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CASE SERIES

The Utility of IVIG in the Management of Autoimmune Encephalitis: A Retrospective Case Series

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Abstract

Autoimmune encephalitis (AE) involves inflammation of the brain parenchyma due to autoantibodies targeting neuronal cell surfaces or synaptic proteins [1]. It is a rapidly progressive disorder and can lead to significant morbidity, prolonged hospital stays, and possible mortality. Intravenous immunoglobulin (IVIG) is a treatment for AE that may be used when other acute treatments are ineffective or contraindicated. It has been proven useful in many autoimmune disorders [2-5], though is underutilized in AE due to lack of controlled studies. We report a retrospective case series, in which the use of IVIG was a life-saving measure for two patients with autoimmune encephalitis. These cases demonstrate that IVIG may be an important treatment option to consider for both acute and maintenance management of AE.

Introduction

Autoimmune encephalitis (AE) involves inflammation of the brain parenchyma due to autoantibodies targeting neuronal cell surfaces or synaptic proteins [1]. It is a rapidly progressive disorder with various neurological symptoms [6] that can lead to significant morbidity, a prolonged hospital stay with its own set of complications, and possibly mortality. Intravenous immunoglobulin (IVIG) as a treatment for AE that may be used when other acute treatments are ineffective or contraindicated. It is derived from the healthy donor plasma [7] and neutralizes the pathogenic antibodies, modulating lymphocytic activation and effector function [8]. It has been proven useful in many autoimmune disorders [2-5], though unfortunately due to lack of controlled studies, may be underutilized in AE. Early intervention with appropriately-dosed IVIG can be lifesaving, and monthly IVIG may be a safe, noninvasive alternative to plasma exchange or chronic immunosuppressive agents.

In this retrospective case series, we report two patients with autoimmune encephalitis who were responsive only to IVIG acutely and required maintenance IVIG therapy to control their AE.

Case # 1: NMDA-R AE

A 25-year-old previously healthy black female was admitted as a transfer from a psychiatric hospital with acute psychosis refractory to 3 different antipsychotic medications, insomnia, dysautonomia and new-onset seizures requiring intubation. Initial EEG showed status epilepticus requiring multiple antiseizure medications. MRI Brain was remarkable for mild diffuse leptomeningeal enhancement (Figure 1). Labs were significant for 1:1280 NMDA-R serum and 1:80 CSF titer. Plasma exchange was initiated along with 1g IV methylprednisolone for 5 days, followed by 60 mg prednisone daily. No clinical improvement was noted. Rituximab was initiated on hospitalization day 19 with minimal response. Hospital course was further complicated by multiple infections, precluding the use of plasma exchange and steroids. No obvious ovarian teratoma was noted on initial pelvic ultrasound. Patient was eventually started on IVIG at 2 g/kg (actual weight) divided over 5 days on 28th day of admission. Significant clinical improvement was noted on day 3 of IVIG. She received 4 additional courses of IVIG every 5 weeks

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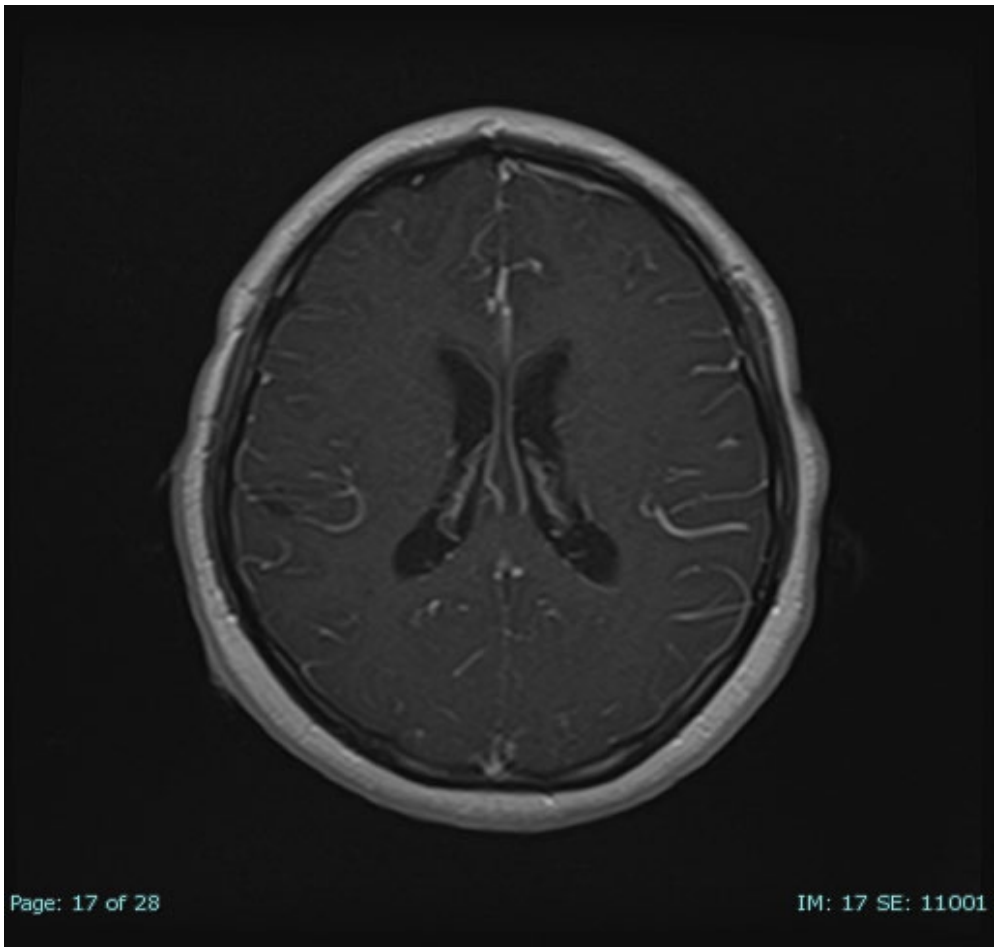

Figure 1: T1-weighted image with contrast revealing diffuse leptomeningeal enhancement.

as inpatient and then continued IVIG at home at a dose of 1 g/kg divided over 3 days every 28 days. She was eventually able to regain her independence and employment with resolution of her psychosis.

Currently, she is 2 years post-admission. Her day-to-day functioning has returned close to baseline, though her learning ability, processing speed, and memory are still affected, and a new diagnosis of narcolepsy has recently been made.

Case # 2: LGI-1 Mediated AE

A 74-year-old female was initially admitted to the hospital for altered mentation and new-onset seizure. MRI Brain showed right medial temporal lobe hyper intensity without enhancement (Figure 2). EEG showed periodic lateralized discharges over the right hemisphere. Initially, she was covered broadly with antibiotics and antivirals for suspected encephalitis and showed some improvement clinically, but without complete return to baseline. Infectious work up returned negative. She was ultimately given a course of IVIG with clinical improvement, but still had significant cognitive problems. Hospital stay was further complicated by lower extremity DVT, hyponatremia from SIADH, and sepsis. She was eventually discharged to subacute rehabilitation 3 weeks later and ultimately to home.

Unfortunately, patient's memory and cognition continued to worsen, and her hyponatremia recurred. Concurrently, serum returned positive for VGKC antibody with Leucine- Rich Glioma Inactivated protein 1 (LGI-1) antibody. Despite the diagnosis of LGI-1 encephalitis, IVIG was not approved, causing irreversible and persistent deterioration of patient's clinical status. Four months after her initial hospitalization, she was readmitted with status epilepticus and sepsis.

MRI brain showed progression of inflammation of left temporal lobe along with new mild atrophy of the right temporal lobe. IVIG was started at 2 g/kg divided over 5 days with significant improvement in her mentation and resolution of status epilepticus. Some of her seizures were consistent with fascio-brachial dystonic seizures typical of LGI-1 encephalitis. She required multiple antiseizure medications for optimal seizure control.

IVIG authorization request was resent to her insurance, but despite multiple appeals, peer to peer reviews, and even a case review by the court, her IVIG was not approved as outpatient. She required multiple readmissions for seizures and altered mentation, necessitating IVIG administration over several months.

Patient eventually switched insurance, and with monthly IVIG at 1 g/kg doses, her clinical condition

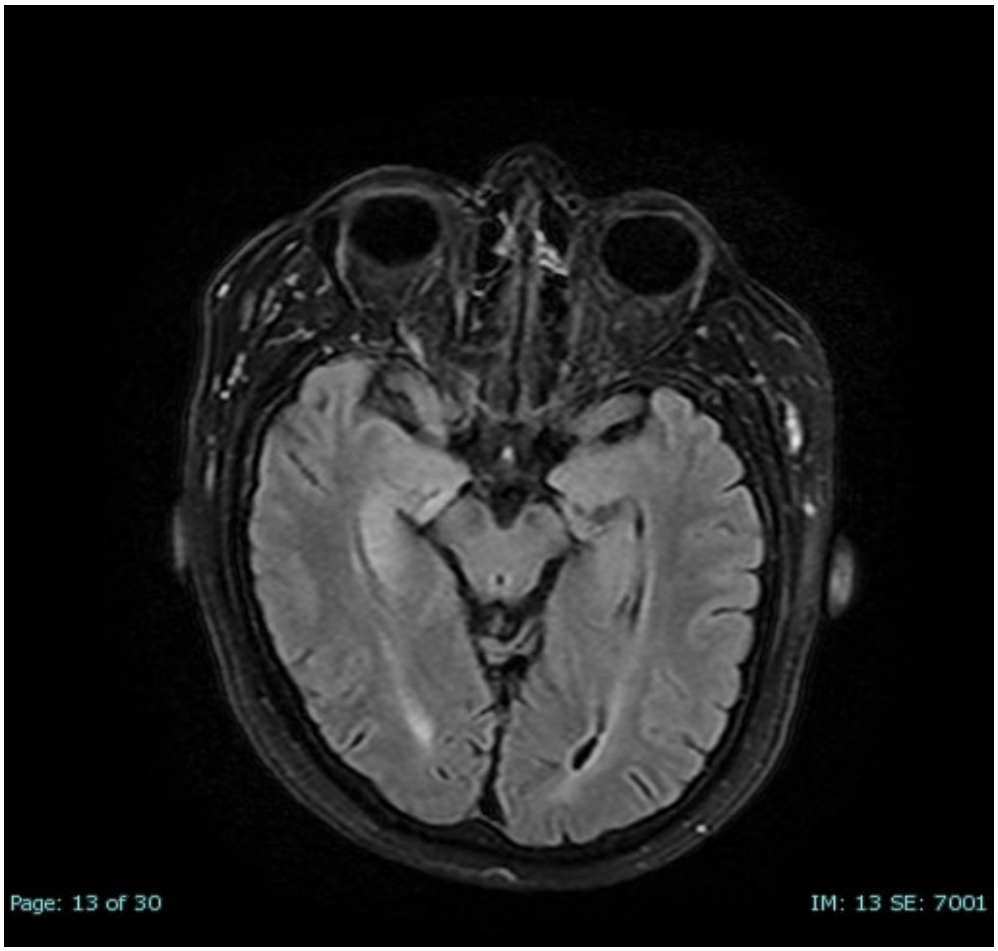

Figure 2: T2 FLAIR revealing medial right temporal lobe hyper intensity without enhancement.

started to improve, though she continues to have severe memory and cognitive deficits to this day. The patient was eventually cleared for the use of Rituximab, and currently continues Rituximab in addition to IVIG.

Currently, about 2-years after her initial presentation, this patient still has significant difficulty with ambulation and has very limited short-term memory. Repeat MRI Brain, nearly two years after initial presentation, showed significant progression of bilateral temporal lobe atrophy over time without evidence of ongoing inflammatory changes (Figure 3).

Discussion

We describe two patients with autoimmune encephalitis, both with aggressive and complicated clinical courses. Ongoing sepsis and recurrent infections precluded the use of immunosuppressive therapy with corticosteroids or longer-term immunosuppressive options, such as rituximab, necessitating monthly IVIG both in the hospital and outpatient setting.

Corticosteroids, which decrease immune cell function and inflammation [9], are typically first-line for acute treatment of autoimmune encephalitis. However, they are associated with side effects, including increased risk of infection and psychiatric symptoms, such as agitation and psychosis, which can already be a manifestation of autoimmune encephalitis [9]. Often, corticosteroids alone are insufficient to combat the robust autoimmune response, thus are given in combination with plasma exchange or IVIG. However, not all patients are responsive to plasma exchange, and it can be contraindicated in hemodynamically unstable patients [10]. In such patients, IVIG can be especially useful not only in the acute setting, but also in the outpatient setting to allow recovery post-hospitalization without increasing the risk of potentially lethal infections and related complications.

Delays in transitioning to maintenance outpatient IVIG can be detrimental and lead to a protracted clinical course, seizure breakthrough and worsening hyponatremia, resulting in repeated ICU admissions, continued deconditioning, and increased risk of hospitalization-related complications. As demonstrated in our patient of the second case, delays in treatment with IVIG, as well as under dosage using 1 g/kg, lead to repeated admissions and likely irreversible neurologic damage. We therefore argue in cases where patients experience multiple hospital-related complications, outpatient IVIG should be made more easily available for 6-12 months to allow recovery, prevent readmissions, eventually bridging patients to immunosuppressive therapy. Monthly IVIG in such cases could not only

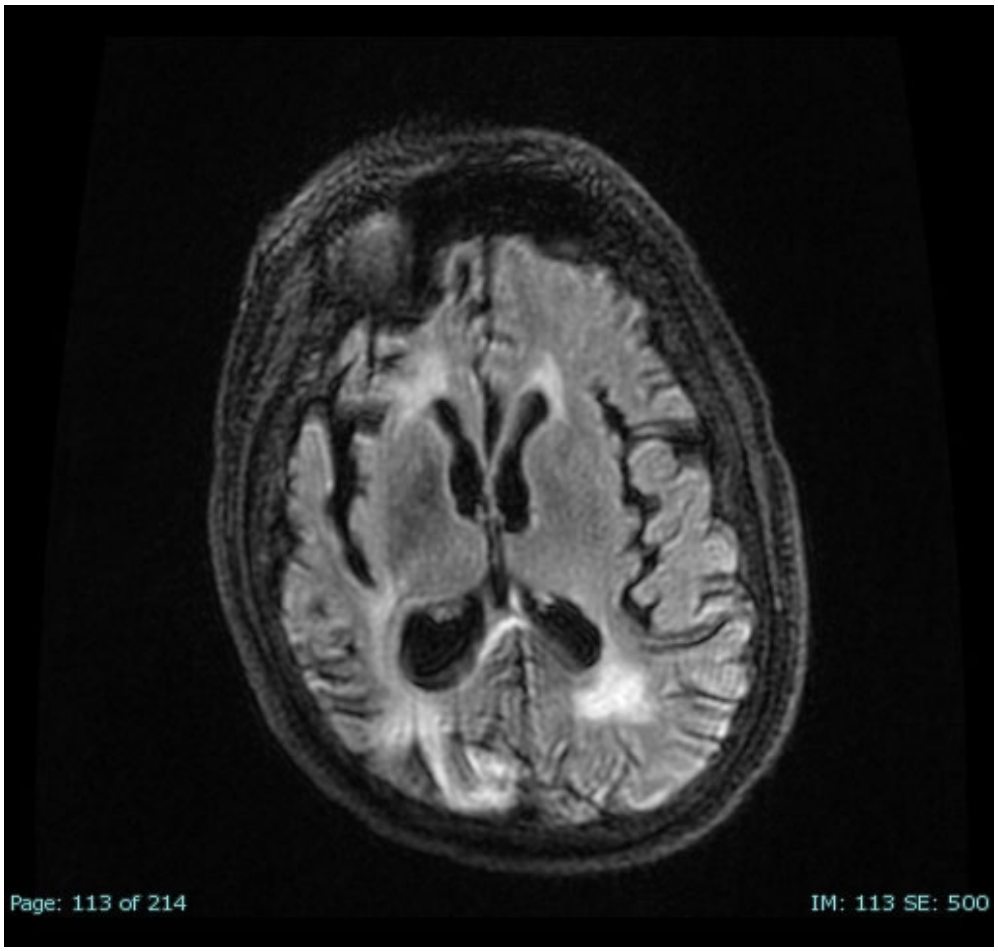

Figure 3: T2 FLAIR revealing extensive atrophy bilateral hemisphere with bilateral medial temporal atrophy and enhancement.

reduce medical costs associated with readmissions, but also prevent further damage related to the pathogenic autoantibodies. Furthermore, we posit that doses of 2 g/kg be used based on actual weight, as under dosing may lead to more damage and result in long-term sequelae, such as cognitive dysfunction or sleep disorders.

Unfortunately, IVIG is not commonly used in the hospital setting, and even less so in the outpatient setting. Due to the aggressive nature and the rarity of the disease, there is a lack of randomized controlled trials and evidence for its use in AE, thus there is also difficulty with insurance approval. We therefore present these cases to add to the growing literature on the benefits of using IVIG both acutely and for maintenance therapy, and its role in allowing for recovery and promoting survival in patients with AE.

In conclusion, physicians should consider early and prompt treatment with IVIG in severe cases of AE, as it may be crucial in reducing the disease morbidity and mortality. We also argue if shown to be effective in the inpatient setting, IVIG should also be continued in the outpatient setting as monthly maintenance therapy.

References

1. Dalmau J, Graus F (2018) Antibody-mediated encephalitis. N Engl J Med 378: 840-851.
2. Kazatchkine MD, Kaveri SV (2001) Immunomodulation of autoimmune and inflammatory diseases with intravenous immune globulin. N Engl J Med 345: 747-755.
3. Lunemann JD, Nimmerjahn F, Dalakas MC (2015) Intravenous immunoglobulin in neurology-mode of action and clinical efficacy. Nat Rev Neurol 11: 80-89.
4. Shimoni Z, Bulvik S, Froom P (2013) Intravenous immune globulin in autoimmune and inflammatory diseases. N Engl J Med 368: 776-777.
5. Morales Ruiz V, Juarez Vaquera VH, Rosetti Sciutto M, Sanchez Munoz F, Adalid Peralta L (2022) Efficacy of intravenous immunoglobulin in autoimmune neurological diseases. Literature systematic review and meta-analysis. Autoimmun Rev 21: 103019.
6. Graus F, Titulaer MJ, Balu R, Benseler S, Bien CG, et al. (2016) A clinical approach to diagnosis of autoimmune encephalitis. Lancet Neurol 15: 391-404.
7. Galeotti C, Kaveri SV, Bayry J (2017) IVIG-mediated effector functions in autoimmune and inflammatory diseases. Int Immunol 29: 491-498.
8. Bayry J, Thirion M, Misra N, Thorenoor N, Delignat S, et al. (2003) Mechanisms of action of intravenous immunoglobulin in autoimmune and inflammatory diseases. Neurol Sci 24: S217-S221.
9. Shin YW, Lee ST, Park KI, Jung KH, Jung KY, et al. (2018) Treatment strategies for autoimmune encephalitis. Ther Adv Neurol Disord 11: 1756285617722347.
10. Mokrzycki MH, Kaplan AA (1994) Therapeutic plasma exchange: Complications and management. Am J Kidney Dis 23: 817-827.