspected diagnosis.

Six patients had a mass on MRI (a single lesion in 3 cases and multiple lesions in 3 other cases), with edema and mass effect in 5 and 3 cases, respectively. In 7 other patients, MRI showed white matter infiltrative lesions with edema and mass effect (Fig. 1A).

Cerebral angiography/magnetic resonance angiography was performed in 4 of the 13 patients, and only 1 showed changes characteristic of vasculitis (Table 3).

3.4. Biopsy results

All 13 patients had positive cerebral biopsy (stereotactic in 10, open-wedge in 3). Granulomatous vasculitis was found in 8 patients, accompanied by vascular deposits of β-amyloid peptide in 6 (Fig. 1B). Three patients had granulomatous and necrotizing vasculitis on histologic examination, accompanied by vascular deposits of β-amyloid peptide in 1, while the other 2 patients had a lymphocytic vasculitis.

Histological stains for fungi and mycobacteria were performed in 9 patients and were negative in all 9 patients as well as polymerase chain reaction (PCR) tests and cultures of cerebral biopsies for zoster and herpes simplex viruses which were performed in 8 and 6 patients.

3.5. Treatment and outcome

All 13 patients received prednisone therapy. In 4 patients, only oral prednisone was used. In 9, intravenous pulse methylprednisolone 1 g/day for 3–5 days was administered before oral prednisone therapy was started. The median initial oral prednisone dose was 60 mg/day (range: 60–120 mg/day). The median duration of oral prednisone therapy was 7 months (range: 1–98 months).

Three patients received cyclophosphamide in addition to prednisone at the beginning of the treatment and one during a disease flare: 3 patients received oral cyclophosphamide, the fourth intravenous pulse cyclophosphamide. Mycophenolate mofetil was used in 3 patients, and azathioprine in one patient.

Five patients with associated amyloid angiopathy and the 2 patients with lymphocytic vasculitis were treated with prednisone alone, while the other 6 patients with granulomatous or granulomatous/necrotizing vasculitis were treated with an immunodepressant in addition to prednisone.

Five patients had PCNSV flares that led to a change in the therapy.

Overall, all 13 patients responded to therapy and recovered with no, slight or moderate residual disability. The median modified Rankin disability score at the last visit was 0 (range: 0–3), whereas, at presentation the median score was 2 (range: 1–5). Furthermore, 8/13 (61.5%) had a Rankin disability score of 0 at last visit.

3.6. Comparison of patients presenting with and without tumor-like mass lesion

The 13 cases with TLM were compared with the 178 cases without as shown in Tables 1 and 2 Patients with TLM were more likely to be male, (p = 0.04) and to present with seizures (p = 0.02), and were less like to present with headaches (p = 0.046) and transient ischemic attacks (TIA) (p = 0.023). No significant differences in spinal fluid findings at diagnosis were observed between the two groups. Gadolinium-enhancing lesions (intracerebral or meningeal) on MRI were more common in patients with TLM (p = 0.007). Intracerebral gadolinium-enhanced lesions were more common in patients with a TLM but only a trend towards statistical significance was observed (p = 0.077). No difference in the frequency of meningeal gadolinium-enhanced lesions was observed. Multiple bilateral infarcts at MRI and vasculitic lesions at angiogram were less frequent in patients with TLM (p = 0.018 and p = 0.047, respectively). Amyloid angiopathy was more frequently found in patients with TLM compared to those without such lesions [7/13 (53.8%) versus 14/58 (24.1%); p = 0.046]. The frequency of patients with relapsing disease, without the need for immunosuppressive medication at the end of follow-up, and of patients who responded to the treatment was similar in the two groups.

Even though patients with TLM were less likely to have poor outcome (Rankin scores of 4 or greater) (8% versus 26%) the difference was not significant.

The median duration of follow-up for the 13 patients was 6.7 months with a range from 27 days to 3.9 years. At the end of the follow-period, only 1 patient died 15 months after the diagnosis. The cause of

Table 3
Characteristics of the 13 patients with tumor-like presentation.

	Age(y)/ gender	Clinical findings at presentation	Tumor localization (suspected diagnosis)	Type of biopsy	Histological findings	Vascular lesions at DSA/MRA	Treatment	Relapse/ recurrence (n)	Follow-up time (m)	MRS presentation/ last follow-up
Case 1	63/F	Confusion, headache, visual impairment	Temporal and occipital lobes, and right parietal lobe (gliomatosis cerebri)	Stereotactic	ABRA (granulomatous)	ND	PDN	1	106	4/1
Case 2	37/M	Difficulty with memory, personality changes, and subacute decline in balance and coordination	Corpus callosum and corona radiata bilaterally (glioblastoma multiforme)	Stereotactic	Granulomatous and necrotizing	ND	PDN, CYC, MMF	2	81	4/2
Case 3	30/M	Headache, confusion, and difficulty in coordination	Right posterior fronto-parietal region (high grade malignancy cerebral neoplasia)	Stereotactic	Granulomatous	ND	PDN, CYC	1	17	2/1
Case 4	75/M	Seizures	Right frontal lobe (oligodendroglioma)	Stereotactic	ABRA (granulomatous)	–	PDN	0	6	2/0
Case 5	43/M	Left visual field defect and left hemiparesis	Right cerebellum and brain (metastases)	Stereotactic	Granulomatous	+	PDN, CYC	0	20	2/1
Case 6	84/M	Confusion and agitation	Frontal lobes and right temporal lobe (glial neoplasm)	Open-wedge	ABRA (granulomatous and necrotizing)	ND	PDN, CYC	0	5	3/0
Case 7	75/F	Seizures	Right temporal lobe (glioma)	Open-wedge	ABRA	ND	PDN	0	6	1/0
Case 8	31/M	Seizures, headache, confusion	Left temporal lobe (glioma)	Stereotactic	Lymphocytic	ND	PDN	0	2	3/0
Case 9	25/F	Seizures	Left frontal lobe (multifocal glioma)	Stereotactic	Granulomatous and necrotizing	ND	PDN, AZA, MMF	4	46	1/0
Case 10	75/M	Aphasia	Left temporal and parietal lobes (glioma)	Stereotactic	ABRA (granulomatous)	ND	PDN	0	15	2/0
Case 11	66/M	Seizures, headache, confusion	Right frontal lobe (glioma)	Open-wedge	ABRA (granulomatous)	–	PDN	0	43	4/2
Case 12	73/M	Subacute cognitive decline, confusion	In particular, left temporal lobe, but also both cerebral hemispheres (metastases)	Stereotactic	ABRA (granulomatous)	–	PDN, MMF	0	4	5/3
Case 13	34/M	Seizures, right hemiparesis	Left frontal and left occipital lobes and (multifocal glioma)	Stereotactic	Lymphocytic	ND	PDN	1	27	2/0

DSA = digital subtraction angiography; MRA = magnetic resonance angiography; MRS = Modified Rankin Score; ABRA = Aβ-related angiitis; ND = not done; PDN = prednisone; CYC = cyclophosphamide; MMF = mycophenolate mofetil; AZA = azathioprine.

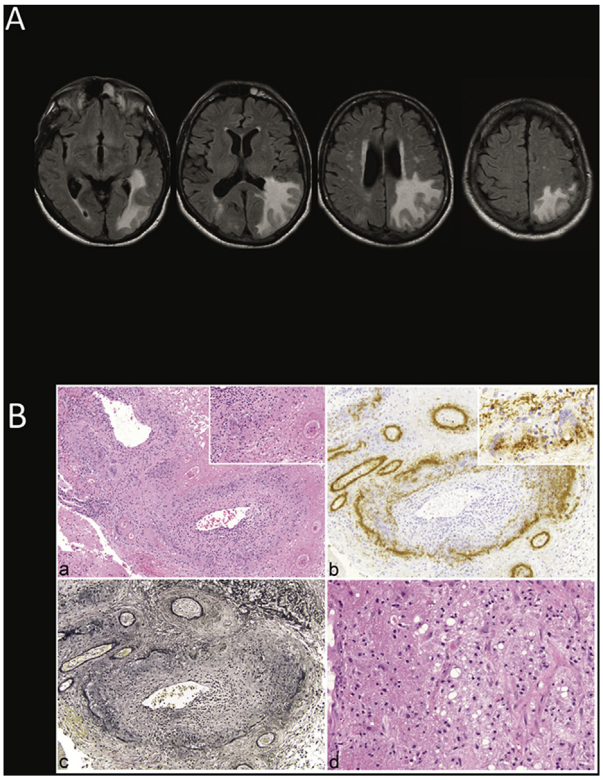

Fig. 1. Magnetic resonance imaging (MRI) and pathologic findings of case 10 with ABRA and tumor-like presentation: A) MRI showing infiltrative white matter process mimicking low grade glioma. Fluid attenuation inversion recovery (FLAIR)-weighted MRI images show infiltrative white matter T2 hyperintensity in left temporal/parietal lobes with associated mass effect; mild contralateral infiltrative T2 hyperintensity is also present. The images are negative for enhancement. B) It illustrate extensive vasculitic involvement of leptomeningeal arteries (a) with granulomatous inflammation with giant cells (inset). Severe beta-amyloid deposition is present in the vascular wall (b) and amyloid is present inside the giant cells. The Verhoeff-Van Gieson stain for elastic fibers highlights the destruction of the internal elastic lamina (c). Subacute organizing infarct with dense macrophage infiltration contributes to the mass-like appearance of the lesion (d). Magnification a x100, b,c,d x140, inset a x200, inset b x400.

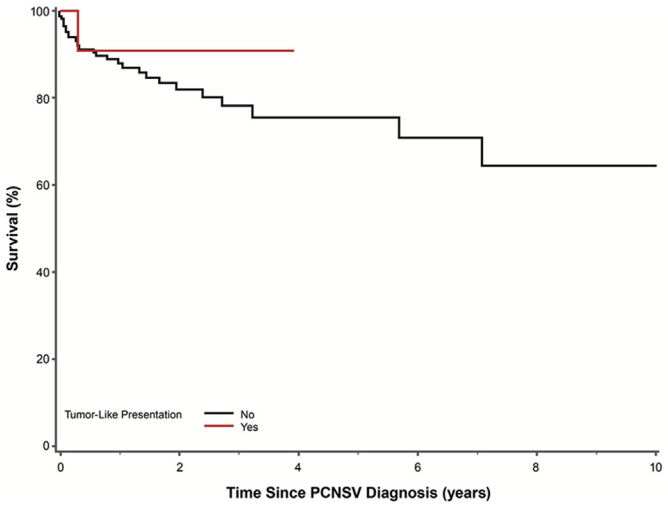

Fig. 2. Survival curves of patients with PCNSV with and without tumor-like mass lesion: survival of the patients with tumor-like mass lesion was not different compared to patients without (p = 0.57).

death was unknown. Fig. 2 shows the survival curves of patients with PCNSV with and without ML. No significant difference in survival between the 2 groups of patients was observed (p = 0.57) (Fig. 2).

In the entire cohort of 191 patients, univariate Cox proportional analysis showed four findings to be associated with an increased mortality rate: increasing age at diagnosis (calculated per 10-year increments) (HR, 1.37; 95%CI: 1.06–1.76; p = 0.02), cerebral infarction seen on MRI at presentation compared to those without an infarction (HR, 2.95; 95%CI: 1.28–6.80; p = 0.01), and the presence of large vessel involvement on angiogram (HR, 3.23; 95%CI: 1.21–8.63; p = 0.02). Patients with gadolinium enhancing lesions or meninges on MRI at presentation had a lesser risk of death during follow up than patients who had no such lesions (HR, 0.29; 95%CI: 0.11–0.76; p = 0.01).

Univariate logistic analysis showed that high disability scores (Rankin scores 4–6) at last follow-up were associated with increasing age (OR, 1.49; 95%CI: 1.18–1.87; p = 0.0008), and cerebral infarction on MRI at presentation (OR, 3.47; 95%CI: 1.59–7.57; p = 0.002). Patients with gadolinium enhancing meninges or lesions on MRI at presentation (OR, 0.36; 95%CI: 0.16–0.80; p = 0.01) and those with amyloid angiopathy at biopsy (OR, 0.21; 95%CI: 0.06–0.82; p = 0.02) had lower disability at follow-up.

4. Discussion

These findings suggest that TLM presentation occurs in patients with PCNSV with a frequency of about 7%. Our 13 patients with TLM presentations represent the largest series derived by a single institution cohort. Many of previously reported cases were from small series or individual case reports [6–23]. These data from a large group of unselected consecutive cases from a single centre, diagnosed with uniform criteria and frequent pathologic verification of vasculitis with extensive clinical data and follow-up provides a unique view of this condition. Therefore, our cohort may provide a more accurate estimate of the frequency of this manifestation, spectrum of clinical findings, and outcomes.

These patients differ from the cases without TLM. They were more likely to be male, and present with seizures, and were less likely to present with headache or TIA. Gadolinium-enhancing lesions at MRI were more frequently observed in patients with TLM, while multiple bilateral infarcts and vascular lesions at angiogram were less frequent. Cerebral amyloid angiopathy at biopsy was more frequently observed in patients with TLM. All patients with TLM had a favourable response to treatment with control of disease activity and improvement of Rankin scores over time. 61.5% of the patients had a Rankin disability score of 0 at last visit.

Recently, de Boysson et al. reported 10 cases presenting with TLM lesions enrolled in the French PCNSV cohort and compared them with other 75 patients without TLM within the same cohort [7]. Similar to our results, their patients were more like to have seizures and gadolinium-enhancing lesions at diagnosis. Most patients with TLM had negative vascular imaging but positive biopsy in both series, suggesting that the vessels involved were small and beyond the resolution of arteriography or MRA.

Our histologic findings were similar to those reported by Molloy et al. [6] who reported 38 cases of PCNSV with TLM, including 30 identified from the medical literature. Most of our patients had a granulomatous vasculitis (61.5% compared to 53% in the Molloy et al. study). Vascular deposits of β-amyloid peptide were observed in 53.8% of our cases compared to 34% of the cases described by Molloy et al. and in 24.1% of our patients with positive biopsies but without TLM [6]. A granulomatous vasculitis was observed in only 13% of the cases with TLM in the French study and lymphocytic vasculitis was the most frequent histopathological pattern, observed in 89% of cases with TLM and 82% of patients without. We observed a lymphocytic vasculitis in 15.3% of patients with TLM and in 22% of the total cohort of PCNSV

patients [3]. These differences in the histopathological pattern may be related to differences in the referral of the patients: in the French cohort, patient population was referred to 25 tertiary centers, while in our study to a single centre providing a more uniform estimate of PCNSV clinical spectrum.

As we observed in our previous studies, angiography-negative patients, in whom cerebral biopsy is required for diagnosis, are characterized by evidence of gadolinium enhancing lesions, the absence of cerebral infarcts, as well as the presence of amyloid angiopathy and have a more benign disease that responds favourably to treatment [3,4,28–31]. Our PCNSV patients with TLM are part of this subgroup of PCNSV patients with less aggressive cerebral vasculitis with the inflammation mainly restricted to the small cortical and leptomeningeal vessels. This study confirms our previous results, in which patients with Aβ-related angiitis (ABRA), who represented half of our patients with TLM presentation, are a definable subset of PCNSV with favourable response to glucocorticoids alone or in combination with immunodepressants [28,29]. In these patients the vascular inflammation more than Aβ deposition alone has a major influence in determining disease manifestations, therapy response, and outcomes. 5/7 (71%) of our patients with ABRA and presenting with TLM were successfully treated with prednisone alone, furthermore, the 2 patients with lymphocytic vasculitis responded to prednisone without adding any immunodepressive treatment confirming our previous observation that lymphocytic vasculitis appears to define a subset of PCNSV with a more benign vasculitis [3].

Limitations of this study include its retrospective nature, the potential for an unrecognized referral bias of cases, and the frequent lack of tissue diagnosis in the overall cohort even though the angiograms were highly suggestive of vasculitis and follow-up showed no evidence of other conditions than vasculitis.

In conclusion, a TLM presentation is not a rare occurrence in PCNSV and should prompt a CNS biopsy to establish the correct diagnosis. Cognitive dysfunction and seizures are frequent presenting findings. Evidence of cerebral infarctions on MRI is uncommon in these patients, while gadolinium enhancing lesions are frequent. The predominant vasculitic histopathologic pattern is granulomatous and half of the patients have an associated CAA. These patients generally respond well to glucocorticoid therapy alone or combined with immunodepressives. Early recognition and treatment may reduce poor outcomes.

Contributors

All authors were involved in drafting the manuscript or revising it critically, and approved the final version. CS had full access to all the data in the study and takes responsibility for the integrity of the data and accuracy of the data analysis. Study design: CS, RDB, TJHC, JH III, CG, GGH. Statistical analysis: TJCH. Data Collection: CS, RDB, JH III, CG, GGH.

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Conflicts of interest

Authors declares no conflict of interest.

Ethics approval

The study was approved by the Mayo Clinic Institutional Review Board and informed consent was obtained from all patients or their relatives.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jaut.2018.10.001.

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