Journal of
Medical Case Reports

CASE REPORT

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Probable chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids syndrome: management with corticosteroids and intravenous immunoglobulin—a case report

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Abstract

Background Chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids is a rare, subacute inflammatory disorder of the central nervous system with an unknown etiology. It is characterized by distinct clinical (diplopia, ataxia, dysarthria, and altered facial sensation), radiological (punctiform lesions detected on magnetic resonance imaging), and histopathological (predominantly perivascular lymphocytic infiltration, mainly affecting the pons and cerebellum) features. The condition typically demonstrates a favorable response to corticosteroid therapy.

Case presentation We report the case of a 54-year-old Caucasian European male who presented with clinical and radiological findings consistent with chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids. The patient attended the emergency department at his referral hospital following a 1-month history of progressive neurological symptoms, including diplopia, blurred vision, facial paresis, and gait disturbance attributed to lower limb weakness.

Given the clinical presentation and magnetic resonance imaging findings, treatment with oral prednisolone (70 mg/day) was initiated. At 2 weeks post-treatment initiation, the patient exhibited significant clinical improvement, with complete resolution of neurological symptoms.

A follow-up brain magnetic resonance imaging scan, performed at the referral center 1 month after starting corticosteroid therapy, demonstrated a reduction in both the size and number of hyperintense lesions in the brainstem on T2-weighted sequences, along with resolution of contrast enhancement. These radiological findings indicated a favorable therapeutic response to chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids treatment.

At the 1-month follow-up, the patient remained asymptomatic, leading to a gradual tapering of corticosteroid therapy in light of both clinical and radiological improvement.

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Conclusion Chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids is a rare neurological disorder that typically presents with ataxic gait, diplopia, and dysarthria. Diagnosis is based on a combination of clinical features, neuroimaging, and histopathology, although brain biopsy is not always feasible. The cornerstone of treatment is immunosuppressive therapy, primarily with corticosteroids, often supplemented with other immunosuppressive agents to prevent relapse.

Keywords CLIPPERS, Corticosteroids, Diplopia, Ataxia, Case report

Introduction

Chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS) is a subacute inflammatory process of the central nervous system of unknown etiology [1]. It is defined by several clinical (diplopia, ataxia, dysarthria, and altered sensation in the facial region), radiological (punctiform lesions that can be seen on magnetic resonance imaging [MRI] following administration of intravenous [IV] contrast [gadolinium]), and histopathological (largely perivascular inflammatory lymphocytic infiltrate, mainly located in the pons and cerebellum) characteristics, and responds well to steroid treatment [2, 3]. It may be confused with other entities, which gives rise to the need for an exhaustive differential diagnosis and the definition of clear diagnostic criteria based on clinical, radiological, and histological aspects. It was first described by Pittock in 2010 [4]. Precise incidence and prevalence remain unclear owing to its rarity and the potential for misdiagnosis; however, CLIPPERS predominantly affects middle-aged adults, with a slight male predominance. It may occur sporadically worldwide, without a clear geographical or ethnic predisposition. The median age at diagnosis is approximately 45–50 years [5].

Case report

The patient with white European ethnicity is a 54-year-old European Caucasian male who is allergic to iodine and was undergoing psychiatric monitoring for anxiety–depressive disorder treated with venlafaxine. The patient presented to the emergency department of his referral hospital following a 1-month history of progressive neurological symptoms, including diplopia, blurred vision, and facial paresis. He also reported gait instability, which he described as lower limb weakness. Given the clinical presentation, he was admitted to the neurology department for further evaluation and management.

The patient was not taking any medications at the time of admission. Regarding social history, he is a nonsmoker, does not consume alcohol, and lives independently with no recent travel or known exposure to infectious agents.

The following complementary test were performed. A lumbar puncture (LP) was performed, with cytological analysis revealing a serous-based smear in which highly occasional and isolated mature lymphoid elements were observed, without epithelial representation or the presence of neoplastic cells. The LP was repeated several weeks later, with no significant changes in the findings (Table 1).

A brain MRI with intravenous contrast, conducted at an associated center (images not available), revealed an inflammatory-demyelinating process. A computed tomography (CT) scan of the thorax, abdomen, and

Table 1 CSF analysis

Test	Patient's value	Reference range
CSF—cell count	10–50 cells/μL (lymphocytic predominance)	< 5 cells/μL
CSF—proteins	50–100 mg/dL	15–45 mg/dL
CSF—glucose	50–70 mg/dL	50–80 mg/dL
CSF—oligoclonal bands	Positive	Negative
CSF—IgG index	Elevated (> 0.7)	< 0.7
CSF—bacterial culture	Negative	Negative
CSF—PCR for infections	Negative (to rule out infections)	Negative
CSF—cytological smear	Serous base smear showing very occasional and isolated mature lymphoid elements, with no epithelial representation or neoplastic cells	No neoplastic cells or inflammation
CSF—repeat lumbar puncture	No significant changes in findings	-

CSF: cerebrospinal fluid; PCR: polymerase chain reaction; IgG: immunoglobulin G

pelvis with IV contrast showed mild signs of emphysema, with no other significant findings.

Blood tests including immunoglobulins, complement, antinuclear antibody (ANA), antineutrophil cytoplasmic antibodies (ANCA), anti-proteinase 3, anti-myeloperoxidase (MPO), connective tissue disease (CTD) screening, anti-thyroid peroxidase (TPO), antithyroglobulin, ANOEs, and antiphospholipid antibodies were all within normal limits.

Serological testing for hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV), Epstein–Barr virus (EBV), Lyme disease, and Brucella was negative. Toxoplasma serology showed positive immunoglobulin G (IgG) and negative immunoglobulin M (IgM), while cytomegalovirus Immunoglobulin G (CMV IgG) was positive. No onconeural antibodies were detected in serum. Vitamin B12, folate, thyroid-stimulating hormone (TSH), and thiamine levels were tested and found to be within normal limits.

With a diagnosis of ischemic-inflammatory disease, it was decided to initiate pulse treatment with steroids and intravenous immunoglobulin (IVIG) at a dose of 0.4 g/kg/day for five consecutive days, after which the patient showed relative improvement. It was decided to repeat the brain MRI in the same associated center (no images available) and no significant changes were observed. In light of these findings, the diagnosis was oriented towards neoplasia, with the most plausible options being a low-grade glioma or cerebral lymphoma.

With this diagnosis, the patient was referred to radiation oncology for treatment as a biopsy could not be taken owing to the location of the possible tumor.

When the patient was reassessed after steroid pulse treatment, clinical improvement of the instability and facial paresis was seen, although the patient continued to present blurred vision.

In light of this relative improvement, a control brain MRI with IV contrast and perfusion study was performed in a referral center (Figs. 1, 2, 3, 4, 5, 6, 7) before radiotherapy treatment to better characterize the lesion and confirm the diagnosis. In sequences with long repetition time (TR), a mild, diffuse, and patchy hypersignal was identified in the central portion of the medulla oblongata, rear of the pons, and the midbrain. It was not accompanied by tumefaction or an increase in volume, and there was no restriction in diffusion sequences. Following the administration of IV contrast, patchy and heterogeneous enhancement of the lesions and the cortex of both insulas was observed, in addition to an increase in the vascularization of both striata, which is not associated with a clear hypersignal in T2 sequences. These radiological findings would suggest CLIPPERS as the main diagnostic possibility, without ruling out cerebral lymphoma.

Given the presence of compatible clinical characteristics and MRI results, it was decided to initiate treatment with 70 mg/ 24 hours of prednisolone. A full blood panel and positron emission tomography (PET)–computed tomography (CT) were also performed as an extension study to rule out other pathologies.

At 2 weeks after initiating steroid treatment (70 mg/day of prednisolone), the patient displayed clinical improvement and no longer presented with neurological symptoms. Consequently, the same treatment was continued and prophylaxis was started for *Pneumocystis* infection with sulfamethoxazole–trimethoprim and for steroid-induced osteoporosis with calcium carbonate and cholecalciferol.

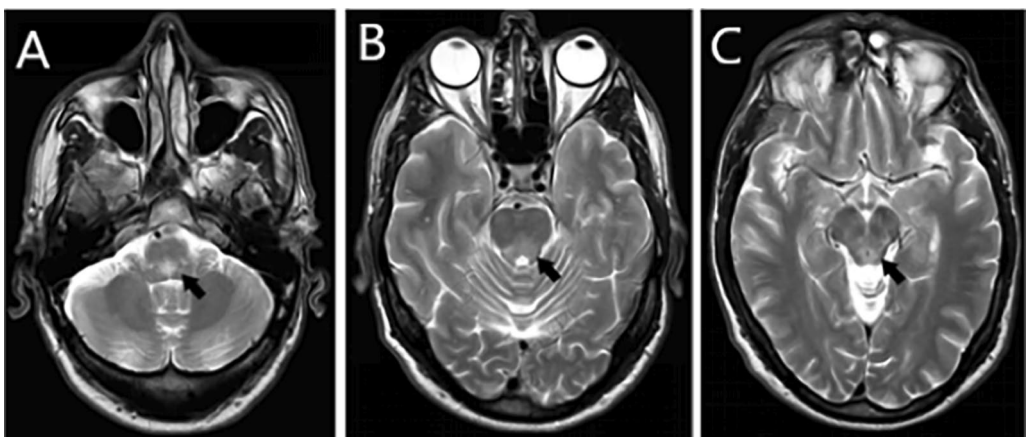

Fig. 1 Axial turbo spin echo T2-weighted magnetic resonance imaging sequences. **A** Patchy hyperintensity in the central portion of the medulla oblongata (black arrow). **B** Hyperintensity in the posterior region of the pons (black arrow). **C** Hyperintensity in the midbrain, involving the tegmentum (black arrow)

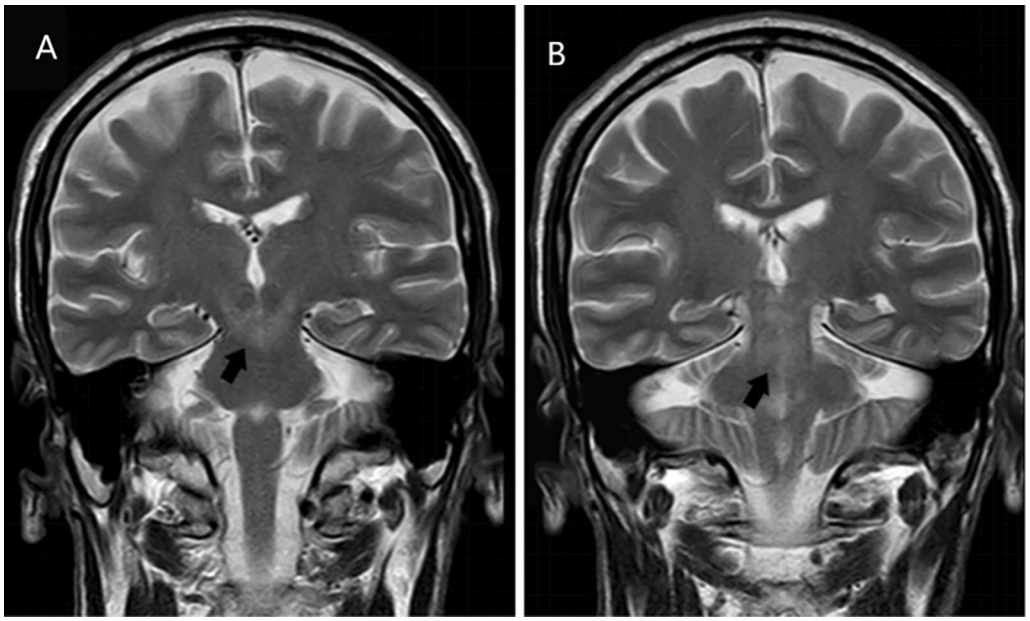

Fig. 2 Coronal turbo spin echo T2-weighted magnetic resonance imaging sequences. **A** Patchy hyperintensity in the midbrain and cerebral peduncles (black arrow). **B** Hyperintensity involving the central and posterior portion of the pons and medulla oblongata (black arrow)

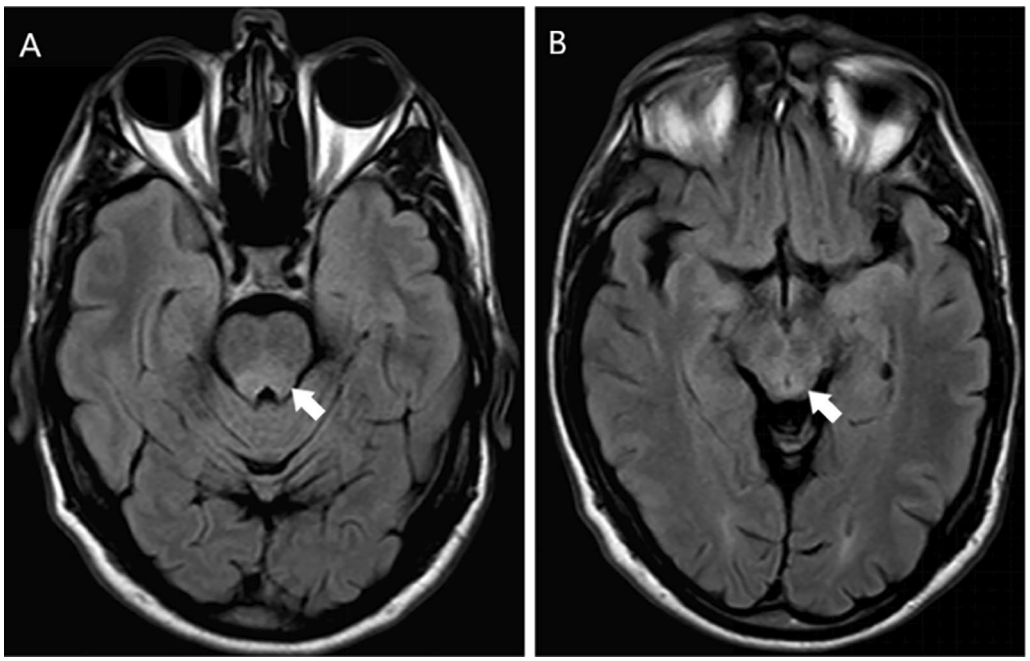

Fig. 3 Axial fluid attenuation inversion recovery T2-weighted magnetic resonance imaging sequences. **A** Slight hyperintensity in the posterior portion of the pons (white arrow). **B** Slight hyperintensity in the midbrain tegmentum (white arrow)

Another control brain MRI was performed in the referral center 1 month after steroid treatment was started (Figs. 8, 9). It showed a reduction in the size and number of hyperintense lesions located in the brainstem in T2 sequences, in addition to resolution of the enhancement compared to previous MRI. These radiological findings were attributed to a good response to CLIPPERS treatment.

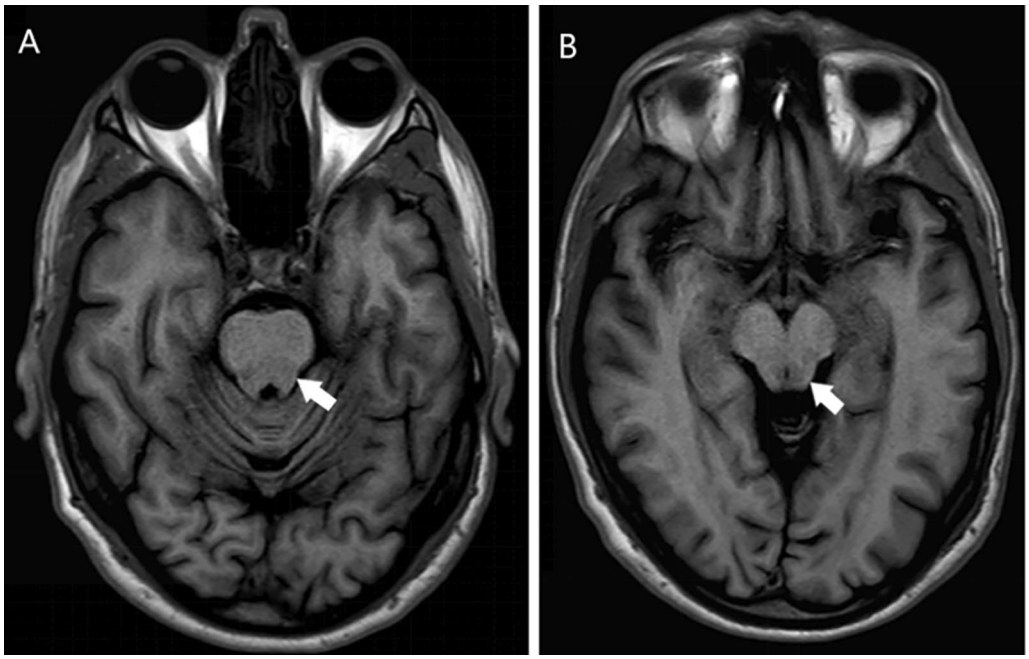

Fig. 4 Axial T1-weighted fluid attenuation inversion recovery magnetic resonance imaging sequences. **A** Patchy hypointensity in the posterior portion of the pons (white arrow). **B** Hypointensity in the midbrain tegmentum (white arrow)

At 1 month after initiating treatment, the patient continued to have no symptoms and it was decided to gradually reduce the dose of steroids in light of the clinical and radiological improvement observed. The dose of prednisolone was tapered by 10 mg every 2 weeks until reaching 30 mg/day, and then by 5 mg every 2 weeks until a maintenance dose of 10 mg/day was achieved. Further tapering was done more cautiously, decreasing by 1 mg every month, with close clinical and radiological monitoring to avoid relapse.

Discussion

Clinical presentation, neuroimaging, and histopathology are the three fundamental pillars of CLIPPERS diagnosis. Therefore, in 2017, Tobin *et al*. [6] proposed the only diagnostic criteria available to date.

Clinical presentation is based on subacute pontocerebellar dysfunction, regardless of whether it is associated with other central nervous system symptoms. These symptoms characteristically respond to high-dose steroid therapy [7].

The diagnostic test of choice is an MRI scan of the brain with the usual sequences (sagittal and axial T1, coronal and axial T2, and T2 fluid-attenuated inversion recovery (FLAIR), in addition to magnetic susceptibility and diffusion sequences), in addition to sequences following the administration of IV contrast (axial volumetric 3DT1 sequence and an axial T1 sequence with fat suppression) [6, 8].

It is characterized by the presence of homogeneous, punctiform, and curvilinear lesions that usually measure less than 3 mm but can reach 9 mm. They are often symmetrical and are mainly located in the pons of the brainstem, although they can less frequently be found in the cerebellar hemispheres, other areas of the brainstem, the internal capsule, the thalamus, or the spinal cord, among others. The lesions appear hypo- to isointense on T1-weighted sequences and hyperintense on T2-weighted and T2-FLAIR sequences. Furthermore, punctiform areas of signal loss and venous engorgement can be observed in magnetic susceptibility sequences. They do not exert mass effects but may present mild vasogenic edema and have a slight tendency to converge. Following the administration of IV contrast, homogeneous enhancement can be seen and the damaged areas therefore take on the characteristic heterogeneous "salt and pepper" appearance. Furthermore, the enhancing areas do not show a significant increase in size compared to sequences without contrast, which coincides with the absence of marked vasogenic edema. Lastly, the lesions show clear improvement after steroid treatment is initiated and worsen when it is discontinued.

The third diagnostic pillar is histopathology. Histopathology observes intense, largely perivascular lymphocytic inflammation accompanied by diffuse infiltration of

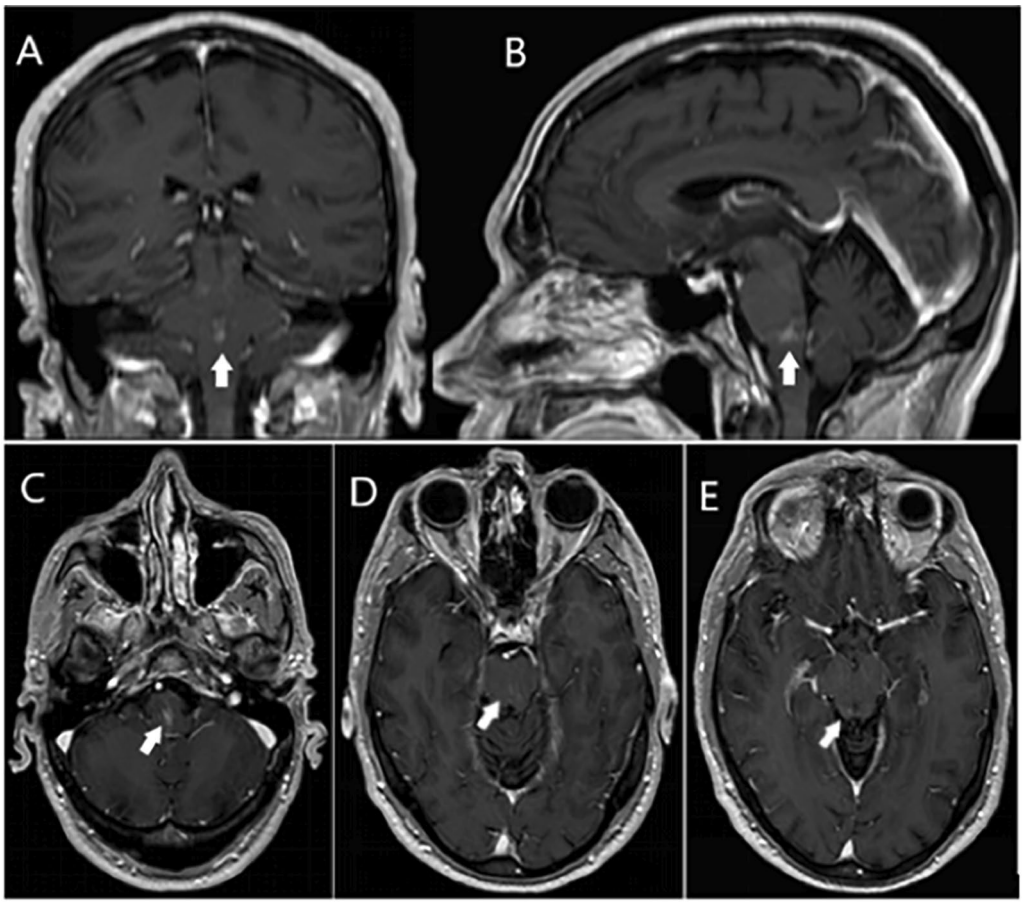

Fig. 5 Post-contrast three-dimensional T1-weighted magnetic resonance imaging sequences in coronal, sagittal, and axial planes. **A** Heterogeneous enhancement in the midbrain tegmentum (white arrow). **B** Contrast enhancement in the posterior region of the pons (white arrow). **C** Subtle enhancement in the medulla oblongata (white arrow). **D** Patchy enhancement in the pons (white arrow). **E** Mild enhancement in the midbrain (white arrow)

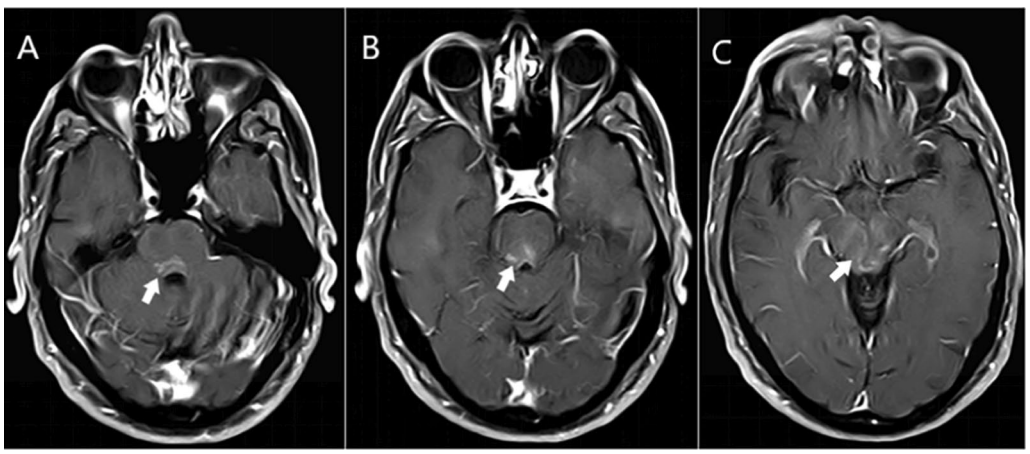

Fig. 6 Axial post-contrast T1-weighted magnetic resonance imaging sequences with fat suppression. **A** Heterogeneous enhancement in the posterior portion of the pons (white arrow). **B** Patchy enhancement in the central pons (white arrow). **C** Focal enhancement in the midbrain tegmentum (white arrow)

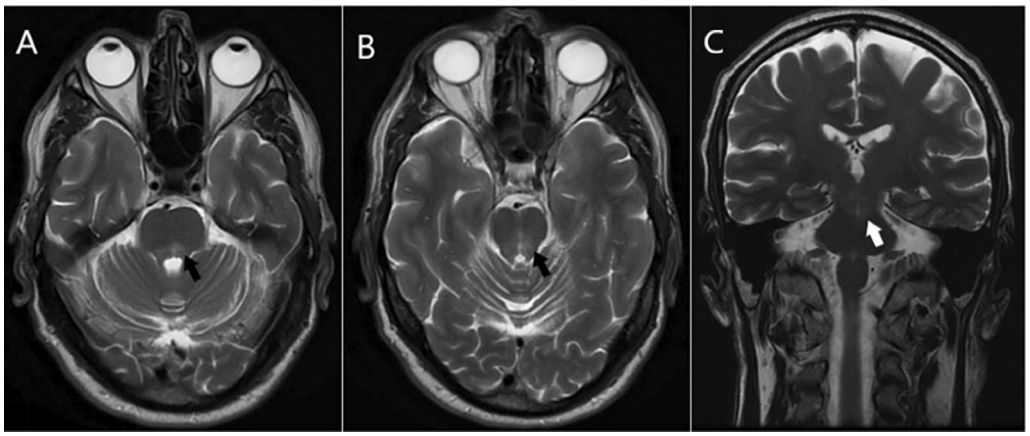

Fig. 7 Axial and coronal turbo spin echo T2-weighted magnetic resonance imaging sequences. **A** Partial resolution of the hyperintense lesion in the posterior portion of the pons (black arrow). **B** Persistent but reduced hyperintensity in the midbrain tegmentum (black arrow). **C** Coronal view showing decreased signal intensity in the midbrain compared to initial study (white arrow)

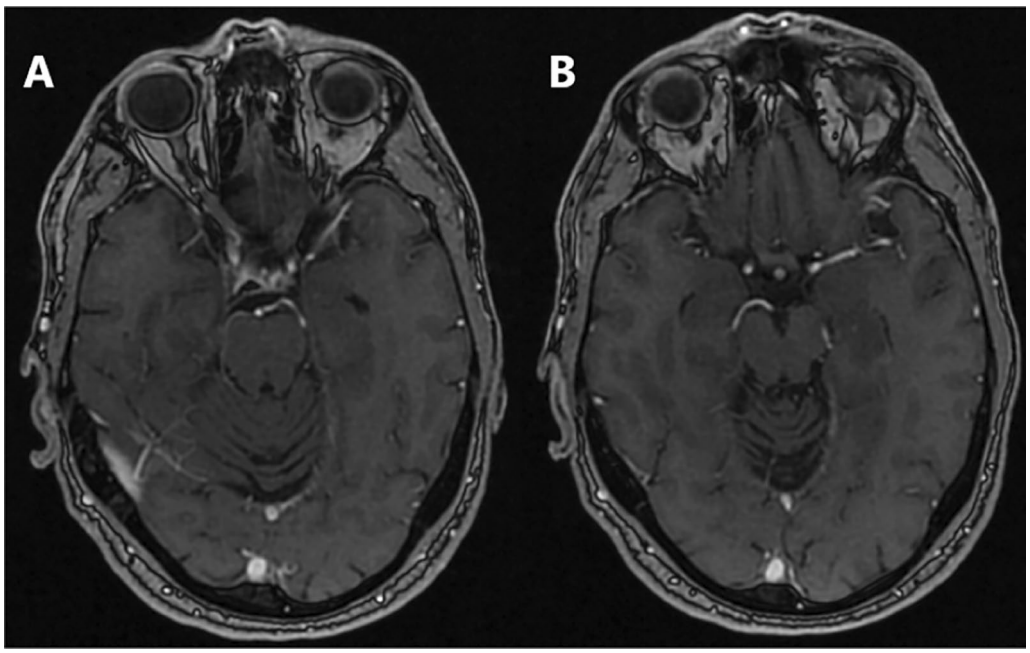

Fig. 8 Axial three-dimensional T1-weighted magnetic resonance imaging sequences after intravenous contrast administration. **A** No residual enhancement in the pons, indicating complete resolution of previously observed lesions. **B** Absence of contrast enhancement in the midbrain, confirming radiological resolution. Compare with Fig. 5

the parenchyma. Both white and grey matter are affected and lymphoid cells are mostly $CD3^+$ (T lymphocytes). Most of these are $CD4^+$, although there are also some $CD8^+$. A variable quantity of macrophages can also be identified. There is no demyelination, or it is focal and secondary to inflammation if it is present.

In accordance with all of these criteria, two diagnostic categories can be established for CLIPPERS [3, 4, 6]: *Definite CLIPPERS*: patients who meet all clinical, radiological, and histopathological criteria. *Probable CLIPPERS*: patients who meet clinical and radiological criteria, but may or may not meet histopathological criteria as no biopsy is available (as is our case).

Several clinical and radiological features should prompt reconsideration of the diagnosis. These include a lack of response to steroid therapy, the absence of lesions predominantly located in the brainstem, and the rapid onset—within days—of severe neurological

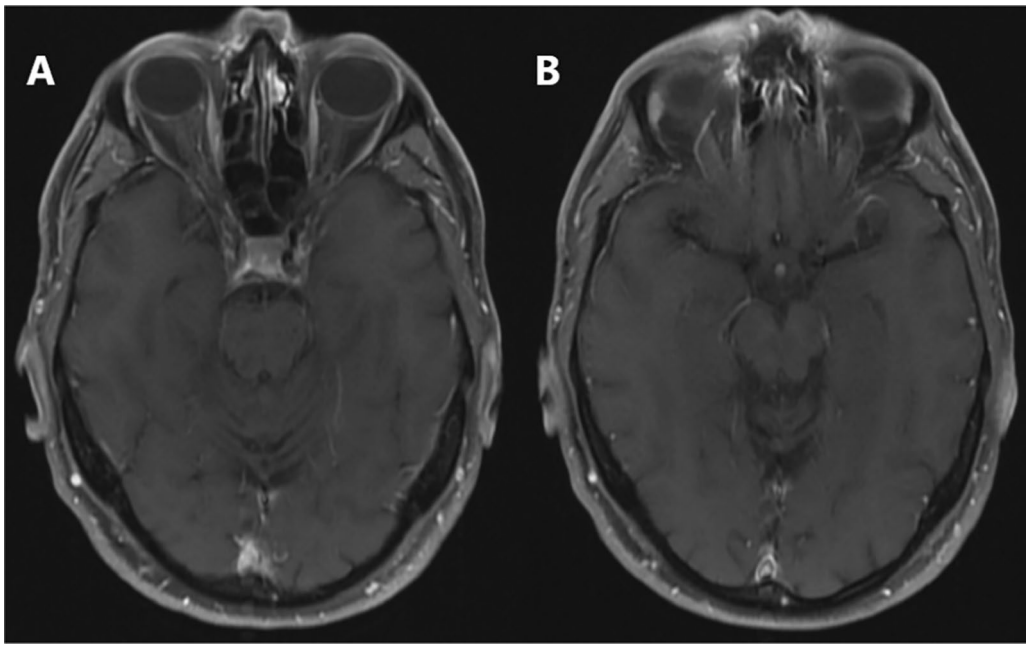

Fig. 9 Axial post-contrast T1-weighted magnetic resonance imaging sequences with fat suppression. **A** Complete resolution of prior contrast enhancement in the posterior pons. **B** Absence of residual enhancement in the midbrain. Compare with Fig. 6

deficits. Additional warning signs include the presence of fever or B symptoms, early-onset seizures, a decrease in the level of consciousness, and the appearance of systemic manifestations outside the central nervous system (CNS).

In our case, brain MRI initially revealed mild, patchy hyperintensities on T2 and FLAIR sequences affecting the central medulla oblongata, posterior pons, and midbrain, with corresponding subtle, heterogeneous contrast enhancement on post-contrast T1-weighted images. These findings were consistent with an inflammatory pattern predominantly involving the brainstem. Follow-up imaging demonstrated partial resolution of the hyperintense lesions and complete resolution of the pathological contrast enhancement, indicating a favorable radiological response to treatment.

MRI [3, 4, 9] may also reveal features inconsistent with the typical presentation, such as lesions associated with significant vasogenic edema and/or mass effect, a normal scan despite clear clinical symptoms, or the presence of ring-enhancing lesions following the administration of intravenous contrast. Other atypical findings include marked asymmetry in lesion distribution, and localization of abnormalities in areas such as the cortex, meninges, hypothalamus, or pituitary gland.

Given the broad differential diagnosis, a comprehensive diagnostic workup is warranted. In selected cases, a brain biopsy may be necessary to confirm the diagnosis and exclude alternative pathologies.

The differential diagnosis is broad and justifies an extensive diagnostic study, in addition to cerebral biopsy in selected cases.

The main differential diagnosis is performed with primary cerebral lymphoma (PCNSL). Both PCNSL and CLIPPERS have subacute and progressive presentation, but the clinical manifestations of lymphoma are more variable. The latter often presents with a headache accompanied by focal neurological symptoms and signs of intercranial hypertension due to mass effect, an aspect that is not present in the case of CLIPPERS. Furthermore, neuropsychiatric symptoms and epileptic seizures can be some of the initial symptoms of PCNSL. Another important difference is the appearance of symptoms outside of the CNS in the case of lymphoma such as B symptoms (fever, weight loss, and sweating), while there are no nonneurological symptoms with CLIPPERS [3, 6, 9]. Another differential diagnosis is the infectious rhombencephalitis. Infectious rhombencephalitis and CLIPPERS syndrome may appear similar but have key differences. Infectious rhombencephalitis is caused by bacteria such as *Listeria*, viruses, fungi, or parasites, and typically presents with fever, confusion, difficulty speaking or moving, and sometimes neck stiffness [8, 10]. MRI shows large lesions with inflammation and, in some cases, abscesses, while cerebrospinal fluid (CSF) analysis reveals a high number of inflammatory cells, elevated protein levels, and, if bacterial, low glucose. Treatment depends on the causative agent, with

antibiotics or antivirals [11, 12]. In contrast, CLIPPERS syndrome is an autoimmune inflammation without infection, causing progressive difficulties in walking, speaking, and eye movement, but without fever or altered consciousness. MRI reveals small lesions with a "salt-and-pepper" pattern, and CSF findings are usually near normal or show mild inflammation. The key to differentiating them is that infectious rhombencephalitis has a more abrupt onset with fever and potential consciousness impairment, whereas CLIPPERS is more progressive and responds well to corticosteroids. Before starting immunosuppressive treatment, infection must always be ruled out.

Besides these clinical entities, there are more conditions that can be mistaken for CLIPPERS syndrome. We analyze the differences in Table 2.

With regard to neuroimaging, in brain MRIs, lymphomas are normally located in deep supratentorial regions, affect the basal ganglia and periventricular white matter, and often involve the corpus callosum. Hypointensity is observed in T1 sequences and hypo-isointensity in T2 sequences, and restriction can be identified in diffusion sequences owing to high cellularity. Following the administration of IV contrast, intense and homogeneous enhancement can often be appreciated; however, enhancement may be mild or absent in low-grade tumors. Furthermore, "ring" enhancement can be identified in immunocompromised patients. Lastly, it exerts mass effects and may be associated with vasogenic edema.

Neoplastic cells identical to those found in systemic lymphomas are observed in the anatomopathological study. In contrast, no neoplastic cells are observed with CLIPPERS, but rather perivascular lymphocytic inflammation [13].

With regard to treatment, both PCNSL and CLIPPERS respond very well to steroids, with an objective clinical and radiological improvement. The main difference lies in early recurrence despite steroid treatment in the case of PCNSL.

Some authors have considered the possibility that CLIPPERS could be a premalignant lesion or an initial stage of primary CNS lymphoma [14].

Other differential diagnoses are Bickerstaff brainstem encephalitis, sarcoidosis, histiocytosis, vasculitis, and demyelinating diseases.

Treatment [15–20] begins with the administration of intravenous methylprednisolone at a dose of 1 g per day for five consecutive days. Following this initial phase, oral prednisolone should be introduced at a dosage of 1 mg/kg/day. This regimen is to be maintained until satisfactory clinical and radiological improvement is observed. During this period, it is essential to implement prophylactic measures to mitigate the risks of infections, osteoporosis, and weight gain.

Once the desired therapeutic response has been achieved, the oral prednisolone dosage may be gradually reduced; however, it is generally not advisable to go below 20 mg per 24 hours. At this stage, the addition of a steroid-sparing agent, such as methotrexate (MTX),

Table 2 Differential diagnoses of CLIPPERS syndrome

Diagnosis	Key characteristics	Differences from CLIPPERS
Infectious rhombencephalitis	Acute onset, fever, altered consciousness, MRI with heterogeneous lesions, edema	More acute onset, fever, possible altered consciousness, responds to antibiotics
Multiple sclerosis	Demyelinating lesions on MRI, multifocal involvement, oligoclonal bands in CSF	More extensive demyelinating lesions, white matter involvement, oligoclonal bands in CSF
Behçet's disease	Oral/genital ulcers, uveitis, thrombosis, multisystem involvement	Multisystem involvement with oral/genital ulcers and vasculitis, not just brainstem
CNS sarcoidosis	Granulomas on MRI, systemic or pulmonary involvement, elevated ACE	More diffuse granulomatous lesions, systemic involvement, elevated ACE
CNS lymphoma	Single or multiple lesions on MRI with homogeneous enhancement, diagnosed by biopsy	Focal or multifocal lesions with homogeneous enhancement, poor response to corticosteroids
CNS vasculitis	Multifocal involvement, systemic symptoms, diagnosed by angiography or biopsy	Clear vascular involvement, diagnosed by angiography, associated systemic symptoms
Paraneoplastic syndromes	History of cancer, presence of onconeural antibodies	Underlying cancer history, positive onconeural antibodies
Neuropsychiatric lupus	Systemic autoimmune disease, positive ANA, multisystem involvement	Diffuse CNS involvement, positive ANA, part of systemic autoimmune syndrome
Susac syndrome	Triad of encephalopathy, retinal artery occlusion, sensorineural hearing loss	Characteristic triad with encephalopathy, sensorineural hearing loss, and retinal lesions
Neurosyphilis	History of syphilis, positive serology, meningeal involvement	History of syphilis, positive serology, chronic meningeal involvement

CSF: cerebrospinal fluid; PCR: polymerase chain reaction; IgG: immunoglobulin G

azathioprine (AZA), or mycophenolate mofetil (MMF), is recommended to maintain disease control [21, 22].

This combined treatment should be continued for a minimum duration of 12 months. Thereafter, a gradual tapering of therapy may be considered, accompanied by regular MRI monitoring to evaluate for possible relapse.

Literature review and comparison with the current case

Since its initial description, various cases of CLIPPERS have been reported in the literature, generally presenting with a subacute onset of cerebellar and brainstem signs such as ataxia, dysarthria, diplopia, and facial paresis [23]. MRI findings have been characteristic, showing punctate lesions with perivascular enhancement in the posterior fossa, without swelling or diffusion restriction, and responding positively to corticosteroid treatment.

Compared with other published cases, our patient shares several clinical and radiological features typical of CLIPPERS syndrome, including diplopia, facial paresis, and ataxia, along with a good response to steroid therapy. However, some relevant particularities are noted:

Initial diagnosis of ischemic disease or neoplasia: in this case, the initial suspicion focused on neoplastic pathologies such as lymphoma or low-grade glioma owing to the atypical presentation of radiological findings in the initial MRIs performed at another center.

Absence of swelling or diffusion restriction on MRI: although characteristic lesions were observed in the posterior fossa, no swelling was evident, which could suggest a less aggressive phenotype of the disease.

Clinical course and therapeutic management: the response to corticosteroids was favorable and sustained, with a progressive reduction of lesions on follow-up MRI. A controlled tapering of prednisolone was implemented to prevent relapses, a strategy that has been suggested in recent reviews to improve long-term prognosis.

Contributions to existing knowledge

This case contributes to the understanding of CLIPPERS syndrome in several ways:

Importance of differential diagnosis with neoplasms: the initial diagnostic confusion with lymphoma or glioma highlights the need to consider CLIPPERS in patients with brainstem involvement and perivascular enhancement on MRI. In this case, the clinical course and good response to steroids were key to the definitive diagnosis.

Relevance of follow-up with high-resolution MRI: the initial MRI did not allow proper characterization of the lesions, emphasizing the importance of advanced imaging studies to improve diagnostic accuracy.

Corticosteroid tapering strategy: a gradual prednisolone tapering regimen was adopted with clinical and radiological monitoring, which could be a useful strategy to prevent relapses, in line with recent reports in the literature.

Limitations

Despite the detailed clinical, radiological, and therapeutic evaluation performed in this case, several limitations must be considered:

Absence of histopathological confirmation: The lack of a brain biopsy is the primary limitation of this case. Although the clinical presentation and brain MRI findings are highly suggestive of CLIPPERS, a definitive diagnosis requires histological confirmation of perivascular lymphocytic inflammation without evidence of neoplasia. In this case, the lesion location prevented the acquisition of a tissue sample, necessitating classification as probable CLIPPERS rather than definitive CLIPPERS.

Difficulty in generalizing management: the corticosteroid tapering strategy employed in this case was based on previous guidelines and literature reports; however, no standardized protocol exists for the optimal management of CLIPPERS.

Conclusion

In clinical practice, professionals faced with subacute brainstem syndromes characterized by ataxic gait, diplopia, and dysarthria should consider CLIPPERS as part of the differential diagnosis, especially when MRI shows punctate and patchy contrast-enhancing lesions predominantly located in the brainstem and cerebellum. Maintaining a high index of suspicion is essential, particularly in the absence of systemic involvement and after ruling out infectious, neoplastic, and autoimmune etiologies. Early initiation of corticosteroid therapy can lead to rapid clinical and radiological improvement, which supports the diagnosis and helps prevent further neurological deterioration. However, these findings are not specific and can also be seen in many other conditions (such as Bickerstaff brainstem encephalitis, sarcoidosis, histiocytosis, vasculitis, primary central nervous system lymphoma, and demyelinating diseases). Therefore, it is necessary to perform a thorough differential diagnosis to reach a diagnosis of exclusion. This makes CLIPPERS a true diagnostic challenge.

For long-term management, sustained immunosuppression is usually required to prevent relapses. Current literature recommends maintaining corticosteroid therapy at the lowest effective dose, in combination with a steroid-sparing agent (such as methotrexate, azathioprine, or mycophenolate mofetil), for at least 12 months, followed by gradual tapering. Regular follow-up with MRI is advised to detect subclinical disease activity. Although the prognosis is generally favorable with appropriate treatment, relapses may occur, especially if

immunosuppression is discontinued prematurely. Therefore, careful long-term follow-up is essential to optimize outcomes and minimize the risk of recurrence or progression.

Acknowledgements
There are no acknowledgements.

Author contributions
Juan Antonio Encarnacion conducted the information search, drafted the manuscript, and obtained consent forms. The other authors reviewed the manuscript and the bibliography.

Funding
Not applicable.

Data availability
Data available for readers and reviewers.

Declarations

Ethics approval and consent to participate
Accepted by the ethical committee of Virgen de la Arrixaca.

Consent for publication
Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests
Not applicable.

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Received: 28 January 2025 Accepted: 6 June 2025
Published online: 17 July 2025

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