Diagnostic and therapeutic challenges of isolated spinal vasculitis: A case report

YAJUN YAO[1], GE-HONG DONG[2] and DE-CAI TIAN[1]

[1]Department of Neurology, Beijing Tiantan Hospital, Capital Medical University, Beijing 100070, P.R. China;
[2]Department of Pathology, Beijing Tiantan Hospital, Capital Medical University, Beijing 100070, P.R. China

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Abstract. The present case report describes a 31-year-old male patient with isolated spinal vasculitis. The patient initially presented with right-hand numbness and weakness, which later extended to both lower limbs, causing gait instability. MRI scans performed after the symptoms had extended to both lower limbs revealed a cervical lesion with T1 hypointensity, T2 hyperintensity and heterogeneous enhancement, initially suspected to be a tumor. Histopathological analysis of the spinal cord biopsy specimen revealed lymphocytic infiltration surrounding the small vessels of spinal cord, supporting a diagnosis of primary isolated spinal vasculitis. The patient was treated with high-dose intravenous methylprednisolone for 9 days (500 mg for 3 days, 250 mg for 3 days and 120 mg for 3 days), resulting in pronounced clinical improvement on follow-up neurological examination and no recurrence at the 2-year follow-up without additional immunosuppressive therapy. The present case underscores the diagnostic challenge of distinguishing vasculitis from spinal tumors and highlights the uncertainty regarding long-term recurrence prevention strategies.

Introduction

Primary angiitis of the central nervous system (PACNS) is a rare condition characterized by inflammation of the blood vessels in the CNS, without systemic vascular involvement (1). The incidence rate of PACNS has been reported to be 2.4 cases per million individuals per year. PACNS primarily affects adults aged 30-60 years, with no clear sex predominance (58 women and 43 men in a 101-patient cohort), and is further associated with a number of neurological symptoms including headaches, cognitive impairment, seizures and hemiparesis (1,2). Serum inflammatory markers are typically normal (for example, acute-phase reactants and autoantibodies, including antinuclear antibodies, antineutrophil cytoplasm antibodies and antiphospholipid antibodies); however cerebrospinal fluid abnormalities are present in 80-90% of cases, typically showing a mildly increased leucocyte count and total protein concentration (1). Diagnosis can be made through magnetic resonance angiography, conventional angiography or tissue biopsy, revealing characteristic histopathological patterns that are commonly classified as granulomatous, lymphocytic or necrotizing vasculitis (1,3). Given the severity of the disease and its associated high mortality rate (reported to range from 6 to 17% across cohorts), early detection and timely initiation of treatment are important for reducing morbidity and mortality, as they help prevent irreversible damage and improve long-term outcomes (1,3).

Spinal cord vasculitis is a rare subtype of PACNS that primarily affects the blood vessels of the spinal cord, leading to localized inflammation and ischemic damage. Spinal cord vasculitis is typically characterized by symptoms such as limb weakness, numbness and urinary or bowel dysfunction (4). Due to its rarity and the overlap of clinical and imaging features with other conditions (for example, intramedullary tumors, inflammatory myelitis and spinal cord infarction), spinal cord vasculitis is often misdiagnosed or overlooked. The present report outlines a case of spinal cord vasculitis diagnosed through biopsy, with the aim to elucidate the clinical diagnostic challenges and underlying pathophysiology of this subtype and to enhance the understanding of this rare disease for improved clinical recognition and early diagnosis.

Case report

In March 2023, a 31-year-old male patient presented to the Department of Neurosurgery, Beijing Tiantan Hospital (Beijing, China) with a 4-month history of progressive right-hand numbness and weakness. Initially, the numbness and weakness were localized to the right hand, along with muscle atrophy and pain in the right shoulder, back and upper arm. The symptoms progressed to involve the right lower limb, with a walking-on-cotton sensation. A cervical spine MRI revealed a longitudinally extensive intramedullary lesion with cord swelling, showing T1 hypointensity and T2 hyperintensity from C3 to T1 with heterogeneous enhancement (Fig. 1A a-1). These findings, combined with the clinical presentation,

Correspondence to: Dr De-Cai Tian, Department of Neurology, Beijing Tiantan Hospital, Capital Medical University, 119 South Fourth Ring West Road, Beijing 100070, P.R. China
E-mail: decaitian@hotmail.com

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led to the suspicion of an intramedullary spinal cord tumor, given the expansile, mass-like appearance on MRI and the relatively mild clinical deficits despite the marked imaging abnormalities.

In June 2023, after a waiting period for hospital admission, the patient underwent microsurgical biopsy of the intramedullary spinal cord lesion, which was preoperatively suspected to be neoplastic based on the clinical presentation and MRI findings. No corticosteroids were administered prior to the biopsy. In the immediate postoperative period, the patient experienced neurological worsening, with a new onset of bilateral lower limb numbness, particularly on the right, along with stiffness and gait instability. Although there was no bladder or bowel dysfunction, a postoperative MRI revealed persistent intramedullary signal abnormality with T1 hypointensity and T2 hyperintensity, along with residual linear enhancement, raising further diagnostic uncertainty, as it was difficult to determine whether these postoperative findings reflected surgical changes, ongoing inflammation or residual neoplastic pathology (Fig. 1A a-2).

A neurological examination revealed atrophy of the right thenar and hypothenar muscles, decreased strength in wrist flexion and extension, as well as finger adduction/abduction on the right side. Reflexes were diminished in the right upper limb but hyperactive in both lower limbs. A sensory examination demonstrated decreased pinprick and vibratory sensations in the right hand and both lower limbs. The Babinski sign (extensor plantar response) was positive on the right side. These findings pointed to a severe, possibly inflammatory spinal cord lesion, yet differentiation from a neoplasm remained challenging based on the clinical and imaging data alone.

Laboratory tests were unremarkable, including routine blood, urine and stool tests, serum biochemistry, coagulation profile, infectious disease screening and tumor markers. The immunological work-up was negative, including an autoantibody panel, inflammatory markers (C-reactive protein and erythrocyte sedimentation rate), antistreptolysin O, rheumatoid factor, anticardiolipin antibody, antineutrophil cytoplasmic antibody, thyroid autoantibodies, complement component 3 and complement component 4, and angiotensin-converting enzyme. Cerebrospinal fluid analysis showed no abnormalities except for mildly elevated total protein levels. Notably, serological and cerebrospinal fluid antibody tests against aquaporin-4, myelin oligodendrocyte glycoprotein, glial fibrillary acidic protein (GFAP) and myelin basic protein (MBP), as well as paraneoplastic antibody tests (including anti-Hu, anti-Yo, anti-Ri, anti-CV2/CRMP5, anti-Ma2 and anti-amphiphysin) were negative. The absence of serological and cerebrospinal fluid markers added to the difficulty in establishing a clear diagnosis.

The development in diagnosis came with the histopathological analysis of the spinal cord biopsy in June 2023 conducted by the Department of Pathology, Beijing Tiantan Hospital (Beijing, China), which revealed lymphocytic infiltration surrounding the small blood vessels of spinal cord and occasional epithelioid cell nodules, suggestive of small vessel vasculitis. No well-formed granulomas or multinucleated giant cells were identified. Immunohistochemical staining demonstrated inflammatory cell markers (CD3, CD20 and CD68), supporting a lymphocytic inflammatory infiltrate. Markers of vascular structures (CD34 and α-smooth muscle actin) highlighted small vessels, whereas neural/glial markers (GFAP, neurofilament, MBP and oligodendrocyte transcription factor 2) characterized the surrounding spinal cord tissue; tumor-associated markers [OCT4, enhancer of zeste inhibitory protein (EZHIP), histone H3K27M, histone H3K27me3 and Spalt-like transcription factor 4 (SALL4)] and the proliferation marker Ki-67 were included to evaluate for a neoplastic process (Fig. 1B). The biopsy tissue was fixed in 10% neutral buffered formalin at room temperature (overnight) and then paraffin-embedded according to routine diagnostic procedures in the Department of Pathology, Beijing Tiantan Hospital. The blocks were sectioned at a thickness of 4 μm, deparaffinized in xylene and rehydrated through a descending ethanol series, and then stained with H&E using a commercial H&E staining kit (cat. no. G1120; Beijing Solarbio Science & Technology Co., Ltd.), according to the manufacturer's instructions. Immunohistochemistry was performed on the sections following standard diagnostic protocols, including antigen retrieval and blocking with 3% bovine serum albumin at room temperature for 30 min, followed by HRP-based visualization with 3,3'-diaminobenzidine, with hematoxylin counterstaining. Primary antibody incubation was performed at 4˚C overnight. The primary antibodies used were CD3 (ab16669; 1:150 dilution; Abcam), CD20 (ab78237; 1:250 dilution; Abcam), CD68 (ab955; 1:3,000 dilution; Abcam), α-smooth muscle actin (ab124964; 1:400 dilution; Abcam), CD34 (ab81289; 1:50 dilution; Abcam), GFAP (ab4674; 1:6,000 dilution; Abcam), neurofilament (ab7794; 1:1,000 dilution; Abcam), MBP (ab7349; 1:4,000 dilution; Abcam), oligodendrocyte transcription factor 2 (Olig2) (ab109186; 1:100 dilution; Abcam), OCT4 (ab181557; 1:1,000 dilution; Abcam), Ki-67 (ab16667; 1:200 dilution; Abcam), EZHIP (ab316856; 1:500 dilution; Abcam), histone H3 (mutated K27M) (ab190631; 1:1,000 dilution; Abcam), histone H3 (tri methyl K27) (ab192985; 1:500 dilution; Abcam) and SALL4 (ab29112; 1:100 dilution; Abcam), which were used according to the manufacturer's instructions. Signal detection was performed using the EnVision™ + System-HRP (Dako; Agilent Technologies, Inc.), i.e., species-specific HRP-labeled polymer reagents selected according to the host species of the primary antibodies, followed by DAB visualization, according to the manufacturer's instructions. Slides were examined and imaged using a bright-field light microscope. The final pathology interpretation supporting small-vessel vasculitis became available 2 weeks after the biopsy (after completion of the histopathological review and ancillary immunohistochemistry analysis of the specimen). With these findings, a diagnosis of PACNS was established. Therefore, the present case report underscores the diagnostic complexity, as the longitudinally extensive spinal cord lesion with persistent enhancement mimicked a tumor.

In July 2023, 4 weeks after the biopsy, the patient was admitted to the Department of Neurology, Beijing Tiantan Hospital and treated with high-dose intravenous methylprednisolone, followed by rehabilitation. During this hospitalization, intravenous methylprednisolone was administered for 9 days (500 mg for 3 days, 250 mg for 3 days and 120 mg for 3 days), followed by oral prednisone acetate (60 mg/day), initiated after completion of intravenous methylprednisolone, and tapered

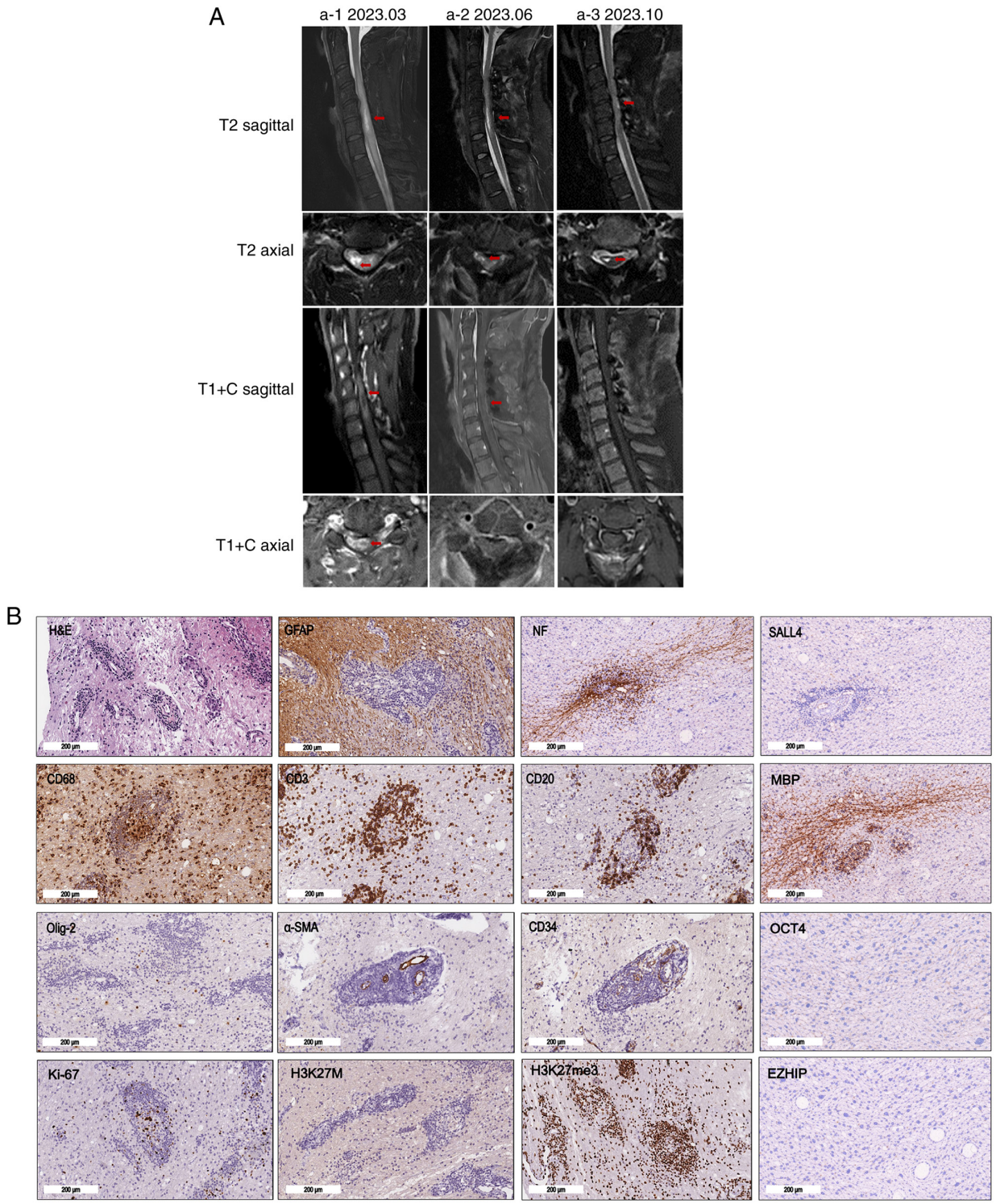

Figure 1. Cervical lesions detected through MRI scans and pathological findings. (A) Serial cervical spine MRI findings. (a-1) Baseline MRI demonstrated a longitudinally extensive intramedullary lesion with cord swelling on T2-weighted images and heterogeneous enhancement on post-contrast T1-weighted images (arrows). (a-2) Immediate postoperative MRI showed persistent intramedullary signal abnormality with residual enhancement (arrows). (a-3) Follow-up MRI after high-dose corticosteroid therapy showed interval reduction of the lesion and no residual enhancement (arrows). (B) H&E staining showing vasculocentric lymphocytic infiltration involving small vessel walls, consistent with small-vessel vasculitis. Immunohistochemistry showed $CD3^+$, $CD20^+$, $CD68^+$, α-SMA^+, $CD34^+$, $GFAP^+$, NF^+, MBP^+, Olig-2^-, $OCT4^-$, $H3K27me3^+$, $EZHIP^-$, $SALL4^-$, $H3K27M^-$ and Ki-67^+ (scattered) staining, supporting small-vessel vasculitis and arguing against a neoplastic process. Scale bar, 200 μm. α-SMA, α-smooth muscle actin; GFAP, glial fibrillary acidic protein; NF, neurofilament; MBP, myelin basic protein; Olig2, oligodendrocyte transcription factor 2; EZHIP, enhancer of zeste inhibitory protein; SALL4, Spalt-like transcription factor 4; H3K27M, histone H3 (mutated K27M); H3K27me3, histone H3 (tri methyl K27); C, contrast-enhanced.

by 5 mg (one 5-mg tablet) each week until discontinuation, for a total duration of 12 weeks. Concomitant medications during corticosteroid therapy included potassium chloride sustained-release (1 g twice daily), calcitriol (0.25 μg twice daily), calcium carbonate (0.75 g three times daily) and omeprazole (20 mg once daily) to prevent steroid-induced side

effects, with supportive therapy using mecobalamin (0.5 mg three times daily) and vitamin B1 (10 mg three times daily) for nerve nutrition. At the 4-month follow-up, the patient exhibited an improvement in limb weakness and gait stability. MRI scans at the follow-up in October 2023 demonstrated a reduction in lesion size and absence of enhancement (Fig. 1A a-3). Cyclophosphamide or other immunosuppressive agents were not administered during this period. Given the spinal cord-limited, biopsy-proven small-vessel vasculitis and the excellent response of the patient to corticosteroids, careful long-term clinical and MRI follow-up were opted for, rather than immediate additional immunosuppression. At the last follow-up, 2 years after the initiation of corticosteroid therapy (June 2025), the modified Rankin scale value (5) of the patient was 2 (slight disability; unable to carry out all previous activities but able to look after own affairs without assistance), without relapse. The clinical treatment timeline of the patient is summarized in Fig. S1.

Discussion

PACNS is a rare condition characterized by inflammatory lesions confined to the blood vessels of the brain and spinal cord (1). The present case report highlights two key challenges, namely the difficulty in distinguishing isolated spinal vasculitis from spinal cord tumors, given their similar radiographic presentations, such as marked swelling and persistent enhancement, as well as the uncertainty regarding the prevention of recurrence. While corticosteroid treatment led to clinical improvement, the long-term strategy for preventing recurrence without immunosuppression remains unclear. In a number of cases, immunosuppressive agents such as cyclophosphamide may be needed, but the timing and choice of such treatments must be individualized based on patient response (for example, relapse or radiological/clinical progression despite glucocorticoid treatment) and risk factors (for example, disease severity). In the present report, 'isolated spinal vasculitis' referred to spinal cord-limited PACNS. Given that the Calabrese and Mallek diagnostic criteria were developed for cerebral disease and have not been specifically validated for spinal cord-limited vasculitis, histopathological analysis remains key in diagnosis (6,7). Histopathologically, PACNS is commonly classified into granulomatous, lymphocytic and necrotizing pattern categories. The biopsy conducted in the present study showed vasculocentric lymphocytic inflammation involving small vessel walls with occasional epithelioid cell nodules, consistent with predominantly lymphocytic small-vessel vasculitis with possible focal granulomatous features (1,8). These nodules likely represent focal epithelioid histiocyte aggregates, as well-formed granulomas or multinucleated giant cells were not identified. CD4 and CD8 immunostaining was not performed in the present case, therefore information on the CD4 and CD8 staining pattern or the CD4/CD8 ratio is not available. Future studies with expanded T-cell subset profiling may further characterize the inflammatory microenvironment. IgG4-related disease is a recognized mimic of inflammatory CNS disorders and should be considered in the differential diagnosis of suspected CNS vasculitis (9). In the present case, IgG4 immunostaining was not performed as it was not included in the initial immunohistochemistry panel at the time of biopsy, and IgG4-related disease was not specifically considered given the absence of typical clinicoradiologic features, such as dural thickening/enhancement or systemic manifestations (9). Examples of such clinical manifestations of IgG4-RD include swelling of salivary glands (especially the parotid glands), fever, weight loss and multi-organ involvement. Radiologically, IgG4-RD is often associated with uniform organ enlargement and enhancement, which can be detected using MRI or CT scans. However, IgG4 staining may be useful when feasible in similar cases. Advanced imaging may provide complementary information beyond conventional spinal MRI when CNS vasculitis is suspected. While a high-resolution contrast-enhanced vessel wall MRI may add diagnostic specificity in cerebral vasculitis (10), its application in spinal cord-limited disease remains technically challenging and is not routinely available due to the small size and complex anatomy of spinal cord vessels, as well as the influence of surrounding bone structures and artifacts. Therefore, this was not performed on the present patient. Neurological deterioration after primary spinal cord biopsy has previously been reported. For example, in a multicenter series of 61 primary spinal cord biopsies, postoperative neurological worsening (for example, new or worsened motor and/or sensory deficits) occurred in 47.5% (29/61) of patients; of those who worsened, 48.3% (14/29) recovering within 3 weeks (11).

For severe, rapidly progressive or generalized PACNS, induction therapy with high-dose corticosteroid combined with cyclophosphamide is commonly used in clinical practice and supported by retrospective cohort experience and contemporary reviews (3,12,13). Despite the absence of immunosuppressants, the patient described in the present study has remained free from recurrence for 2 years, raising an important therapeutic question, namely under what circumstances immunotherapy should be initiated. Recurrence in PACNS, particularly when limited to the spinal cord, is a recognized risk and cases in the literature report that relapses may occur after prolonged intervals of ≥1 year (for example, 13 months later, or cerebral involvement emerging 5 years later) (4,13,14). In large cohorts of patients with PACNS, relapses have been observed in 27% of cases. Accordingly, long-term surveillance is warranted even after apparent clinical stability. The optimal duration of therapy remains uncertain and maintenance strategies using steroid-sparing agents (such as azathioprine, mycophenolate mofetil, methotrexate or other immunosuppressants), are often considered (3,12,13). Previous studies appear to advocate combination induction and/or maintenance immunosuppression to mitigate relapse risk in PACNS (3,12,13). Furthermore, although agents such as cyclophosphamide are commonly used as part of induction and relapse-prevention strategies in PACNS, their associated toxicities, particularly in younger patients, complicate this decision, given the risks of bladder toxicity (hemorrhagic cystitis reported in 12-41% in high cumulative-dose cohorts), gonadal toxicity (ovarian failure reported in 26% in a classic SLE cohort), and late malignancies (e.g., increased risks of bladder cancer and acute myeloid leukemia reported after exposure in vasculitis cohorts) (15,16). In addition, late-onset brain involvement (namely, delayed intracranial extension after an initially spinal cord-limited presentation), further complicates therapeutic decisions and underscores the need for long-term clinical/MRI surveillance and individualized consideration of treatment duration.

PACNS involving the spinal cord is rare. In the Mayo Clinic 40-year cohort, spinal cord involvement occurred in 10/216 cases (4.6%), whereas truly spinal cord-limited disease was exceptionally rare (1/216, 0.5%) (6). These occurrence rates add to the diagnostic complexity, as spinal cord tumors and other inflammatory conditions (such as inflammatory myelitis, demyelinating diseases such as NMOSD or MS, and spinal cord infarction) are often more strongly considered. The course of the present case report suggests that isolated spinal vasculitis may have a favorable prognosis, particularly when diagnosed early and managed appropriately. However, further studies are required to clarify the long-term outcomes and role of immunosuppressive therapy in preventing recurrence. From a mechanistic perspective, emerging work in neurovascular inflammation highlights the role of endothelial dysfunction and inflammatory mediators in regulating CNS vascular integrity (1,17). Although not examined in the present case, future studies integrating immunophenotyping and molecular profiling may help clarify the pathophysiology of spinal cord-limited vasculitis and identify potential therapeutic targets, consistent with the evolving perspective that CNS tissues are not absolutely immune-privileged.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

DCT contributed to the conception and design of the study, supervised the clinical management of the patient and critically revised the manuscript. YY contributed to data collection, clinical data review and analysis, interpretation of imaging findings, and drafting of the manuscript. GHD contributed to the histopathological analysis and interpretation, and preparation of the pathological figures. All authors have read and approved the final version of the manuscript. YY and DCT confirm the authenticity of all the raw data.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Written informed consent for publication of the clinical information and images was obtained from the patient.

Competing interests

The authors declare that they have no competing interests.

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