ISSN: 2692-5370
Anaesthesia & Surgery Open Access Journal
DOI: 10.33552/ASOAJ.2025.06.000632
Iris Publishers

Case Report

Rare Neurological Manifestation Under Hydroxychloroquine in a Patient with Systemic Lupus Erythematosus (SLE): A Case Report

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Received Date: February 25, 2025

Published Date: March 04, 2025

Abstract

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease that can lead to central nervous system involvement, including seizures, which occur in 2-8% of patients. The pathogenesis of seizures in SLE may involve immune-mediated mechanisms or direct neuronal injury. In some cases, patients with antiphospholipid antibodies or certain genetic predispositions may be more susceptible to seizures. Accurate diagnosis requires excluding other causes such as vasculitis or thrombosis, with neuroimaging playing a key role. This review examines the prevalence, clinical characteristics, and treatment strategies for seizures in SLE patients. We report the case of a 17-year-old female with SLE who developed tonic-clonic seizures after initiating hydroxychloroquine therapy, suggesting a potential drug-induced cause. Although hydroxychloroquine is generally safe, it may cause seizures in predisposed individuals. The review discusses the role of antimalarial medications in inducing seizures, the difficulties in distinguishing between neuropsychiatric manifestations of SLE and drug side effects, and the importance of individualized treatment. Early recognition and personalized management of seizures in SLE are essential to improve long-term outcomes and quality of life for patients.

Introduction

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease that can affect the central nervous system, either through direct neuronal damage, vascular injury, or by immune-mediated mechanisms induced by the production and deposition of immune complexes. The prevalence of explicit epilepsy episodes in patients with SLE ranges from 2% to 8%. In some cases, patients with positivity for antiphospholipid antibodies or anti-β2 glycoproteins are more prone to seizures compared to seronegative patients. Other at-risk individuals may have genetic abnormalities encoding ion channels. Exclusion of vasculitis or thrombosis is essential for accurate treatment, and imaging studies with alternative sequences are mandatory in SLE patients who present with seizures. Several aspects of seizures in SLE remain unclear. In this literature review, we analyzed published information on the prevalence, pathogenesis, clinical characteristics, diagnosis, and treatment of patients with SLE who experience seizures, aiming to provide useful information for rapid diagnosis and individualized treatment.

Patient and Observation

We report the case of a 17-year-old woman with disseminated lupus erythematosus (SLE), with a clinical history of complex partial

seizures, who developed a tonic-clonic seizure after receiving hydroxychloroquine for 2 weeks at a dose of 200 mg/day (5 mg/kg). The absence of previous similar episodes and the lack of recurrence after discontinuation of the medication over the following months, along with the short latency after administration and favorable short-term evolution, led to the suspicion of a potential role of the drug in the development of the isolated seizure. It is possible that hydroxychloroquine may cause tonic-clonic seizures in predisposed individuals.

Discussion

Hydroxychloroquine sulfate is a widely used medication for the treatment of mild SLE. Patients with inactive SLE experience fewer exacerbations of the disease when hydroxychloroquine therapy is continued [1]. In patients with SLE, treatment can typically be continued for a longer period [2], and discontinuation is primarily due to insufficient disease control rather than toxicity [3]. In a prospective placebo-controlled trial of hydroxychloroquine for arthropathy in 71 patients with mild SLE, only two patients withdrew from the study due to severe drug reactions (rash and dizziness) [1]. Hydroxychloroquine remains an important part of therapy for SLE [4].

We report the case of a young woman with SLE characterized by cutaneous, cardiac, and hematological involvement, along with complex partial seizures. No signs or symptoms of active SLE were detected. The patient had normal glucose-6-phosphate dehydrogenase (G6PD) levels, and there was no family history of epilepsy. No other side effects related to hydroxychloroquine, such as ototoxicity, were identified.

We propose that hydroxychloroquine may have played a crucial role in the presentation of the tonic-clonic seizures in our patient. Firstly, the chronological criteria were met: short latency after administration, favorable short-term evolution, and no relapse in the following months. The medical history was negative for previous tonic-clonic seizures or other potential triggering agents. Neuro-imaging, including CT, MRI, and PET scans, was negative. The electroencephalogram (EEG) trace was not different from previous recordings. We could not exclude a new neurological manifestation of SLE, although it is also possible that CNS involvement by SLE may have exacerbated the risk of CNS toxicity associated with hydroxychloroquine.

In our internal medicine service (a tertiary referral center), approximately 30% of patients with SLE receive hydroxychloroquine (including those with neurological involvement). None of them experienced epilepsy or other serious problems.

We reviewed the literature on antimalarial medications and seizures. Various neuropsychiatric events have been reported following the use of chloroquine [5]. In formal treatment, the occurrence of seizures is rare but not impossible [6-8].

In autoimmune rheumatic diseases, side effects from chloroquine have been described in 15 out of 100 patients with rheumatoid arthritis and SLE. These included neurological effects, such as headaches, confusion, ototoxicity, and polyneuropathy, but not epilepsy. Side effects are related to serum drug concentrations, not the total dose administered [9]. Hydroxychloroquine and chloroquine likely have similar mechanisms of action and similar toxicities. The differing incidence of ocular toxicity between chloroquine and hydroxychloroquine may be due to the addition of the hydroxy group, which limits the permeability of the blood-retinal barrier [10]. The lower incidence of CNS side effects with hydroxychloroquine may also be due to the permeability of the blood-brain barrier (which differs).

To our knowledge, no previous reports have described the adverse effects we observed. We emphasize the difficulties in differential diagnosis between neuropsychiatric manifestations in patients with SLE. We recommend using hydroxychloroquine with caution in SLE patients with a history of epilepsy, and perhaps even in those with neurological involvement. Input from other colleagues experienced in this field would be appreciated.

Seizures may be an early manifestation of SLE, often characterized by focal seizures. Neuro-imaging with MRI, EEG recording, and cerebrospinal fluid (CSF) analysis can aid in diagnosis. Treatment should be individualized, considering disease activity and seizure recurrence.

Although there is no consensus on the therapeutic approach for seizures in SLE, many authors emphasize the use of immunosuppressive medications. The addition of antiepileptic drugs (AEDs) is recommended only for patients with recurrent seizures (2 events within 24 hours) and for those with structural abnormalities on MRI, focal neurological signs, focal disturbances of consciousness, and epileptiform spikes on EEG.

Conclusion

As we advance in understanding the pathogenic role of inflammatory cells and autoantibodies in the genesis of seizures, new therapeutic targets may be discovered. In the meantime, prompt recognition and personalized treatment could impact the reduction of comorbidities associated with the chronic administration of antiepileptic drugs, leading to better long-term outcomes in terms of functionality and quality of life.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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