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ACIDENTES VASCULARES CEREBRAIS ISQUÊMICOS RECORRENTES MÚLTIPLOS COMO MANIFESTAÇÃO INICIAL DE PROVÁVEL ANGIITE PRIMÁRIA DO SISTEMA NERVOSO CENTRAL: UM RELATO DE CASO EM CONFORMIDADE COM O PROTOCOLO CARE

MULTIPLE RECURRENT ISCHEMIC STROKES AS THE INITIAL MANIFESTATION OF PROBABLE PRIMARY ANGIITIS OF THE CENTRAL NERVOUS SYSTEM: A CARE-COMPLIANT CASE REPORT

ACCIDENTES CEREBROVASCULARES ISQUÉMICOS RECURRENTES MÚLTIPLES COMO MANIFESTACIÓN INICIAL DE PROBABLE ANGIÍTIS PRIMARIA DEL SISTEMA NERVIOSO CENTRAL: UN INFORME DE CASO CONFORME A LAS DIRECTRICES CARE

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Resumo

Contexto: A angiite primária do sistema nervoso central (APSN) é uma doença inflamatória rara com

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manifestações clínicas inespecíficas e desafios diagnósticos significativos. **Apresentação do caso**: Relatamos o caso de um homem de 57 anos, previamente saudável, que apresentou múltiplos acidentes vasculares cerebrais isquêmicos recorrentes em um curto período, apesar da terapia antiplaquetária adequada. Os exames de imagem convencionais foram inconclusivos. A neuroimagem avançada com imagem da parede vascular demonstrou realce concêntrico da parede arterial, sugestivo de vasculite. O líquido cefalorraquidiano e diversos exames laboratoriais não apresentaram alterações. A biópsia cerebral revelou alterações inflamatórias sem vasculite granulomatosa definitiva. O diagnóstico de APSN provável foi estabelecido com base na correlação clínico-radiológica e na exclusão de causas secundárias. **Intervenção e desfecho**: O paciente foi tratado com altas doses de corticosteroides, seguidas de ciclofosfamida, evoluindo com melhora clínica, estabilização radiológica e recuperação funcional. **Conclusão**: Este caso destaca a importância de considerar a APSN em pacientes com acidentes vasculares cerebrais recorrentes sem causa aparente e ressalta o papel da neuroimagem avançada e da avaliação multidisciplinar.
Palavras-chave: Angiíte primária do sistema nervoso central; Vasculite do sistema nervoso central; Acidente vascular cerebral isquêmico; Neuroimagem avançada; Estudo da parede vascular.

Abstract

Background: Primary angiitis of the central nervous system (PACNS) is a rare inflammatory disorder with nonspecific clinical manifestations and significant diagnostic challenges. **Case presentation:** We report a 57-year-old previously healthy man presenting with multiple recurrent ischemic strokes over a short period despite adequate antiplatelet therapy. Conventional imaging was inconclusive. Advanced neuroimaging with vessel wall imaging demonstrated concentric arterial wall enhancement suggestive of vasculitis. Cerebrospinal fluid and extensive laboratory tests were unremarkable. Brain biopsy revealed inflammatory changes without definitive granulomatous vasculitis. The diagnosis of probable PACNS was established based on clinicoradiological correlation and exclusion of secondary causes. **Intervention and outcome:** The patient was treated with high-dose corticosteroids followed by cyclophosphamide, evolving with clinical improvement, radiological stabilization, and functional recovery. **Conclusion:** This case highlights the importance of considering PACNS in patients with recurrent unexplained strokes and underscores the role of advanced imaging and multidisciplinary evaluation.

Keywords: Primary Angiitis of the Central Nervous System; Central Nervous System Vasculitis; Ischemic Stroke; Advanced Neuroimaging; Vessel Wall Imaging.

Resumen

Antecedentes: La angiítis primaria del sistema nervioso central (PACNS) es un trastorno inflamatorio poco frecuente con manifestaciones clínicas inespecíficas y desafíos diagnósticos significativos.

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Presentación del caso: Presentamos el caso de un hombre de 57 años, previamente sano, que presentó múltiples accidentes cerebrovasculares isquémicos recurrentes en un corto período a pesar de un tratamiento antiplaquetario adecuado. Las imágenes convencionales no fueron concluyentes. Las neuroimágenes avanzadas con imágenes de la pared vascular demostraron un realce concéntrico de la pared arterial sugestivo de vasculitis. El líquido cefalorraquídeo y las pruebas de laboratorio extensas no mostraron alteraciones. La biopsia cerebral reveló cambios inflamatorios sin vasculitis granulomatosa definitiva. El diagnóstico de probable PACNS se estableció con base en la correlación clínico-radiológica y la exclusión de causas secundarias. **Intervención y resultado**: El paciente fue tratado con corticosteroides en dosis altas seguidos de ciclofosfamida, evolucionando con mejoría clínica, estabilización radiológica y recuperación funcional. **Conclusión:** Este caso resalta la importancia de considerar la PACNS en pacientes con accidentes cerebrovasculares recurrentes inexplicables y subraya el papel de las imágenes avanzadas y la evaluación multidisciplinaria.
Palabras clave: Angiitis primaria del sistema nervioso central; Vasculitis del sistema nervioso central; Accidente cerebrovascular isquémico; Neuroimagen avanzada; Imagen de la pared vascular.

1. Introducion

Primary angiitis of the central nervous system (PACNS) is a rare, noninfectious inflammatory vasculitis restricted to small- and medium-sized vessels of the brain and spinal cord, without evidence of systemic involvement (KRAWCZYK et al., 2021). Its estimated incidence is approximately 2.4 cases per million inhabitants per year, making it an entity that remains unfamiliar even to experienced neurologists and general clinicians. Despite its low prevalence, PACNS is associated with substantial morbidity and potential mortality when diagnosis and treatment are delayed (SALVARANI et al., 2007).

The principal challenge in PACNS lies in its heterogeneous and nonspecific clinical presentation. Initial symptoms frequently mimic far more prevalent neurological conditions, such as atherothrombotic or cardioembolic ischemic stroke and transient ischemic attacks (TIA). Headache, focal neurological deficits, cognitive impairment, and seizures may occur in isolation or combination, without a pathognomonic clinical pattern. This “kaleidoscopic” presentation contributes to diagnostic delays, inappropriate therapeutic approaches, and progression of neurological damage (AGARWAL et al., 2022; BEUKER et al., 2021).

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Initial complementary investigations, including computed tomography and conventional magnetic resonance imaging, often reveal only nonspecific findings, such as areas of gliosis, microangiopathy, or infarcts at different stages of evolution. Similarly, systemic laboratory tests may remain unremarkable, further complicating the distinction between PACNS and other causes of recurrent ischemic stroke (EKKERT; ŠAULYTĖ; JATUŽIS, 2022). In this context, patients presenting with multiple cerebral ischemic events over a short period, particularly in the absence of classical vascular risk factors or despite adequate antiplatelet therapy, should raise suspicion for less common etiologies, including vasculitides of the central nervous system (HECKER et al., 2022; RESCH; OVSIEW; SOBLE, 2022; SARTI et al., 2020).

Recent advances in neuroimaging techniques, such as magnetic resonance vessel wall imaging (VWI, “black-blood vessel wall imaging”), have expanded diagnostic capabilities by allowing direct visualization of inflammatory vessel wall thickening and enhancement (EKKERT; ŠAULYTĖ; JATUŽIS, 2022). Nevertheless, even with these tools, definitive diagnosis of PACNS frequently requires an integrated approach combining clinical, radiological, and laboratory data and, in selected cases, histopathological confirmation through brain biopsy.

Given this scenario, case reports remain essential to enhance recognition of PACNS, highlight clinical red flags, and illustrate the role of advanced diagnostic strategies. In this study, we describe a rare case of a patient with multiple recurrent ischemic strokes as the initial manifestation of PACNS, emphasizing the diagnostic challenges, the contribution of advanced neuroimaging, and the importance of early clinical suspicion for appropriate disease management.

2. Case Report

The study protocol was approved by the Ethics Committee of the Federal University of Mato Grosso do Sul (UFMS) under CAAE number 68676923.9.0000.0021.

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2.1 Patient Information

A 57-year-old Brazilian man with no previous comorbidities presented with recurrent neurological deficits characterized by ischemic cerebrovascular events over a short period.

2.2 Clinical Findings

Initial symptoms included left hemiparesis and paresthesia. Over subsequent months, the patient developed recurrent episodes involving paraparesis, sensory deficits, and transient sphincter dysfunction. Episodes of mental confusion appeared later in the disease course.

2.3 Timeline

Table 1 – Clinical timeline

Date	Event
Jun 2021	First ischemic stroke (left hemiparesis)
Sep 2021	New episode – suspected TIA
Oct 2021	Recurrent paraparesis
Nov 2021	MRI: nonspecific ischemic changes
Nov 25 2021	Confusional episode
Dec 01 2021	Advanced MRI with vessel wall imaging
Dec 2021	Brain biopsy
Dec 2021	Start immunosuppressive therapy
Jan 2022	Radiological improvement
Aug 2022	New ischemic event
Follow-up	Clinical stabilization

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2.4 Diagnostic Assessment

Laboratory Investigations:

CSF analysis demonstrated normal cell count, protein and glucose levels.

- ESR and CRP: were within normal reference ranges
- ANA: negative
- ANCA: negative
- Infectious serologies: negative

Cerebrospinal Fluid:

- Analysis demonstrated normal cell count, protein and glucose levels.
- Oligoclonal bands: negative

  All findings within normal reference ranges.

Neuroimaging

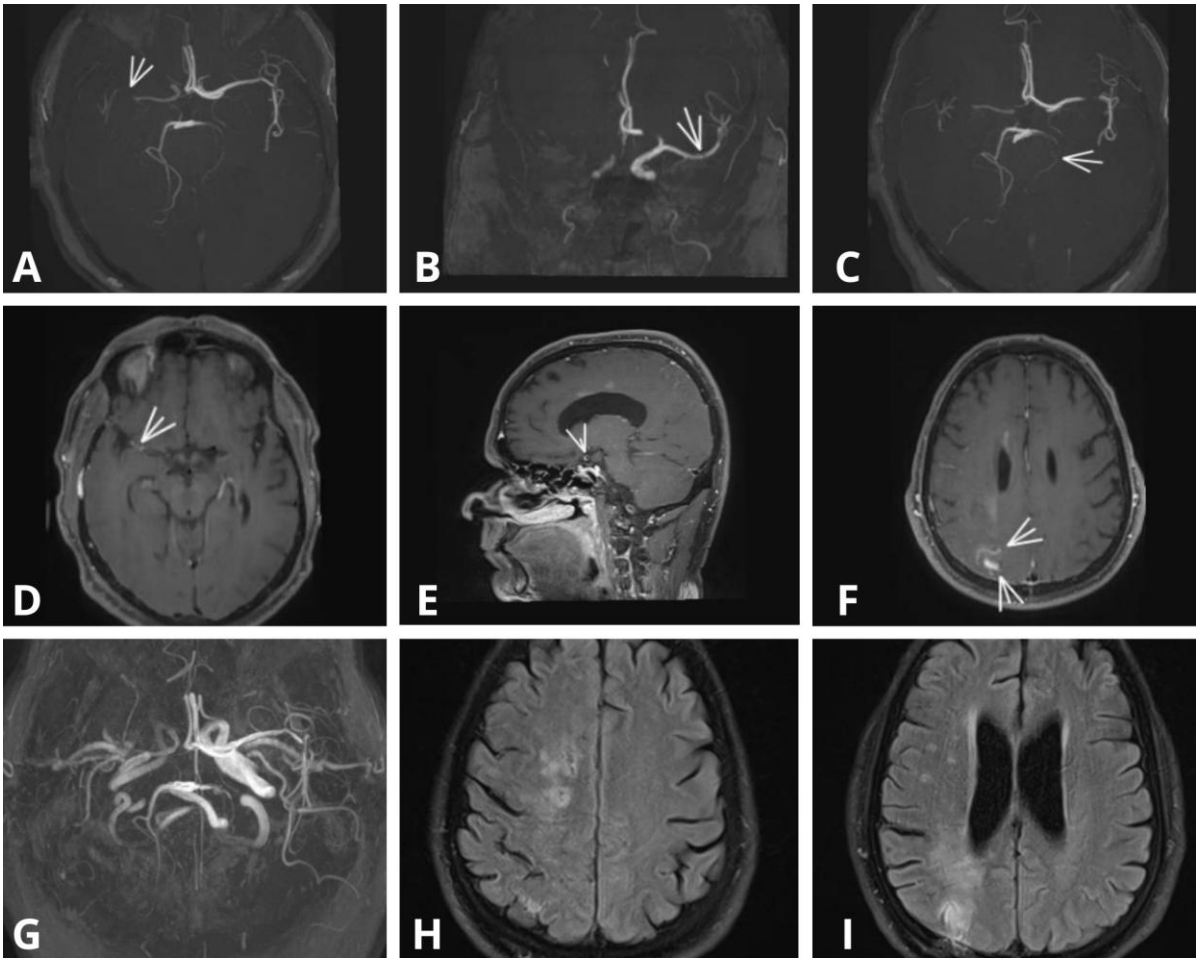
Conventional MRI demonstrated nonspecific white matter changes. Advanced MRI with vessel wall imaging revealed, as shown in figure 1A (arrow)**:**

- arterial narrowing
- concentric vessel wall enhancement
- perivascular contrast enhancement

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Figure 1 – Brain magnetic resonance imaging (MRI) with intracranial magnetic resonance angiography and vessel wall imaging (VWI).



Caption: Images A–C (baseline study, December 1, 2021) demonstrate: (A) marked luminal narrowing of the mid-to-distal M1 segment of the right middle cerebral artery, associated with concentric vessel wall enhancement (arrow), a pattern suggestive of inflammatory vasculitis; (B) irregular narrowing of the left middle cerebral artery (arrowhead); (C) focal stenosis of the left posterior cerebral artery (arrow). Images D–F show areas of perivascular and leptomeningeal contrast enhancement (arrows), predominantly in the right parietal lobe, indicative of blood–brain barrier disruption and active inflammatory process. Images G–I (follow-up study, January 13, 2022) demonstrate: (G) persistent narrowing of the right M1 segment (arrow); (H) evolution of ischemic lesions to the subacute phase, with reduced diffusion restriction; (I)

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marked reduction in perivascular contrast enhancement (arrow), indicating partial therapeutic response.

No new ischemic lesions were identified during the interval.

Differential Diagnosis

Table 2 – Differential diagnoses

Diagnosis	Supporting features	Arguments against
Atherosclerosis	Carotid plaques	No significant stenosis; rapid recurrence
RCVS	Recurrent deficits	No thunderclap headache; enhancement present
Dissection	Focal stenosis	No wall hematoma
Infectious vasculitis	CNS involvement	Negative CSF/serologies
Secondary vasculitis	Inflammation	No systemic disease
PACNS	VWI pattern	Most consistent

Brain Biopsy

A stereotactic biopsy of the right parietal lobe was performed during hospitalization without complications. Histopathological examination revealed cerebral parenchyma with findings consistent with organizing ischemic injury, characterized by neuronal loss, reactive gliosis, and areas of neovascularization, as shown in figure 2 and Table 3.

An inflammatory infiltrate was observed, predominantly composed of macrophages, along with scattered lymphocytes. Vessels exhibited endothelial prominence; however, no unequivocal evidence of granulomatous or necrotizing vasculitis was identified. Additionally, no neoplastic features were observed.

Immunohistochemical analysis further characterized the inflammatory profile, demonstrating:

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- CD163 positivity, confirming a macrophage-rich infiltrate;
- presence of T lymphocytes (CD3 positive);
- absence of B lymphocyte predominance (CD20 negative);
- low proliferative index (Ki-67 approximately 5%), arguing against a neoplastic process.

Markers associated with alternative diagnoses were negative, including IDH-1 (excluding glioma), β-amyloid (arguing against amyloid angiopathy), and infectious markers (including HSV-1/2, CMV, and fungal stains), effectively excluding infectious and neoplastic etiologies.

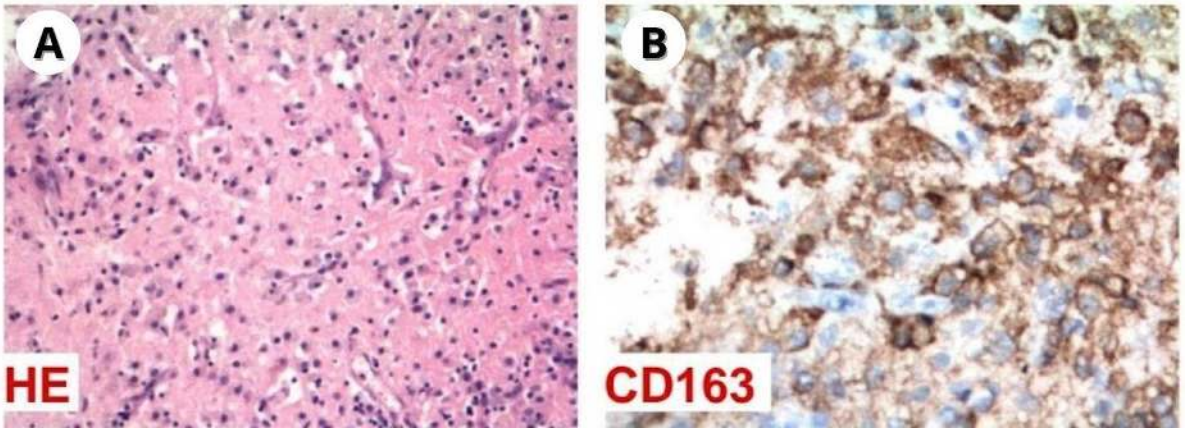
Overall, the histopathological and immunohistochemical findings support an inflammatory, non-neoplastic, and non-infectious process, compatible with ischemic injury in an inflammatory context. Importantly, the absence of definitive granulomatous vasculitis does not exclude primary angiitis of the central nervous system (PACNS). This limitation is well recognized and is attributed to the segmental and patchy distribution of the disease, particularly in cases involving medium- and large-caliber vessels. Thus, when interpreted in conjunction with the clinical presentation and advanced neuroimaging findings—especially the presence of concentric vessel wall enhancement—the results were considered supportive of a diagnosis of probable PACNS, based on clinicoradiological correlation and systematic exclusion of secondary causes.

These histopathological findings, although not definitive in isolation, were crucial when integrated with clinical and radiological data to support the diagnosis.

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Figure 2 – Histopathological and immunohistochemical findings from right parietal lobe brain biopsy.



Caption: (A) Hematoxylin and eosin (H&E) staining showing cortical parenchyma with features of organizing ischemic injury, including neuronal loss, reactive gliosis, and inflammatory infiltrate (arrow). No evidence of neoplasia is observed. (B) Immunohistochemistry for CD163 demonstrating a macrophage-rich inflammatory infiltrate (arrows), consistent with an active inflammatory process. Additional immunohistochemical analysis revealed: presence of T lymphocytes (CD3 positive); absence of B lymphocytes (CD20 negative); low proliferative index (Ki-67 ≈ 5%)

No definitive features of granulomatous vasculitis were identified. Findings are consistent with an inflammatory process associated with ischemic injury, requiring clinicoradiological correlation for diagnosis. The absence of unequivocal granulomatous vasculitis does not exclude PACNS due to the segmental nature of the disease.

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Table 3 – Immunohistochemical findings of brain biopsy and diagnostic interpretation

Marker	Result	Interpretation
CD163	Positive	Macrophage-rich inflammatory infiltrate
CD3	Positive	Presence of T lymphocytes
CD20	Negative	Absence of B lymphocyte predominance
Ki-67	~5%	Low proliferative index; argues against neoplasia
GFAP	Positive	Reactive gliosis
OLIG2	Positive	Glial cell involvement
IDH-1	Negative	No evidence of glioma
β-amyloid	Negative	Excludes amyloid angiopathy
SV-40	Negative	No viral infection
HSV-1/2, CMV	Negative	No neurotropic infection
PAS	Negative	No fungal infection

These findings support an inflammatory, non-neoplastic, and non-infectious process, reinforcing the diagnosis of probable PACNS.

2.5 Therapeutic Intervention

Cyclophosphamide was administered as monthly intravenous pulses (1 g per cycle), with cumulative dose monitoring and regular hematological, renal, and hepatic surveillance.

- Methylprednisolone: 1 g/day for 5 days
- Cyclophosphamide: 1 g per pulse
- Planned monthly cycles
- Supportive rehabilitation (physiotherapy and occupational therapy)
- 12

2.6 Follow-up and Outcomes

- Clinical improvement

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- Radiological stabilization
- Return to daily activities

Functional scales were not systematically applied, representing a limitation.

3. Discussion

Primary angiitis of the central nervous system (PACNS) is characterized by a heterogeneous and often nonspecific clinical presentation, which frequently leads to delayed diagnosis and inappropriate initial management (AGARWAL et al., 2022; BEUKER et al., 2021). In the present case, the patient experienced multiple recurrent ischemic events over a short period despite appropriate antiplatelet therapy, a pattern that should raise suspicion for uncommon etiologies, including inflammatory vasculitides of the central nervous system.

The most reported clinical features include focal neurological deficits, headache, nausea, and vomiting, while seizures may occur in up to 70% of cases (EKKERT; ŠAULYTĖ; JATUŽIS, 2022). This clinical nonspecificity represents one of the major challenges in the early recognition of probable PACNS and management, the disease. In the present case, the patient initially presented with sudden-onset paresis and paresthesia and was treated as an isolated ischemic cerebrovascular event. The recurrence of symptoms within the same year led to the consideration of transient ischemic attack, delaying the recognition of an underlying inflammatory etiology.

The disease exhibits a segmental and patchy distribution, which significantly reduces the sensitivity of the procedure, particularly in cases involving medium- and large-caliber vessels. Consequently, negative or nonspecific histopathological findings do not exclude the diagnosis. In this case, the integration of histopathological findings with advanced neuroimaging was crucial. While the biopsy did not provide definitive confirmation, it effectively excluded alternative diagnoses, such as neoplastic, infectious, and amyloid-related processes. This exclusionary value, combined with the highly suggestive VWI pattern and the clinical course marked by

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recurrent ischemic events, supported the diagnosis of probable PACNS based on clinicoradiological correlation.

This integrative diagnostic approach aligns with contemporary recommendations, which emphasize that PACNS diagnosis should not rely solely on a single modality but rather on a combination of clinical presentation, imaging findings, laboratory exclusion of secondary causes, and, when available, histopathological data.

Another important aspect illustrated by this case is the role of immunosuppressive therapy. The patient demonstrated a favorable clinical and radiological response to high-dose corticosteroids followed by cyclophosphamide, with reduction of vessel wall enhancement on follow-up imaging and stabilization of neurological deficits. These findings further support the inflammatory nature of the disease process and highlight the potential reversibility of vascular changes when treated early.

In this context, advanced neuroimaging plays a pivotal role. In our case, vessel wall imaging (VWI) demonstrated concentric arterial wall enhancement, a finding that strongly favors an inflammatory vasculitic process. This pattern contrasts with eccentric enhancement typically seen in atherosclerosis, the absence of enhancement in RCVS, and the intramural hematoma pattern characteristic of arterial dissection, highlighting the diagnostic relevance of this modality. Despite the growing importance of neuroimaging, histopathological analysis remains traditionally regarded as the reference standard for diagnosing PACNS. In the present case, brain biopsy revealed findings consistent with organizing ischemic injury associated with a macrophage-rich inflammatory infiltrate, without evidence of neoplasia or infection. However, no unequivocal granulomatous vasculitis was identified. This finding underscores a well-recognized limitation of brain biopsy in PACNS (EKKERT; ŠAULYTĖ; JATUŽIS, 2022). Neuropsychiatric disturbances such as a mental confusion, anxiety, depression, and personality changes have also been reported with relative frequency (HECKER et al., 2022; SARTI et al., 2020). In the present case, episodes of mental confusion emerged approximately five months after

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symptom onset, reinforcing the multifoc al and progressive nature of cerebral involvement, a pattern consistent with inflammatory vascular processes affecting the central nervous system.

Clinical presentations of PACNS also vary according to the caliber of the affected vessels. Predominant small-vessel involvement is more commonly associated with seizures, cognitive impairment, and movement disorders, whereas involvement of médium - and large-sized- caliber vessels tends to manifest as focal neurological deficits and recurrent ischemic events. The clinical course observed in this patient, marked by multiple ischemic episodes and recurrent focal deficits, suggests predominant involvement of medium- and large-sized vessels, a finding later corroborated by vessel wall neuroimaging studies (EKKERT; ŠAULYTĖ; JATUŽIS, 2022)

The classical diagnostic criteria proposed by Calabrese e Mallek (1988) establish that the diagnosis of primary angiitis of the central nervous system should be based on the presence of acquired neurological deficits associated with angiographic and/or histopathological evidence of vascular inflammation, in the absence of systemic or secondary causes. In this context, the diagnosis in the present case was achieved through integration of clinical data, neuroimaging findings, and histopathological analysis, requiring extensive investigation at a specialized center and careful exclusion of alternative diagnoses.

More recent diagnostic algorithms emphasize the central role of neuroimaging as one of the main pillars for confirming PACNS, as well as its utility in monitoring disease activity and progression (SARTI et al., 2020). In the present case, the initial investigations performed at the patient's place of residence, including computed tomography and non-contrast brain magnetic resonance imaging, revealed only nonspecific findings such as white matter hyperintensities and cortical atrophy. These abnormalities are commonly associated with chronic microangiopathy and, when considered in isolation, do not allow a diagnosis of central nervous system vasculitis.

Vessel wall imaging demonstrated concentric enhancement, a pattern that favors inflammatory vasculitis over: atherosclerosis (eccentric enhancement),

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reversible cerebral vasoconstriction syndrome (absence of enhancement), arterial dissection (intramural hematoma pattern). Although digital subtraction cerebral angiography has traditionally been considered the reference standard for the evaluation of central nervous system vasculitis, its sensitivity is limited, particularly in small-vessel forms, and may be reduced in the absence of significant luminal stenosis. Contrast-enhanced magnetic resonance imaging may demonstrate multiple ischemic lesions and areas of enhancement; however, it also lacks specificity (RICE; SCOLDING, 2020). In this context, the use of advanced neuroimaging techniques, such as vessel wall magnetic resonance imaging (vessel wall imaging – Black Blood), represents a relevant diagnostic advance (RESCH; OVSIEW; SOBLE, 2022). In the present case, this method revealed arterial narrowing associated with concentric vessel wall enhancement and a perivascular enhancement pattern, as well as areas of diffusion restriction compatible with subacute ischemic events. These findings were strongly suggestive of active inflammatory vascular disease and proved decisive for establishing the diagnosis.

The neuroimaging findings observed in this case are also consistent with those reported in published PACNS case series. Previous studies have shown that brain MRI frequently reveals bilateral lesions, predominantly involving the frontal lobes (up to 100% of patients), parietal lobes (approximately 55.6%), and subcortical white matter (66.7%), in addition to signs of cortical atrophy and ventricular enlargement (WANG et al., 2019). Such alterations reflect chronic and recurrent vascular injury, consistent with persistent inflammatory processes. Similarly, the patient described here already demonstrated areas of atrophy and ventricular enlargement on the earliest neuroimaging studies, suggesting a previously subclinical disease course.

In recent years, advances in neuroimaging techniques have further expanded diagnostic capabilities in PACNS. Vessel wall magnetic resonance imaging allows the identification of arterial wall thickening and concentric enhancement, as well as perivascular enhancement and edema—features that favor an inflammatory vasculitis process over atherosclerotic or embolic etiologies (ARNETT et al., 2021). Additional methods, such as ^18F-choline PET/MRI, have been investigated as complementary

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noninvasive diagnostic tools, although their availability remains limited and their role is still being established (ABOUZIED et al., 2021).

The present case clearly illustrates the nonspecific and insidious presentation of PACNS, characterized by multiple recurrent ischemic events over a short period of time despite appropriate antiplatelet therapy. The absence of systemic manifestations or striking neurological features contributed to the initial consideration of more common differential diagnoses, such as transient ischemic attack, representing an additional obstacle to early disease recognition (SARTI et al., 2020).

Another essential component in the diagnosis of PACNS is the careful exclusion of systemic vasculitis and secondary causes, as emphasized both in the criteria proposed by Calabrese e Mallek (1988) and in more recent diagnostic algorithms (SARTI et al., 2020). In the present case, systemic laboratory investigations, including inflammatory and autoimmune markers, did not reveal significant abnormalities, nor did cerebrospinal fluid analysis—findings that are not uncommon in this condition. It is important to emphasize the role of inflammatory and rheumatologic laboratory testing in excluding systemic vasculitis, including the assessment of antineutrophil cytoplasmic antibodies (ANCA), HLA-B51, and rheumatoid factor.

Although cerebrospinal fluid findings may be normal in a subset of patients, studies have shown that abnormalities such as mild lymphocytic pleocytosis and elevated protein levels may be present and can play an auxiliary role in the diagnostic process (JUNEK et al., 2023; STRUNK et al., 2019). Additional biomarkers, including beta-amyloid protein and neurofilament light chains, have been investigated as potential indicators of axonal damage and disease activity, representing promising perspectives for improving the diagnosis and longitudinal monitoring of PACNS in the future (PAWLITZKI et al., 2019; STRUNK et al., 2019).

Brain biopsy has limited sensitivity, particularly in medium- and large-vessel disease, and negative or nonspecific findings do not exclude PACNS. Studies indicate that diagnostic yield may reach up to 100% in predominant small-vessel forms, whereas in patients with medium- and large-vessel involvement, accuracy is

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lower, approximately 57%, reflecting the segmental nature of the disease [23]. In addition, biopsy yield is strongly dependent on the sampled region, surgical technique, and the stage of disease evolution (EKKERT; ŠAULYTĖ; JATUŽIS, 2022).

In the present case, histopathological analysis of brain tissue demonstrated the absence of neoplasia and findings consistent with a cerebral infarct in the organizing phase, with neuronal loss and a predominantly macrophage-rich inflammatory infiltrate. Immunohistochemical analysis showed negativity for beta-amyloid and a low proliferative index, arguing against differential diagnoses such as inflammatory amyloid angiopathy and primary central nervous system neoplasms (PAWLITZKI et a, 2019). Although unequivocal granulomatous vasculitis was not identified, the histological findings, when interpreted in conjunction with the clinical presentation and neuroimaging results, were considered compatible with PACNS, underscoring the importance of clinic-radiological correlation in the diagnosis of this entity (EKKERT; ŠAULYTĖ; JATUŽIS, 2022).

Despite being considered the most specific diagnostic test for confirmation, brain biopsy is an invasive procedure and is not without risk, including bleeding, infection, and neurological deficits, although such complications occur in a minority of cases. In the patient described, the procedure was performed without complications, allowing acquisition of relevant diagnostic information without additional clinical harm.

Immunosuppressive therapy plays a fundamental role in PACNS, reducing inflammatory activity, preventing new ischemic events, and preserving functional capacity. The patient demonstrated favorable clinical and radiological response to pulse therapy with methylprednisolone followed by cyclophosphamide, in accordance with recommended treatment regimens for moderate to severe forms of the disease (EKKERT; ŠAULYTĖ; JATUŽIS, 2022). In addition, multidisciplinary support, including motor physiotherapy and occupational therapy, was essential for functional and cognitive recovery, enabling reintegration into daily activities (AGARWAL et al., 2022; HECKER et al., 2022).

Other therapeutic strategies may be employed for maintenance of remission or in cases of intolerance or refractoriness, including azathioprine, mycophenolate

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mofetil, methotrexate, and rituximab (AGARWAL et al., 2022; HECKER et al., 2022). During the use of cytotoxic agents such as cyclophosphamide, strict monitoring of renal and hepatic function, as well as potential systemic adverse effects, is imperative.

Three-dimensional vessel wall magnetic resonance imaging represents a valuable tool in the longitudinal follow-up of PACNS, allowing assessment of treatment response and residual inflammatory activity (WANG et al., 2019). Despite therapeutic advances, long-term follow-up studies continue to report mortality rates ranging from 11% to 28%, associated with significant morbidity, highlighting the potential severity of the disease (JUNEK et al., 2023).

In the present case, early initiation of immunosuppressive therapy following diagnostic confirmation resulted in sustained clinical stabilization, absence of new ischemic events, and significant functional recovery. Although PACNS is a rare condition, it should be considered in patients with recurrent cerebrovascular events, unexplained focal neurological deficits, and atypical neuroimaging findings. The dissemination of well-documented case reports contributes to increased disease recognition and improved clinical management of a potentially disabling yet treatable condition when diagnosed in a timely manner.

Nevertheless, this case also presents important limitations. The lack of definitive histopathological confirmation represents a diagnostic constraint, although consistent with real-world scenarios in PACNS. Additionally, formal functional and cognitive outcome scales were not systematically applied, limiting objective assessment of recovery.

Despite these limitations, this report emphasizes several key points:
(1) the importance of considering PACNS in cases of recurrent unexplained strokes;
(2) the diagnostic value of vessel wall imaging in identifying inflammatory vascular patterns;
(3) the complementary, rather than definitive, role of brain biopsy; and

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(4) the necessity of an integrated clinicoradiological approach for accurate diagnosis and management.

4. Conclusion

Primary angiitis of the central nervous system remains a significant diagnostic challenge due to its heterogeneous clinical presentation, lack of specific biomarkers, and frequent overlap with more common cerebrovascular conditions. This case highlights the importance of maintaining a high level of diagnostic suspicion in patients with recurrent ischemic strokes and atypical neuroimaging findings, particularly when conventional antithrombotic strategies fail to prevent disease progression.

The integration of clinical data, advanced neuroimaging with vessel wall assessment, and histopathological analysis, even in the absence of unequivocal classical vasculitis, was crucial for establishing the diagnosis and initiating appropriate treatment. Early recognition of PACNS and management in specialized centers can have a decisive impact on prognosis by reducing morbidity, preventing further ischemic events, and enabling meaningful functional recovery. The dissemination of well-characterized cases contributes to increased awareness of this rare but potentially treatable condition and reinforces the central role of clinic-radiological correlation in its management.

5. Patient Perspective

The patient reported significant improvement in quality of life after treatment and expressed satisfaction with recovery and return to normal activities.

6. Informed Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

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