DOI: https://doi.org/10.5114/ait.2025.147585

Cerebral vasculitis secondary to pneumococcal meningitis. Plasmapheresis as adjuvant therapy. Case report

Almudena Domínguez, Carmen Rosa Fraga, Roger Ayala, Pedro Conde, Daida García, Alberto Cereijo

University Hospital of the Nuestra Señora de Candelaria (HUNSC), Tenerife, Canary Islands, Spain

Anaesthesiol Intensive Ther 2025; 57, 1: e46–e49

Received: 26.12.2023, **accepted:** 28.11.2024

Dear Editor,

Cerebral vasculitis is a rare complication of pneumococcal meningitis, associated with high mortality and a substantial incidence of persistent neurological sequelae [1–5]. There is no standardized treatment for this cerebrovascular complication; however, it is evident that intervention should address not only the infectious trigger but also the complex underlying inflammatory cascade [1, 3]. Prophylactic corticosteroid therapy with dexamethasone, administered within the initial four days alongside antibiotic therapy, has been shown to reduce mortality and the incidence of deafness [4]. Nevertheless, there is a lack of necessary evidence to recommend corticosteroid therapy as a treatment within established post-infectious vasculitis [1, 5]. Additionally, there is no evidence regarding the use of immunosuppressants or apheresis in these cases [5]. Many specialists tend to adopt therapeutic regimens established for systemic or primary cerebral vasculitis [2].

A 29-year-old man with a history of childhood traumatic brain injury with post-traumatic cerebrospinal fluid fistula presented with a two-day history of headache before he was found at home with a low level of consciousness (Glasgow Coma Scale, GCS < 7). Orotracheal intubation was performed, and he was transferred to the referral hospital, where a plain computed tomography (CT) scan revealed a generalized reduction in the depth of sulci and fissures. The CT angiogram did not show any pathological findings. In the laboratory tests, there was an elevation in acute phase reactants (procalcitonin on admission of 40 ng mL^{-1}), and a fever of up to 39°C was noted during the examination. A chest X-ray without infiltrates, normal urine sediment, and cultures were obtained. A lumbar puncture was performed, yielding turbid fluid with biochemical evidence of bacterial meningitis. Treatment was initiated with dexamethasone and empiric triple antibiotic therapy. Subsequently, sensitive pneumococcus was cultured from the cerebrospinal fluid and from blood, prompting a switch to targeted treatment with cefotaxime. Despite being kept without sedation, the patient maintained a GCS score of 4 with pathologic extension of upper limbs in response to pain. He retained corneal and cough reflexes but lacked a threat reflex.

Given the poor clinical progression, a lumbar puncture was repeated at 72 hours, revealing aseptic fluid, and a follow-up CT scan was conducted, revealing multiple areas of hypodensity in subcortical and periventricular white matter with bilateral and symmetric involvement of semioval centres. A subsequent magnetic resonance imaging (MRI) scan (Figure 1) demonstrated multiple confluent focal areas of restricted diffusion bilaterally and symmetrically, predominantly in the frontal and bilateral periatrial regions, as well as in the semioval centres, consistent with cytotoxic damage, suggesting acute ischaemic lesions in the context of probable associated vasculitis.

CORRESPONDING AUTHOR:

Almudena Domínguez, University Hospital of the Nuestra Señora de Candelaria (HUNSC), Tenerife, Canary Islands, Spain, e-mail: almudenadg93@hotmail.com

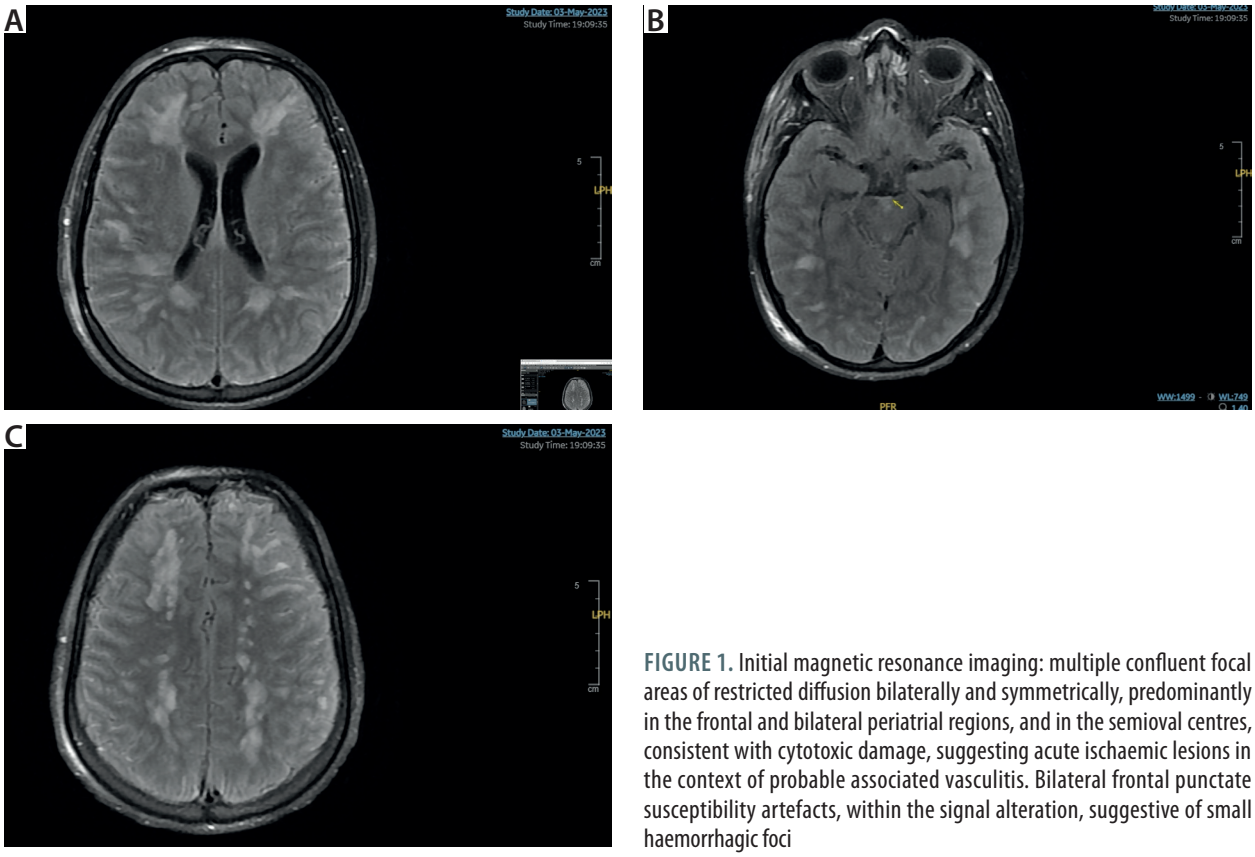

FIGURE 1. Initial magnetic resonance imaging: multiple confluent focal areas of restricted diffusion bilaterally and symmetrically, predominantly in the frontal and bilateral periatrial regions, and in the semioval centres, consistent with cytotoxic damage, suggesting acute ischaemic lesions in the context of probable associated vasculitis. Bilateral frontal punctate susceptibility artefacts, within the signal alteration, suggestive of small haemorrhagic foci

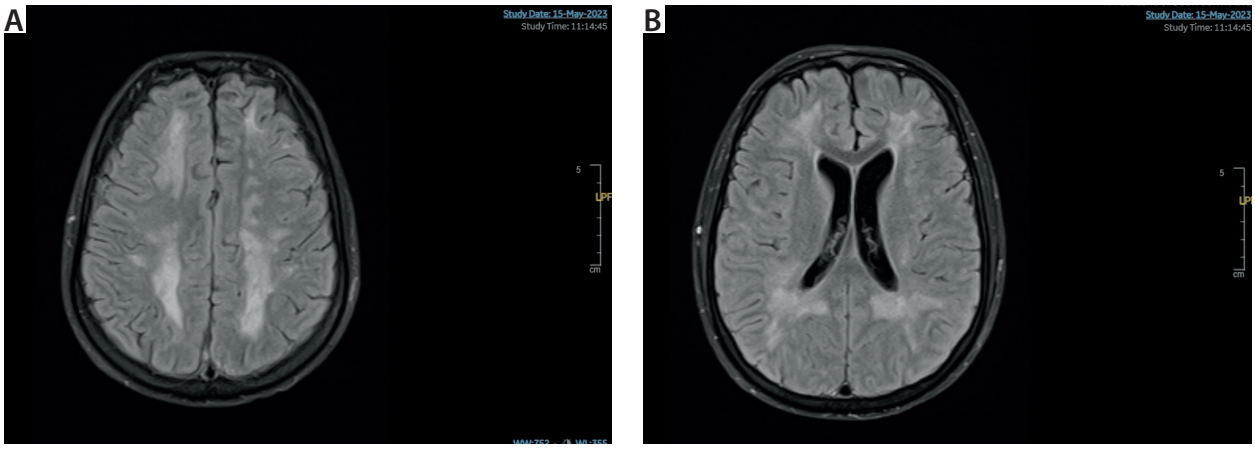

FIGURE 2. Magnetic resonance imaging on 16th day of hospitalisation

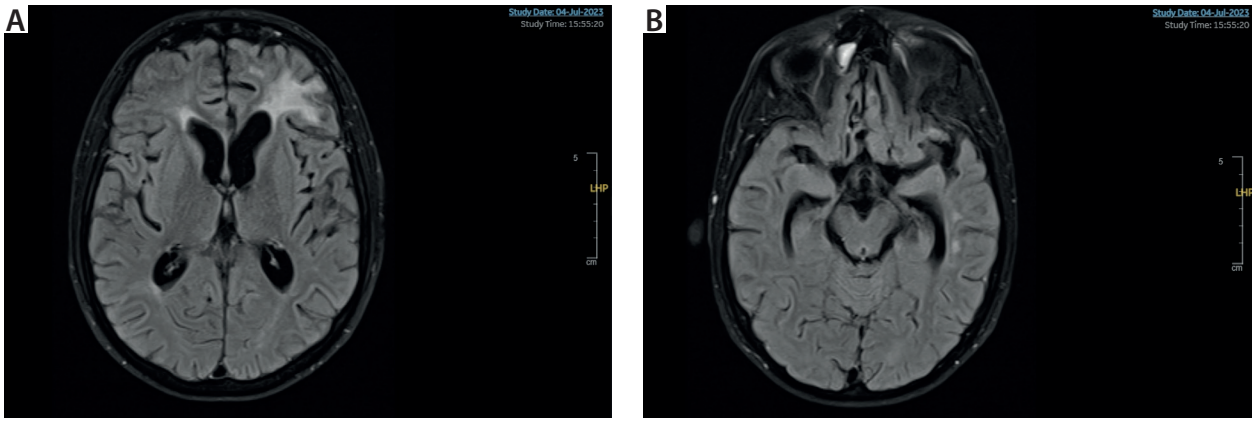

FIGURE 3. Magnetic resonance imaging after 2 months of hospitalisation

Additionally, bilateral frontal punctate susceptibility artefacts were observed within the signal alteration, suggestive of small haemorrhagic foci. A 3D time-of-flight vascular study showed normal morphology of the major vessels of the Willis polygon. No signs of cerebral venous thrombosis were noted. Leptomeningeal enhancement was observed in the context of meningitis. Cerebral angiography and biopsy were not performed.

An extension study was conducted, including a transthoracic echocardiogram and chest-abdomen-pelvis CT, to rule out embolic causes and vasculitis at other levels. The microbiological investigation was expanded, along with a comprehensive rheumatological analysis, all yielding negative results. Multiple electroencephalograms (EEGs) were conducted to rule out non-convulsive status epilepticus as the cause of coma.

The patient was diagnosed with post-infectious cerebral vasculitis due to pneumococcus, and treatment commenced with pulses of 1 g of methylprednisolone for 5 consecutive days, followed by 60 mg per day. By the 7th day, neurological evolution remained unfavourable, resembling the presentation upon admission. Subsequently, plasmapheresis was initiated after ruling out sepsis. A total of 10 cycles were performed with albumin replacement, with a volume of 3000 mL of replaced plasma in each session, spacing them every other day after the 5th session.

MRI was repeated on the 16th day of admission (Figure 2). Changes in signal characteristics were described on this imaging study. Most previously described lesions tended to confluence and increased in size on conventional sequences with normalization in diffusion sequences. Within the described lesions, punctate areas of higher signal intensity were observed in diffusion sequences with clear apparent diffusion coefficient restriction. Following intravenous contrast administration, multiple areas of intraparenchymal enhancement were observed, corresponding to previously described areas of diffusion restriction, without pathological leptomeningeal enhancement. New areas of paraventricular haemorrhagic content adjacent to the right lateral ventricle were noted, with undetermined clinical relevance. Increased visualization of sulci, fissures, and the ventricular system was noted. The findings were interpreted as evolution to chronicity of previously described lesions.

Progressively, the patient showed improvement in neurological examination, and successive control EEGs demonstrated resolution of encephalopathy. At the time of discharge from the Intensive Care Unit, 36 days after admission, the patient was conscious, partially oriented, followed simple commands, and exhibited coherent language. After two months of hospitalization, repeat MRI (Figure 3) showed radiological improvement in the described lesions and stability of haemorrhagic lesions. Increased visualization of sulci, fissures, and the ventricular system was noted.

Upon discharge from the hospital one month later, the patient was able to walk with assistance and was independent in basic activities of daily living, although there were neurocognitive deficits. At present, the patient is fully independent. However, mild cognitive impairment persists. Consent for publication of this case report was given by his legal guardians.

The pathophysiology of post-infectious cerebral vasculitis is poorly understood [6, 10]. It is postulated that following the initial treatment with bactericidal antibiotics, pneumococcal death and lysis occur, leading to the massive release of bacterial components and activation of the inflammatory cascade [10]. This process results in disruption of the blood-brain barrier, recruitment of leukocytes through the endothelium, and cellular damage [6]. However, many researchers believe that the pathophysiology could be more complex and might vary depending on the implicated pathogen [10]. Nevertheless, immune system activation following bacterial lysis in some cases gives rise to the development of cerebral vasculitis [10]. Biopsy confirmation, although the gold standard diagnostic method, is rarely performed [10].

Treatment aims to eradicate the infectious agent while also addressing the inflammatory cascade [6]. Only dexamethasone has demonstrated clinical efficacy as an adjuvant therapy alongside antibiotic treatment during the early days of the disease [8]. However, the impact of corticosteroids on ischaemic brain injury secondary to vasculitis is unknown [6]. Several isolated clinical cases suggesting their effectiveness have been published, including some describing clinical relapse after de-escalation or discontinuation of treatment [9]. Nevertheless, there is no evidence supporting their use, and even less literature supporting the administration of immunosuppressants or plasmapheresis in this context [6]. In fact, based on the literature search conducted, we did not find other clinical cases with a similar therapeutic approach.

We are uncertain whether the clinical improvement in our patient was due to prolonged corticosteroid use, therapeutic apheresis, or the natural course of the disease [6]. In the case of plasmapheresis being a valid therapeutic resource, it is unknown whether the effect could be attributed to the removal of an unknown circulating antibody or to the anti-inflammatory effect of plasmapheresis itself [6].

Our case suggests that plasmapheresis therapy could be beneficial for late complications of pneumococcal meningitis associated with vascular inflammation.

ACKNOWLEDGEMENTS

1. Assistance with the article: none.
2. Financial support and sponsorship: none.
3. Conflicts of interest: none.
4. Presentation: none.

REFERENCES

1. Chen X, Bai Y, Cui W, Wang Z, Zhang G, Xu Y, et al. Effects of B7-H3 on the inflammatory response and expression of MMP-9 in mice with pneumococcal meningitis. J Mol Neurosci 2013; 50: 146-153. DOI: 10.1007/s12031-012-9885-3.
2. Vergouwen MD, Schut ES, Troost D, van de Beek D. Diffuse cerebral intravascular coagulation and

cerebral infarction in pneumococcal meningitis. Neurocrit Care 2010; 13: 217-227. DOI: 10.1007/s12028-010-9387-5.
3. Khedher A, Sma N, Slama D, Fraj N, Hachfi W, Boussarsar M. Cerebral. vasculitis complicating pneumococcal meningitis. Eur J Case Rep Intern Med 2018; 5: 000819. DOI: 10.12890/2018_000819.
4. Engelen-Lee JY, Brouwer MC, Aronica E, van de Beek D. Pneumococcal meningitis: clinical-pathological correlations (MeninGene-Path). Acta Neuropathol Commun 2016; 4: 26. DOI: 10.1186/s40478-016-0297-4.
5. Koedel U, Frankenberg T, Kirschnek S, Obermaier B, Häcker H, Paul R, Häcker G. Apoptosis is essential for neutrophil functional shutdown and determines tissue damage in experimental pneumococcal meningitis. PLoS Pathog 2009; 5: e1000461. DOI: 10.1371/journal.ppat.1000461.
6. Huhn K, Lee DH, Linker RA, Kloska S, Huttner HB. Pneumococcal-meningitis associated acute disseminated encephalomyelitis (ADEM) – case report of effective early immunotherapy. Springerplus 2014; 3: 415. DOI: 10.1186/2193-1801-3-415.
7. Pugin D, Copin JC, Goodyear MC, Landis T, Gasche Y. Persisting vasculitis after pneumococcal meningitis. Neurocrit Care 2006; 4: 237-240. DOI: 10.1385/NCC:4:3:237.
8. Yokoyama D, Ikenouchi H, Miyamoto T, Yamamoto N, Endo K. Steroid rebound phenomenon as a cause of delayed cerebral vasospasm in post-splenectomy pneumococcal meningitis: a case report. Cureus 2023; 15: e33439. DOI: 10.7759/cureus.33439.
9. Malipiero U, Koedel U, Pfister HW, Levéen P, Bürki K, Reith W, Fontana A. TGFbeta receptor II gene deletion in leucocytes prevents cerebral vasculitis in bacterial meningitis. Brain 2006; 129 (Pt 9): 2404-2415. DOI: 10.1093/brain/awl192.
10. Jorens PG, Parizel PM, Demey HE, Smets K, Jadoul K, Verbeek MM, et al. Meningoencephalitis caused by Streptococcus pneumoniae: a diagnostic and therapeutic challenge. Diagnosis with diffusion-weighted MRI leading to treatment with corticosteroids. Neuroradiology 2005; 47: 758-764. DOI: 10.1007/s00234-005-1423-3.
11. Arif S, Liaqat J, Nawaz KH, Hashmat A. Focal hemispheric central nervous system vasculitis: an unusual form of primary angiitis. J Ayub Med Coll Abbottabad 2017; 29: 367.