Clin Neuroradiol (2019) 29:37–44
https://doi.org/10.1007/s00062-017-0622-8

ORIGINAL ARTICLE

Neuroradiologic Characteristics of Primary Angiitis of the Central Nervous System According to the Affected Vessel Size

Christian Thaler[1] · Ann-Katrin Kaufmann-Bühler[1] · Tserenchunt Gansukh[4] · Amarjargal Gansukh[4] · Simon Schuster[2] · Henrike Bachmann[2] · Götz Thomalla[2] · Tim Magnus[2] · Jakob Matschke[3] · Jens Fiehler[1] · Susanne Siemonsen[1]

Received: 11 July 2017 / Accepted: 16 August 2017 / Published online: 5 September 2017

Abstract
Introduction Magnetic resonance imaging (MRI) has an important impact in diagnosing primary angiitis of the central nervous system (PACNS). However, neuroradiologic findings may vary immensely, making an easy and definite diagnosis challenging.
Methods In this retrospective, single center study, we analyzed neuroradiologic findings of patients with PACNS diagnosed at our hospital between 2009 and 2014. Furthermore, we classified patients according to the affected vessel size and compared imaging characteristics between the subgroups.
Results Thirty-three patients were included (mean age 43 [±15.3] years, 17 females) in this study. Patients with positive angiographic findings were classified as either medium or large vessel PACNS and presented more ischemic lesions ($p < 0.001$) and vessel wall enhancement ($p = 0.017$) compared to patients with small vessel PACNS. No significant differences were detected for the distribution of contrast-enhancing lesions (parenchymal or leptomeningeal), hemorrhages, or lesions with mass effect. Twenty-five patients underwent brain biopsy. Patients with medium or large vessel PACNS were less likely to have positive biopsy results.
Discussion It is essential to differentiate between small and medium/large vessel PACNS since results in MRI, digital subtraction angiography and brain biopsy may differ immensely. Since image quality of MR scanners improves gradually and brain biopsy may often be nonspecific or negative, our results emphasize the importance of MRI/MRA in the diagnosis process of PACNS.

Keywords Primary angiitis of the central nervous system · PACNS · MRI · Inflammation · Vessel wall imaging · CNS

Introduction

Primary angiitis of the central nervous system (PACNS) is a rare disorder defined by inflammation of central nervous system (CNS) vessel walls and the absence of secondary causes of vasculitis [1, 2]. Common radiographic findings in PACNS like brain infarction, intracranial hemorrhage, contrast-enhancing lesions, arterial stenosis, and vessel wall enhancement (VWE) are various and nonspecific, making the correct diagnosis challenging [3–5]. Up to date, brain biopsy is still considered the most reliable diagnostic method even though it lacks sensitivity, as samples are nondiagnostic in up to 50% of the cases, and it involves an invasive procedure with the risk of parenchymal damage [6].

Recent studies promote the classification of different disease subgroups according to image findings and detectable vessel pathology [6–9]. Defining PACNS by the affected vessel size has shown meaningful impact on diagnostic processes as well as outcome prediction [10–12]. While

Christian Thaler and Ann-Katrin Kaufmann-Bühler contributed equally to this work.

✉ Christian Thaler
c.thaler@uke.de

[1] Department of Diagnostic and Interventional Neuroradiology, University Medical Center Hamburg-Eppendorf, Martinistrasse 52, 20246 Hamburg, Germany

[2] Department of Neurology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

[3] Institute of Neuropathology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

[4] Mongolian Academy of Sciences, Oyun Onosh Medical Center, Ulaanbaatar, Mongolia

patients with small vessel PACNS present more severe encephalopathic but unrevealing angiographic findings, patients with large/medium vessel affection show angiographic abnormalities and vascular lesions [13]. However, no uniform or internationally accepted classification regarding vessel size exists.

Since radiologic and pathologic findings may vary depending on the affected vessel size, an accurate definition seems to be highly important for diagnostic procedures and algorithms. The purpose of our study was to describe typical combinations of specific MRI characteristics in patients with cerebral vasculitis in consideration of the classification of affected vessel size. We hypothesized that brain lesion patterns, diagnostic yield of brain biopsy, and conventional angiography vary according to affected vessel size.

Methods

Patients

In a retrospective single center study, the records of all patients studied by brain imaging at the Department of Neuroradiology at the University Medical Center Hamburg-Eppendorf between 2009 and 2014 were reviewed. Patients were identified from the hospital's electronic database via full-text search of the term "vasculitis" for clinically suspected diagnosis of cerebral vasculitis. Patients provided written informed consent according to the Declaration of Helsinki. Multidisciplinary investigators including neurologists, neuroradiologists, and neuropathologists verified diagnosis. Patients were included if following inclusion criteria were met: Positive brain biopsy or diagnosis and treatment of CNS vasculitis at the University Medical Center based on comprehensive diagnostics and clinical reasoning, and magnetic resonance imaging (MRI) between 2009 and 2014 at the Department of Neuroradiology. Diagnosis was based on the 2012 German Society of Neurology (DGN) guidelines for diagnosing and treatment of CNS vasculitis [14]. PACNS mimics, including systemic vasculitis with CNS involvement, reversible vasoconstriction syndrome, and atherosclerosis were excluded carefully.

Patients were classified as small, medium, or large vessel PACNS according to Küker et al. [15]. Large vessel PACNS is defined as involvement of internal carotid artery (ICA), basilary, and vertebral arteries, A1 segment and middle cerebral artery (MCA) until distal M1 segment. Medium vessel PACNS complies with detectable changes of M2, A2, or P2 segment and smaller vessels in MRI or digital subtraction angiography (DSA). Small vessel PACNS affects small peripheral arteries that are consequentially not detectable in MRI or DSA.

MR Protocol, Sequences, and Acquisition

MR scans were obtained on a 3 T Magnetom Skyra, 1.5 T Avanto, 1.5 T Symphony, or 1.5 T Sonata (all Siemens, Erlangen, Germany). Among other standard MR sequences such as fluid-attenuated inversion recovery (FLAIR) and T2-weighted (T2w) images, the protocol included a standard multislab 3D time-of-flight angiography (ToF-MRA) centered on the circle of Willis, and in a subgroup of patients also a coronal high-resolution T1-weighted (T1w) spin-echo sequence before and after contrast administration (Gadovist (Gd); Bayer Schering Pharma, Berlin, Germany). Sequence parameters for each scanner are listed in Table 1.

Data Analysis

Clinical Evaluation of MR Images

For image analysis, baseline and follow-up scans were included in this study. Images were read by two experienced neuroradiologists in consensus. We focused on the evaluation of presence and patterns of: (1) Ischemic infarcts (on T2w, diffusion-weighted imaging [DWI], FLAIR); (2) Intracranial hemorrhages (on T2*w or susceptibility weighted images [SWI]); (3) Intracranial arterial stenosis (on ToF-MRA); (4) Vessel wall enhancement (on coronal T1w pre- and postcontrast administration [VW-MRI]); (5) Inflammatory parenchymal and meningeal modifications including contrast-enhancement (CE) and reversible T2w-hyperintense lesions without restricted diffusion (T2w, FLAIR, T1w post Gd); (6) Lesions with mass effect.

Lacunar infarcts were defined as small infarcts (<20 mm in diameter) located in the basal ganglia, the deep cerebral white matter or the brainstem and are the result of occlusion of a single small perforating cerebral artery. Hemodynamic infarcts were defined by an infarction localized at the distal territories at the junction between the 2 main arterial territories.

Presence or absence of arterial VWE was determined by comparing pre- and post-Gd images. For ischemic lesions, location and lesion pattern was determined.

Demographic and Clinical Variables

Collected clinical and demographic data comprised age, sex, rheumatologic work up, and grade of disability at disease onset and at the end of follow-up (modified Rankin scale [mRS]). Median follow-up duration was 13.8 months (range 0–9.9 years).

Table 1 Technical specifications. All scanners by Siemens, Erlangen, Germany

Scanner (Tesla)	Sequence	Repetition time in ms	Echo time in ms	Inversion time in ms	Flip angle	Slice thickness in mm
Avanto (1.5)	FLAIR	6500	104	2200	150°	5
	T2w	4200	106	–	136°	5
	ToF	25	7	–	25°	0.7
	Cor T1w	636	11	–	160°	2
Symphony (1.5)	FLAIR	7900	115	2500	150°	5
	T2w	2700	11	–	160°	5
	ToF	39	7.1	–	25°	0.8
	Cor T1w	636	11	–	160°	2
Skyra (3.0)	FLAIR	9000	90	2500	150°	5
	T2w	2800	18	–	160°	3
	ToF	21	3.4	–	18°	0.5
	Cor T1w	549	11	–	150°	2
Sonata (1.5)	FLAIR	7900	108	2500	150°	5
	T2w	2700	11	–	160°	5
	ToF	36	6	–	25°	0.8
	Cor T1w	595	11	–	160°	2

FLAIR fluid attenuated inversion recovery, *T2w* T2-weighted, *ToF* time of flight, *Cor T1w* coronal T1-weighted

Table 2 Characteristics of ischemic lesion location

Ischemic lesions	Total $n = 19$	
	(n)	(%)
Embolic	11	57.9
Hemodynamic	9	47.4
Lacunar	2	10.5
Multiple ischemic lesions	12	63.2
Location		
Supratentorial	18	94.7
– Bilateral	8	42.1
Infratentorial	6	31.6
– Brainstem	5	26.3
– Cerebellar	4	21.1

Statistical Analysis

Statistical analysis was performed using IBM SPSS 21.0. Two-sided Fisher's exact test was applied to compare categorical data and Mann–Whitney U test was used to compare ordinal data. Two-sided p-values of less than 0.05 were regarded as statistically significant.

Results

Clinical and Demographic Data

We included 33 patients with the final diagnosis of PACNS. Patient mean age at first admission was 43 ± 15.3 years (± standard deviation [sd]), with 17 females and 16 males. Of 26 patients undergoing brain biopsy, histopathologic examination confirmed suspected diagnosis of PACNS in 17 cases. In all other cases diagnosis was based on clinical presentation, imaging findings, and laboratory results. Digital subtraction angiography was performed in 12 patients, with abnormal findings in 11 of them. All patients underwent rheumatologic workup with negative or unspecific results in all cases. Also, all patients underwent lumbar puncture and CSF was abnormal in 29 patients, including elevated leukocyte count, increased protein level, or isolated oligoclonal bands. Induction therapy in all but one case followed the current recommendation of steroid therapy coupled with cyclophosphamide pulse therapy. One patient did not receive any immunosuppressants, but platelet antiaggregant therapy.

Imaging Characteristics

In 25 patients (75.8%) intracranial stenosis was observed: 21 patients (21/25, 84%) presented with multisegmental stenosis and in 17 cases (68%) stenosis was present in ≥2 vessel territories. The vessel most frequently affected by stenosis was the MCA (22 patients [88%] presented MCA stenosis uni- or bilateral), followed by ACA (20, 80%), PCA (14, 56%), ICA (13, 52%), vertebral artery (5, 20%), and basilar artery (1, 4%). DSA was performed in 12 patients with positive results in all but one. In 8 patients with positive DSA, intracranial stenosis was already detected in ToF angiography.

VW imaging was performed in 29 patients and positive findings were detected in 14 (14/29, 48.3%) cases. Considering all patients suffering from arterial stenosis and undergoing VW imaging, VWE was displayed in 14/23 (60.9%)

Table 3 Imaging characteristics in small vessel vs. medium/large vessel primary angiitis of the central nervous system

		Small vessel PACNS (n = 8)	Medium/large vessel PACNS (n = 25)	p
–	Age in years	36.9 (±13.9)	45.5 (±15.7)	0.176
–	mRS baseline	2.33 ± 2.34 (n = 6)	2 ± 1.38 (n = 21)	0.93
–	mRS follow-up	2.4 ± 1.8 (n = 5)	2.28 ± 3.29 (n = 18)	0.86
–	Δ mRS	–0.4 ± 1.3 (n = 5)	0.3 ± 1.9 (n = 18)	0.54
MRI	Stenosis (ToF-MRA)	0	22	<0.001
	VWE	0/6	14/23	0.017
	Ischemic lesion	0	19	<0.001
	Hemorrhage	2	9	0.687
	CE lesion	7	12	0.098
	Lesions with mass effect	2	3	0.078
–	Positive DSA	0/1	11/11	–
–	Positive brain biopsy	7/7	9/18	0.023

PACNS primary angiitis of the central nervous system, *mRS* modified Rankin Scale, *ToF-MRA* Time of Flight MRA, *VWE* vessel wall enhancement, *CE lesion* contrast-enhancing lesion, *DSA* digital subtraction angiography

patients. In comparison, all patients with VWE also presented with arterial stenosis in ToF-MRA or DSA, but only in 8/23 (34.8%) patients were these affecting the same vessel. In patients without stenosis, no VWE was detected.

Cerebral infarction was detected in 19 patients (19/33, 57.6%), of which 12 patients (12/19, 63.2%) presented multiple infarcts of different ages. Embolic lesion pattern was found in 11 (57.9%), hemodynamic lesions in 9 (47.4%), and lacunar infarcts in 2 (10.2%) patients. Two patients presented with embolic as well as hemodynamic infarcts. All patients with cerebral infarctions also had arterial stenosis. An overview of ischemic lesion location is given in Table 2.

CE lesions and mass lesions were apparent in 19 patients (57.6%). Contrast enhancement was observed in brain parenchyma (14/19, 73.7%) and meninges (5/19, 26.3%). Mass lesions were displayed in 5 patients (5/33, 15.2%) and located both infratentorial and supratentorial. Focal susceptibility artifacts, ring enhancement, and an extended surrounding edema appeared as common features of mass lesions.

Eleven patients suffered intracranial hemorrhage (33.3%), including 4 (4/11, 36.4%) cases of subarachnoid hemorrhage (SAH), 4 cases of intracerebral hemorrhage (ICH), and 4 cases of microbleeds. One patient presented SAH as well as microbleeds.

Image Characteristics Depending on Affected Vessel Size

Positive MRA or DSA were detected in 25 patients and were therefore classified as medium/large vessel PACNS, whereas 8 patients presented no angiopathies in MRA or DSA and were accordingly classified as small PACNS. Patients with medium/large vessel PACNS showed significantly higher rates of VWE and ischemic lesions (p = 0.017; p < 0.001). CE lesions were found in 7 patients with small PACNS and in 12 patients with medium/large vessel PACNS. Mass lesions were displayed in 2 patients with small PACNS and in 3 patients with medium/large vessel PACNS. For both items, no significant difference was found. For a detailed description, see Table 3.

Additionally, we compared findings in patients classified as medium vessel PACNS (n = 6) with patients classified as large vessel PACNS (n = 19). No significant differences were found for any of the investigated characteristics.

Temporal Evaluation of Disease Course

The mRS score at admission was available in 27 PACNS patients with 23 being re-evaluated at follow-up. Median follow-up duration was 13.8 months (range 0–9.9 years). At re-evaluation, grade of disability was low in 14 patients (mRS ≤2), whereas 9 patients suffered from severe neurologic deficits (mRS ≥3). In temporal evaluation, we found decreasing or stable symptoms in 15 patients. Grade of disability worsened in 8 patients. Three patients died during the disease course.

There was no significant difference in clinical outcome between patients with medium/large vessel PACNS and patients with small vessel PACNS.

Discussion

Clinical and neuroradiological findings in PACNS may be manifold and nonspecific, making a fast and definite diagnosis challenging. Since prevalence of PACNS is low and only little data have been published about neuroradiologic findings, a detailed description of its characteristics in neuroimaging is needed. We could not describe one uniform lesion pattern of CNS vasculitis. Instead, we classified our

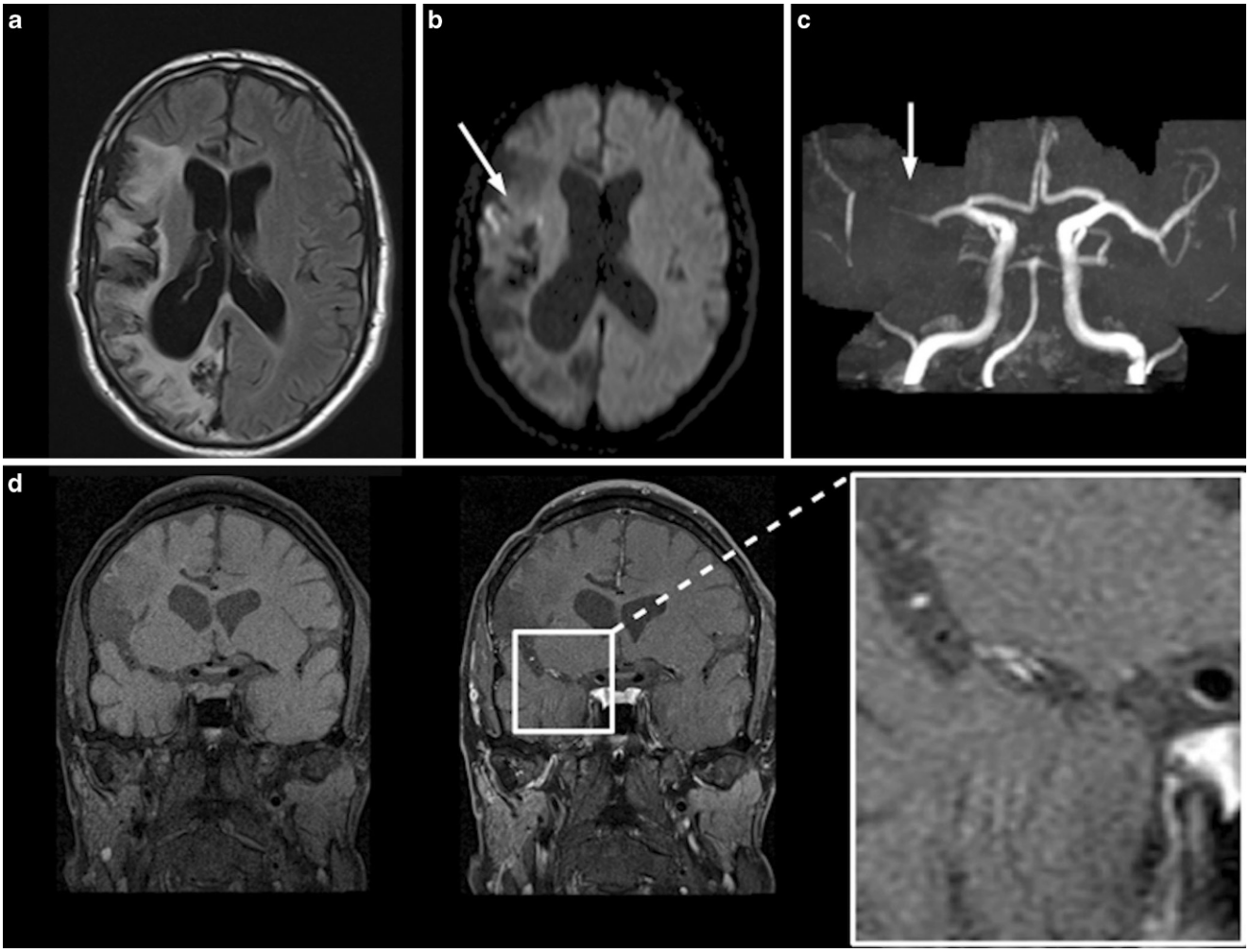

Fig. 1 Typical signs in medium and large vessel primary angiitis of the central nervous system in a patient with advanced course of disease. Hyperintensities on fluid attenuated inversion recovery (**a**) in the right middle and posterior cerebral artery region indicate old ischemic lesions with subacute ischemic areals (diffusion-weighted imaging: **b**, *white arrow*). Three-dimensional time of flight MR angiography (**c**) demonstrates occlusion of the right middle cerebral artery with corresponding vessel wall enhancement (**d**)

study cohort into two subgroups depending on angiographic findings, as supposed by former studies [6–12], and tried to identify specific lesion patterns.

Large and medium vessel PACNS were associated with positive angiographic findings like stenosis of the proximal arteries and VWE and, subsequently, ischemic lesions, which were not detectable in patients with small PACNS ($p < 0.001$) (see Figs. 1 and 2). We could not find significant differences for intracerebral hemorrhages, CE lesions, and lesions with mass effect, though there seemed to be a trend for CE lesions and lesions with mass effect to be more frequent in small PACNS ($p = 0.098$; $p = 0.078$) (see Figs. 3 and 4). By review of the literature, there are two large recent cohort studies, namely the French COVAC and the Mayo Clinic cohort, that aimed to describe image findings of PACNS patients [16, 17]. Our results confirm the findings of both cohort studies with higher rates of ischemic lesions and VWE in large and medium vessel PACNS, while hemorrhages and CE lesions were found increased in small PACNS. However, there is discrepancy between the two studies and our results concerning the occurrence frequency of image findings. The published incidences of ischemic infarcts vary between 54 and 85% (our results: 58%). Mass lesions were described in 5–15% (15%) and vascular pathologies in 40–90% (67%). Differences between the results may be caused by selection of patients and technical standards, since a shorter time of data collection implicates higher consistency in MR protocols and image evaluation.

By identifying specific combinations of lesion patterns, a more defined diagnosis could be established and unnecessary diagnostic procedures could be avoided. According to current guidelines, brain biopsy is still the gold standard for precise diagnosis of CNS vasculitis [14]. How-

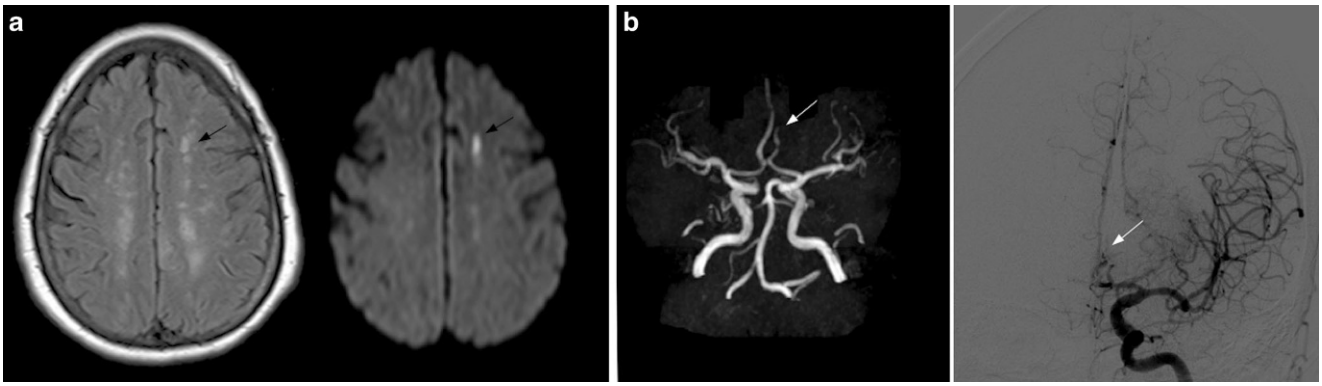

Fig. 2 Subacute, hemodynamic ischemic lesion in the right fontal deep white matter (fluid attenuated inversion recovery and diffusion-weighted imaging: **a**, *black arrow*); three dimensional time of flight MR and digital subtraction angiography reveal occlusion of the anterior cerebral artery (**b**, *white arrows*)

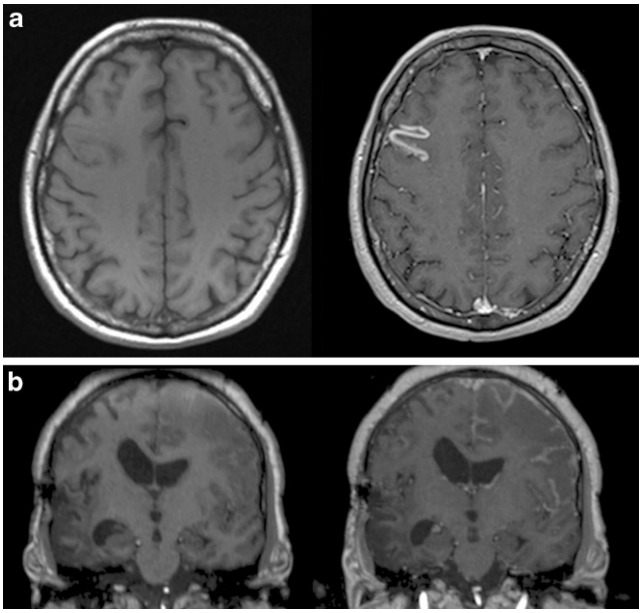

Fig. 3 Pre- and post-gadolinium T1 sequences demonstrate parenchymal (cortical) (**a**) and leptomeningeal enhancement (**b**)

ever, it is the topic of critical debate, since brain biopsy includes certain risks coupled with poor diagnostic yield [6, 18]. In our cohort, in only 9 of 18 patients with diagnosed large and medium vessel PACNS was the diagnosis confirmed by brain biopsy. Nevertheless, patients with negative biopsy were still diagnosed as PACNS according to current guidelines considering their clinical and neuroimaging presentation and benefit from treatment. Reviewing the literature, positive biopsies of patients with involvement of the medium or large intracranial vessels are infrequent and range between 4.9 and 26% [13, 16]. On the other hand, there is no doubt that in cases with suggestive but non-specific MRI and normal angiography, as in small PACNS, brain biopsy is necessary to confirm diagnosis and exclude other inflammatory or neoplastic processes. However, considering the low positive rates in patients with medium or large vessel PACNS, the diagnostic value of brain biopsies will be the focus of further critical debate.

Stenosis of intracranial arteries and beading are highly suggestive for PACNS [3, 7, 9, 15, 16]. Twelve patients of our study cohort underwent DSA with positive results in all but one. However, in 10 of these patients, stenosis or VWE were already detected by MRI/MRA at baseline or in the temporal course. DSA is still considered the diagnostic modality of choice in detecting vessel pathologies, but may lose influence in clinical practice due to improving MR image quality [19]. By applying higher field strengths, detection rates of stenosis can be increased, especially in more distal and small vessels [20]. Moreover, we suggest that in case of clear positive MR angiography, classic angiography will not provide additional diagnostic benefit but increase the risk of periinterventional complications.

In 84% (21/25) of patients with medium or large vessel PACNS, more than one intracranial stenosis was detected. Since the reversible cerebral vasoconstriction syndrome (RCVS) and atherosclerotic disease may also present multisegmental stenosis of the cerebral arteries, it is highly important to distinguish between these entities. VWE has recently been discussed as correlate for the inflammatory process and as possible vasculitis-specific feature in MR imaging [21–24]. Arterial wall thickening with concentric or eccentric enhancement is associated with PACNS, while these findings are absent or only moderately presented in RCVS [21, 22]. Atherosclerotic disease may also cause eccentric stenosis and show vessel wall enhancement of the intracranial arteries [23]. However, in atherosclerotic disease, vessel wall enhancement is generally weaker and does not compromise the whole vessel wall. Furthermore, contrast enhancement is commonly localized at the shoulder region of the atherosclerotic plaque [25]. Our major findings on VWE in PACNS are in accordance with earlier studies, though we found lower incidence of VWE [22].

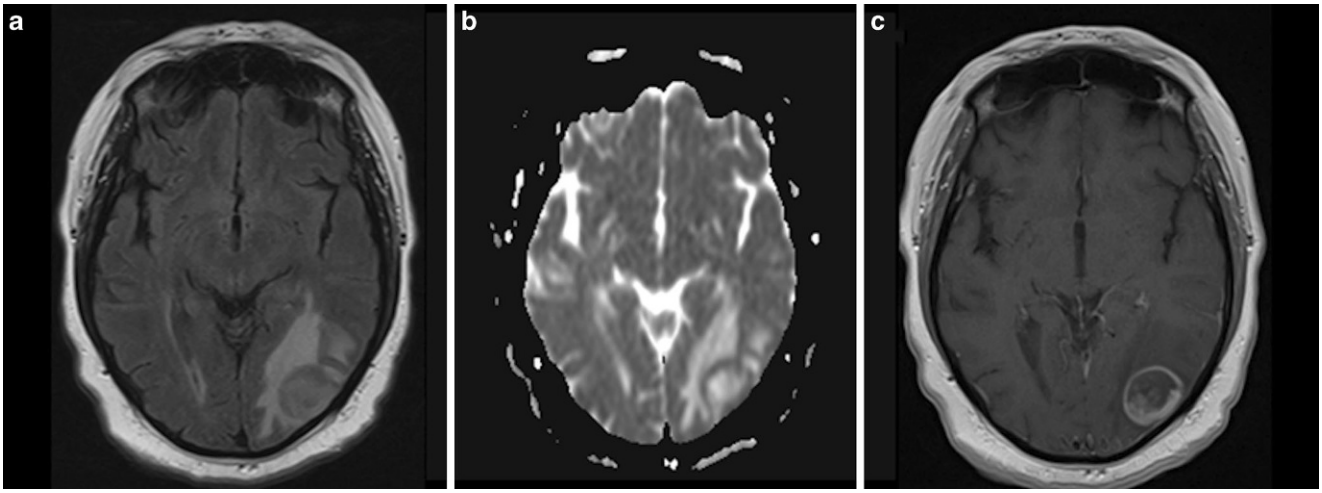

Fig. 4 Tumor-like mass lesion in the left occipital white matter with perifocal edema on fluid attenuated inversion recovery (**a**), peripheral diffusion limitation on apparent diffusion coefficient (**b**) and nodular and ringlike enhancement on post-gadolinium T1 image (**c**) in a patient with biopsy-proven primary angiitis of the central nervous system

Overall, VW imaging might provide further information in the diagnosis work-up, especially in distinguishing between PACNS and RCVS, but still lacks sensitivity in detecting vascular pathologies.

There are some limitations to our study. Data collection was performed retrospectively leading to varying MR imaging protocols. Therefore, four patients did not receive coronal T1w sequences to evaluate VWE. Furthermore, patients were scanned either on 1.5 T or 3 T MR scanners. Nevertheless, since imaging protocols were optimized for each scanner we assume comparability for all major findings. Compared to the French COVAC and the Mayo Clinic cohort study, a high percentage of our patients underwent brain biopsy in our cohort (76%; 25/33). In patients with missing or negative brain biopsy, PACNS was diagnosed clinically by highly experienced neurologists based on a number of clinical, imaging and laboratory findings. Therefore, all included patients were diagnosed very carefully and only clinically diagnosed patients with unambiguous findings were then included in this study.

In conclusion, it is essential to differentiate between small and medium/large vessel PACNS since results in MRI, DSA, and brain biopsy may differ immensely. Thus, clinical and diagnostic algorithms could be optimized and unnecessary diagnostic procedures could be displaced. Our results strongly support the findings of the French COVAC and the Mayo Clinic cohort study, emphasizing the importance of MRI/MRA in the diagnosis process of PACNS.

Conflict of interest C. Thaler, A.-K. Kaufmann-Bühler, T. Gansukh, A. Gansukh, S. Schuster, H. Bachmann, G. Thomalla, T. Magnus, J. Matschke, J. Fiehler and S. Siemonsen declare that they have no competing interests.

References

1. Calabrese LH, Mallek JA. Primary angiitis of the central nervous system. Report of 8 new cases, review of the literature, and proposal for diagnostic criteria. Medicine (Baltimore). 1988;67:20-39.
2. Hajj-Ali RA, Calabrese LH. Primary angiitis of the central nervous system. Autoimmun Rev. 2013;12:463–6.
3. Birnbaum J, Hellmann DB. Primary angiitis of the central nervous system. Arch Neurol. 2009;66:704–9.
4. Ay H, Sahin G, Saatci I, Söylemezoğlu F, Saribaş O. Primary angiitis of the central nervous system and silent cortical hemorrhages. AJNR Am J Neuroradiol. 2002;23:1561–3.
5. Kumar RS, Singh A, Rathore C, Kesavadas C. Primary angiitis of central nervous system: Tumor-like lesion. Neurol India. 2010;58:147–9.
6. Néel A, Pagnoux C. Primary angiitis of the central nervous system. Clin Exp Rheumatol. 2009;27(1 Suppl 52):95–107.
7. de Boysson H, Zuber M, Naggara O, Neau JP, Gray F, Bousser MG, Crassard I, Touzé E, Couraud PO, Kerschen P, Oppenheim C, Detante O, Faivre A, Gaillard N, Arquizan C, Bienvenu B, Néel A, Guillevin L, Pagnoux C; French Vasculitis Study Group and the French NeuroVascular Society. Primary angiitis of the central nervous system: Description of the first fifty-two adults enrolled in the french cohort of patients with primary vasculitis of the central nervous system. Arthritis Rheumatol. 2014;66:1315–26.
8. Küker W, Gaertner S, Nägele T, Dopfer C, Schoning M, Fiehler J, Rothwell PM, Herrlinger U. Vessel wall contrast enhancement: A diagnostic sign of cerebral vasculitis. Cerebrovasc Dis. 2008;26:23–9.
9. Salvarani C, Brown RD Jr, Hunder GG. Adult primary central nervous system vasculitis. Lancet. 2012;380(9843):767–77.
10. Salvarani C, Brown RD Jr, Christianson TJ, Huston J 3rd, Giannini C, Miller DV, Hunder GG. Adult primary central nervous system vasculitis treatment and course; analysis of one hundred sixty-three patients. Arthritis Rheumatol. 2015;67:1637–45.
11. Celluci T, Tyrrell PN, Sheikh S, Benseler SM. Childhood primary angiitis of the central nervous system: Identifying disease trajectories and early risk factors for persistently higher disease acitivity. Arthritis Rheumatol. 2012;64:1665–72.
12. Park MS, Marlin AE, Gaskill SJ. Angiography-negative primary angiitis of the central nervous system in childhood. J Neurosurg Pediatr. 2014;13:62–7.

13. Deutsche Gesellschaft für Neurologie (German Society of Neurology). S1 Leitlinie: Zerebrale Vaskulitis. 2012. https://www.dgn.org/leitlinien/2322-ll-30-2012-zerebrale-vaskulitis (Created 09.2012). Accessed 1 Jan 2017.
14. Salvarani C, Brown RD Jr, Christianson T, Miller DV, Giannini C, Huston J 3rd, Hunder GG. An update of the Mayo Clinic cohort of patients with adult primary central nervous system vasculitis: Description of 163 patients. Medicine (Baltimore). 2015;94(21):e738.
15. Küker W. Cerebral vasculitis: Imaging signs revisited. Neuroradiology. 2007;49:471–9.
16. Boulouis G, de Boysson H, Zuber M, Guillevin L, Meary E, Costalat V, Pagnoux C, Naggara O, French Vasculitis Group. Primary Angiitis of the central nervous system: Magnetic resonance imaging spectrum of Parenchymal, meningeal, and vascular lesions at baseline. Stroke. 2017;48(5):1248–55.
17. Torres J, Loomis C, Cucchiara B, Smith M, Messé S. Diagnostic yield and safety of brain biopsy for suspected primary central nervous system angiitis. Stroke. 2016;47:2127–9.
18. de Boysson H, Boulouis G, Aouba A, Bienvenu B, Guillevin L, Zuber M, Touzé E, Naggara O, Pagnoux C. Adult primary angiitis of the central nervous system: Isolated small-vasculitis represents distinct disease pattern. Rheumatology (Oxford). 2017;56(3):439–44.
19. Amlie-Lefond C. Catheter angiogram in central nervous system vasculitis: Still first among equals. Dev Med Child Neurol. 2010;52:792.
20. Cosottini M, Canovetti S, Pesaresi I, Desideri I, Pizzanelli C, Catarsi E, Puglioli M, Tavoni A, Bonuccelli U, Bartolozzi C. 3-T magnetic resonance angiography in primary angiitis of the central nervous system. J Comput Assist Tomogr. 2013;37(4):493–8.
21. Mandell DM, Matouk CC, Farb RI, Krings T, Agid R, terBrugge K, Willinsky RA, Swartz RH, Silver FL, Mikulis DJ. Vessel wall MRI to differentiate between reversible cerebral vasoconstriction syndrome and central nervous system vasculitis: Preliminary results. Stroke. 2012;43:860–2.
22. Obusez EC, Hui F, Hajj-Ali RA, Cerejo R, Calabrese LH, Hammad T, Jones SE. High-resolution MRI vessel wall imaging: Spatial and temporal patterns of reversible cerebral vasoconstriction syndrome and central nervous system Vasculitis. AJNR Am J Neuroradiol. 2014;35:1527–32.
23. Pfefferkorn T, Linn J, Habs M, Opherk C, Cyran C, Ottomeyer C, Straube A, Dichgans M, Nikolaou K, Saam T. Black blood MRI in suspected large artery primary Angiitis of the central nervous system. J Neuroimaging. 2013;23:379–83.
24. van der Kolk AG, Zwanenburg JJ, Brundel M, Biessels GJ, Visser F, Luijten PR, Hendrikse J. Intracranial vessel wall imaging at 7.0-T MRI. Stroke. 2011;42:2478–84.
25. Saam T, Hatsukami TS, Takaya N, Chu B, Underhill H, Kerwin WS, Cai J, Ferguson MS, Yuan C. The vulnerable, or high-risk, atherosclerotic plaque: Noninvasive MR imaging for characterization and assessment. Radiology. 2007;244:64–77.