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INVITED REVIEW

Glucocorticoid treatment for primary and secondary central nervous system vasculitis

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This manuscript was peer-reviewed by Dr. Ömer Karadağ

ABSTRACT

Although the first-line treatment of central nervous system vasculitis (CNSV) is glucocorticoids (GC), the duration and dose of GC is still unknown. Although CNSVs seem to be a disease limited to a single area, they are a heterogeneous group of diseases clinically, in terms of involvement pattern and course. Due to the highly heterogeneous nature of the disease, patient-specific determination of the initial dose of GC is essential. Considering the disease courses, it may be more appropriate to consider 1mg/kg oral GC treatment if small/distal vessels are involved and intravenous bolus GC treatment if large/proximal vessels are involved in primary-CNSVs. In secondary-CNSVs (Anca-associated vasculitis, Behçet's syndrome, Systemic Lupus Erythematosus) intravenous high dose GC treatment is recommended.

Keywords: central nervous system vasculitis, glucocorticoids, disease management.

Introduction

Central nervous system vasculitis (CNSV) can manifest as either primary or secondary forms. Primary central nervous system vasculitis (P-CNSV) specifically targets the central nervous system, while secondary central nervous system vasculitis (S-CNSV) is a result of systemic disorders affecting the central nervous system.

To avoid mistakes in diagnosing and treating vasculitis in the central nervous system, it is important to look at other conditions that can affect the system, like systemic vasculitis, infection, or connective tissue disease.

What is the primary central nervous system vasculitis?

Primary central nervous system vasculitis is a rare condition that only affects the brain and spinal cord. The median age of diagnosis is 47 years, with 50% of the patients being diagnosed between the ages of 37 and 59 [1]. It is observed with equal frequency in males and females [2].

Previous case reports have characterized P-CNSV as a lethal disease that does not respond to immunosuppressive therapy. However, recent studies have shown that the disease consists of distinct subtypes and that treatment responses differ depending on the extent of clinical involvement [1,3,4].

The symptoms of P-CNSV can manifest across a broad range, encompassing chronic headache, cognitive dysfunction, and ischemic findings [5,6]. A specific algorithm for diagnosis is not available; however, a thorough examination of the patient's medical history and physical condition, along with imaging and laboratory tests, as well as a biopsy of the central nervous system, are crucial for accurate diagnosis [5,7].

Calabrese and Mallek established diagnostic criteria for primary central nervous system vasculitis in 1988. This criterion briefly included the items listed below [8,9];

- The presence of neurological deficits that are not explicable by another disease
- Vasculitis affecting the central nervous system as revealed by histopathology or angiography
- There is no systemic illness that would resemble the results

Birnbaum and Hellmann updated the diagnostic criteria in 2009. They incorporated the definitions of definite and probable into the criteria. Definite P-CNSV necessitates a histopathological diagnosis, whereas Probable P-CNSV requires angiographic evidence of a highly likely disease along with abnormal magnetic resonance imaging (MRI) and cerebrospinal fluid (CSF) findings [9, 10].

P-CNSV is a complex disease characterized by multiple subgroups rather than just one condition entity. These subgroups have different clinical profiles and treatment responses. Therefore, it is important to distinguish them. Some of the subgroups are [11]:

Angiography negative biopsy positive subgroup: Only arterioles and arteries of extremely small diameter are affected. Responds favorably to treatment. The prognosis is favorable [11,12].

Subtype exhibiting substantial leptomeningeal enhancement on MRI: Their clinical presentation is acute. The biopsy reveals the presence of granulomatous vascular inflammation. Typically, patients exhibit a positive response to glucocorticoid therapy [11,13].

Rapidly progressive primary CNS; Rapidly progressive P-CNSV is the most severe form of P-CNSV. This cohort of patients exhibits poor response to glucocorticoids and conventional immunosuppressive treatment. The disease is fatal, despite the administration of high-dose glucocorticoids [11,14].

Solitary tumour-like mass lesion; Immunosuppressive therapies or surgical procedures may be favorable to the patient [11,15].

What is the appropriate dosage of glucocorticoids for treating P-CNSV?

P-CNSV is a rare condition. There is a lack of randomized controlled trials that provide guidance on the appropriate dosage of glucocorticoids for administration. The most important data originates from the patient cohorts studied by Salvarani et al., Over a 35-year period, Salvarani et al., analyzed the treatments and outcomes of 191 P-CNSV patients. For 47% of the patients, induction therapy was combined with intravenous pulse glucocorticoid therapy.Three-fourths of the patients had been administered five or less doses of 1 g of methylprednisolone. Nevertheless, there was no evidence to support the notion that administering this treatment initially provided any benefit. The study is performed retrospectively, and patients with unfavorable prognostic findings may have undergone more intensive treatment. Therefore, when selecting treatment, it is essential to consider both the patient's involvement characteristics and their general characteristics [16].

Patient glucocorticoids strategies vary depending on whether the small/distal vessels or large/proximal vessels are affected. The group with small vessel involvement recommended to be given 1 mg/kg of oral prednisolone daily. The group with large vessel involvement should be administered a methylprednisolone bolus at a dosage of 1g per day for 3-5 days, followed by a daily dose of 1mg/kg [17].

Secondary central nervous system vasculitis

Secondary central nervous system vasculitis refers to the development of central nervous system vasculitis as a result of a systemic inflammatory or infectious condition.

ANCA-associated vasculitis, Behçet syndrome, systemic lupus erythematosus, infectious causes (Streptococcus pneumoniae, Neisseria meningitidis, Mycobacterium tuberculosis, Treponema pallidum, and Borrelia burgdorferi), and malignancies are a few examples of conditions that may affect the central nervous system.

ANCA-Associated Vasculitis

Currently, there is a lack of conclusive data regarding the optimal glucocorticoid dosage for treating

neurological complications associated with ANCA-associated vasculitis. After reviewing the conducted studies, it is worth noting the recommendation to begin treatment with high-dose glucocorticoids.

In cases of nervous system involvement in ANCA-associated vasculitis, immediate intervention is required. There are two types of treatment: induction and maintenance. In addition to the immunosuppressive therapies, administer a remission induction regimen of 1 mg/kg prednisone for approximately 30 days, followed by the initiation of a dose reduction plan. Low-dose glucocorticoid therapy and an appropriate immunosuppressive therapy are recommended in maintenance treatment [18-20].

According to some publications, the first treatment should be a pulse intravenous methylprednisolone dose of 1 gram per day for three days, followed by a reduction to 1 mg/kg of oral glucocorticoid therapy. Additionally, they recommend reducing the glucocorticoid dose to 7.5 to 10 mg/day over a period of three to five months [10,21-23].

The 2021 ACR/vasculitis Foundation ANCA-associated vasculitis guideline suggests the use of intravenous pulse or high-dose oral glucocorticoids [24].

Behcet's Syndrome

Behçet syndrome (BS) is a disease of the blood vessels. Biopsies of people with Neuro Behçet's disease showed perivasculitis instead of vasculitis [25-27].

While there is no definite data on the specific glucocorticoid treatment for BS, there are numerous publications available to provide guidance. For cerebral venous sinus thrombosis(CVST), treatment is typically effective, with the recommendation to use high-dose glucocorticoids [28-30].

Parenchymal involvement is more resistant to treatment than CVST. IV methylprednisolone treatment is recommended for a period of 5-10 days in cases of parenchymal involvement. In addition, it is advised to gradually decrease the glucocorticoid dosage over a period of 3-6 months, depending on the patient's condition [28,30]

Systemic Lupus Erythematosus

Systemic lupus erythematosus can lead to severe central nervous system complications, such as myelitis and cerebritis. For central nervous system involvement in SLE, intravenous pulse methylprednisolone therapy is recommended [31].

Author contribution

Study conception and design: EU; draft manuscript preparation: EU. All authors reviewed the results and approved the final version of the manuscript.

Funding

The authors declare that the study received no funding.

Conflict of interest

The authors declare that there is no conflict of interest.

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