Scientific Research Publishing

Open Journal of Rheumatology and Autoimmune Diseases, 2026, 16(2), 69-71
https://www.scirp.org/journal/ojra
ISSN Online: 2164-005X
ISSN Print: 2163-9914

Prevention of Refractory Headache Secondary to Immunoglobulins Using Diuretics: A Case Report

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How to cite this paper: Rodado Alabau, E., Gabarró Llatge, N., Martín Ozaeta, G. and Moya Valdés, A. (2026) Prevention of Refractory Headache Secondary to Immunoglobulins Using Diuretics: A Case Report. *Open Journal of Rheumatology and Autoimmune Diseases*, **16**, 69-71.
https://doi.org/10.4236/ojra.2026.162008

Received: January 13, 2026
Accepted: March 16, 2026
Published: March 19, 2026

Abstract

Immunoglobulins (IG) are essential in the treatment of autoimmune diseases, although their adverse effects may force treatment withdrawal. We describe the case of a patient with immune-mediated necrotizing myopathy (IMNM) who developed severe refractory headache after IG infusions. Based on the reproducible chronology of symptoms and clinical signs of hypervolemia, a preventive strategy using loop diuretics was implemented. Oral furosemide administered during the risk period prevented the onset of IG-related headache in subsequent cycles, with excellent clinical response. This case highlights the importance of addressing IG-related adverse effects and suggests that short courses of diuretics may be considered in selected patients with reproducible headache patterns.

Keywords

Intravenous Immunoglobulin, Headache, Diuretics, Immune-Mediated Necrotizing Myopathy, Adverse Effects, Case Report

1. Introduction

Immunoglobulins (IG) are essential in the treatment of autoimmune diseases [1], although their adverse effects may force treatment withdrawal in a significant number of cases [2]. While the anti-inflammatory and immunomodulatory effects of high-dose IG are well-documented across multiple approved and off-label indications [3], management of its side effects remains a challenge. We present

the case of a patient with immune-mediated necrotizing myopathy (IMNM) whose refractory headache after IG infusion resolved with a preventive approach based on the chronology of symptoms.

2. Case Presentation

A 45-year-old woman with IMNM and a 5-year history of chronic headache, which began after high-dose corticosteroid therapy. Her medical history included a stable left temporal multinodular and vacuolating neuronal tumor (MVNT). Recent radiologic characterizations of MVNT suggest these are typically benign, non-progressive lesions [4]; in our patient, follow-up brain MRI during acute headache episodes confirmed the stability of the lesion with no perilesional edema, ruling it out as the trigger for the acute exacerbations.

The patient was refractory to multiple therapeutic lines for her headache (amitriptyline, triptans, and valproate, among others). Due to persistent inflammatory activity of her IMNM, monthly IG treatment was initiated (2 g/kg). She initially received Flebogamma DIF®, which intensified her headache to a VAS 10, requiring hospitalization and sedation. Treatment was switched to Privigen®, but severe headache persisted despite better gastrointestinal tolerance. The patient identified a specific pattern: symptoms peaked on day +8 and lasted until day +18, accompanied by slightly elevated blood pressure and mild ankle edema.

Based on the clinical suspicion of transient cerebral edema due to hyperviscosity or volume overload—a mechanism also implicated in more severe conditions like posterior reversible encephalopathy syndrome (PRES) [5]—we opted for a short course of loop diuretics. Oral furosemide 80 mg/day was administered from day +2 to day +7 of the cycle. From the first cycle using this regimen, the patient did not experience IG-related headache again. Muscle cramps occurred on day +5 but resolved with oral potassium gluconate (20 mEq/day).

3. Discussion

The repeated clinical response suggests that preventive treatment with diuretics avoided the onset of headache. A key differential diagnosis is IgIV-associated aseptic meningitis, which typically presents with fever and nuchal rigidity [6]. However, our patient lacked these signs, pointing instead toward a hemodynamic mechanism. Although the 2023 AANEM consensus highlights the importance of IG in neuromuscular disorders [7], it also emphasizes that side effects significantly impact quality of life.

A limitation of this report is the lack of objective intracranial pressure (ICP) measurements during the peak headache phase. However, our hypothesis of transiently increased ICP secondary to cerebral edema is supported by the therapeutic success. Implementing therapeutic strategies that make these effects more tolerable ensures patient well-being and guarantees the continuity of irreplaceable treatments.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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