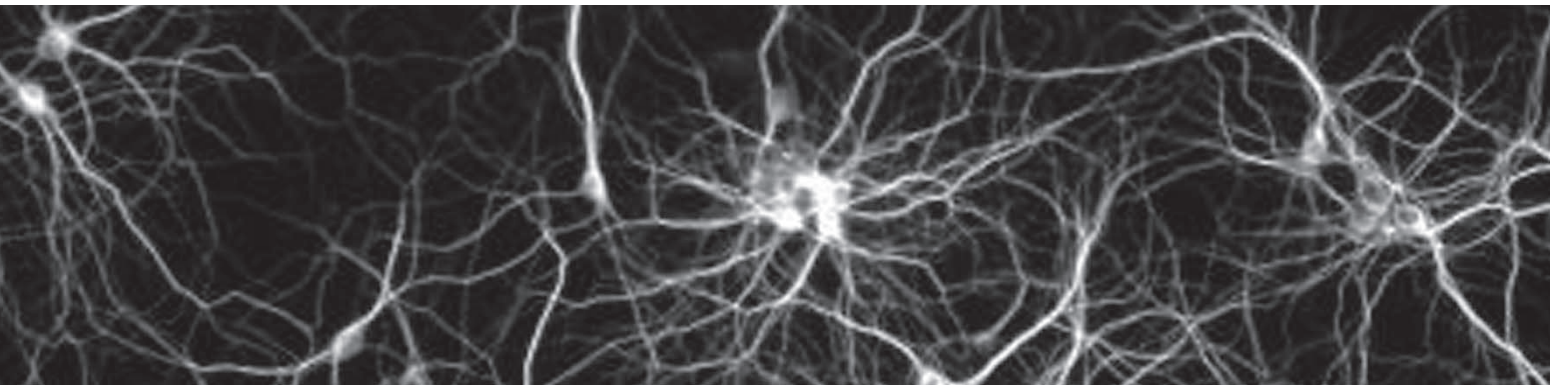

# Juvenile absence epilepsy and myasthenia gravis: a case report

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ABSTRACT – *Objectives:* Juvenile absence epilepsy (JAE) is a genetic generalized epilepsy syndrome that typically starts in adolescence and is characterized by absence seizures and generalized tonic-clonic seizures (GTCS). Myasthenia gravis (MG) is an antibody-mediated autoimmune disease that affects the neuromuscular junction. The management and follow-up of patients affected by both JAE and MG may be challenging due to the potential correlation between increased MG symptoms and epileptic seizures. Antiseizure medications (ASM) that alter Na+ gated channels must be administered with caution in patients affected by both conditions. *Case description:* We present a 43-year-old female patient with JAE who also suffers from generalized seropositive MG. At the age of 23, she had undergone thymectomy as a means of MG treatment. She was treated with pyridostigmine bromide and a low dose of prednisolone with good clinical response and without the need for immunomodulation therapy. The patient has had JAE from the age of 17. For more than 20 years the patient was under ASM comprised of carbamazepine, ethosuximide, and clonazepam seizure free, but in 2023 she had multiple seizures and was admitted to our department. We performed continuous video-EEG monitoring and recorded clinical and electroencephalographic absence seizures. At that point, we introduced levetiracetam to therapy with a positive clinical response. *Results:* Following the successful treatment of both conditions the patient has been seizure free without any relapses of MG symptoms. *Conclusion*: This case report shows that JAE patients with concomitant MG require prudent decision making which considers the best course of treatment for each condition without impacting the other. Further carefully designed studies are needed.

**Keywords:** juvenile absence epilepsy, myasthenia gravis, antiseizure medications

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## INTRODUCTION

Juvenile absence epilepsy (JAE) is a genetic generalized epilepsy syndrome (GGE) that usually starts in adolescence around puberty and is characterized by absence seizures and generalized tonic-clonic seizures (GTCS) (1). In children and adolescents, JAE is responsible for 2.4%–3.1% of cases of newly diagnosed epilepsy (2). Myasthenia gravis (MG) is an antibody-mediated autoimmune disease that affects the neuromuscular junction (3). MG patients, due to the pathophysiology of the disease, require caution when treated with other medications, especially antiseizure medications (ASM) (4). The management and follow-up of patients affected by both JAE and MG may be challenging due to the potential correlation between successful treatment of one of these conditions and concomitant exacerbation of the other one. ASM which affect the neuromuscular junction's Na+ gated channels must be administered with caution.

## CASE PRESENTATION

We report the case of a 43-year-old female patient with JAE and generalized seropositive MG. The patient was born following a normal pregnancy without complications, and her early neurodevelopment was unremarkable. There was no family history of epilepsy, nor did she experience febrile seizures during childhood. She was diagnosed with JAE at the age of 17 and subsequently managed by a paediatric neurologist, later transitioning to adult neurology care at another institution.

Electroencephalograms (EEGs) revealed generalized spike-wave discharges (frequency 2–3 Hz, amplitude up to 200 μV) and polyspike-wave discharges (frequency 3–4 Hz, amplitude up to 250 μV) (Fig. 1). At age 22, she developed nasal speech, swallowing difficulties, ptosis of the upper eyelids, and lower limb weakness. Testing for autoantibodies targeting neuromuscular junction proteins was positive for antibodies against the acetylcholine receptor (AChR-MG) and muscle-specific kinase (MuSK-MG), confirming the diagnosis of generalized seropositive MG. She underwent a thymectomy as part of her MG treatment. Her epilepsy was stable under a regimen of carbamazepine (CBZ), ethosuximide (ESM), and clonazepam (CLN). Following the MG diagnosis, in consultation with a neuromuscular specialist, it was decided not to alter her ASM regimen, as it had been effective. MG symptoms were managed with pyridostigmine bromide and alternate-day prednisolone, with good clinical response and no need for immunomodulatory therapy. Although the removal of CBZ in favour of levetiracetam (LEV) was recommended due to the potential adverse effects of CBZ on the neuromuscular junction, the patient was reluctant to change her treatment. She reported that her epilepsy had remained stable for over 20 years, with seizures occurring only during periods of noncompliance with her medication. In 2023, she had multiple seizures and was admitted to our department, where continuous video-EEG monitoring was performed, and the numerous absence seizures were recorded (Fig. 2). During the hospitalization, the patient disclosed her noncompliance to ASM that provoked multiple epileptic seizures she experienced. An analysis of the patient's blood sample revealed that the levels of ASM were below the therapeutic range. Due to the negative effect CBZ may have on the neuromuscular junction, a removal of CBZ and an implementation of LEV, was recommended. During the transition, serum levels of CBZ and LEV were closely monitored, alongside clinical assessments for seizure activity and potential exacerbation of MG symptoms. Following the successful treatment of both neurological conditions, JAE and MG, the patient has been seizure free without any relapses of MG symptoms.

## DISCUSSION

Patients who have both JAE and MG have been the subject of a limited number of studies. Considering the mechanism of action of ASM, management and follow-up of patients with these conditions, can be complex. JAE tends to be drug-responsive, but lifelong treatment may be necessary (5). The first line of treatment is with valproic acid (VPA) or ethosuximide (ESM) (6). There are several recorded reports of patients with MG, who presented with aggravation of myasthenic symptoms or even unmasked MG following the administration of ASM such as CBZ (7,8,9). CBZ primarily acts on sodium channels, stabilizing hyperexcitable nerve membranes (10). While this mechanism could theoretically worsen MG by disrupting neuromuscular transmission, individual differences in receptor sensitivity or ion channel function may explain the absence of negative effects in certain patients, including ours. In this case, the decision to continue CBZ therapy was made collaboratively between the patient's epileptologist and neuromuscular specialist, carefully balancing the risks and benefits. Regular monitoring and a proactive approach to man-

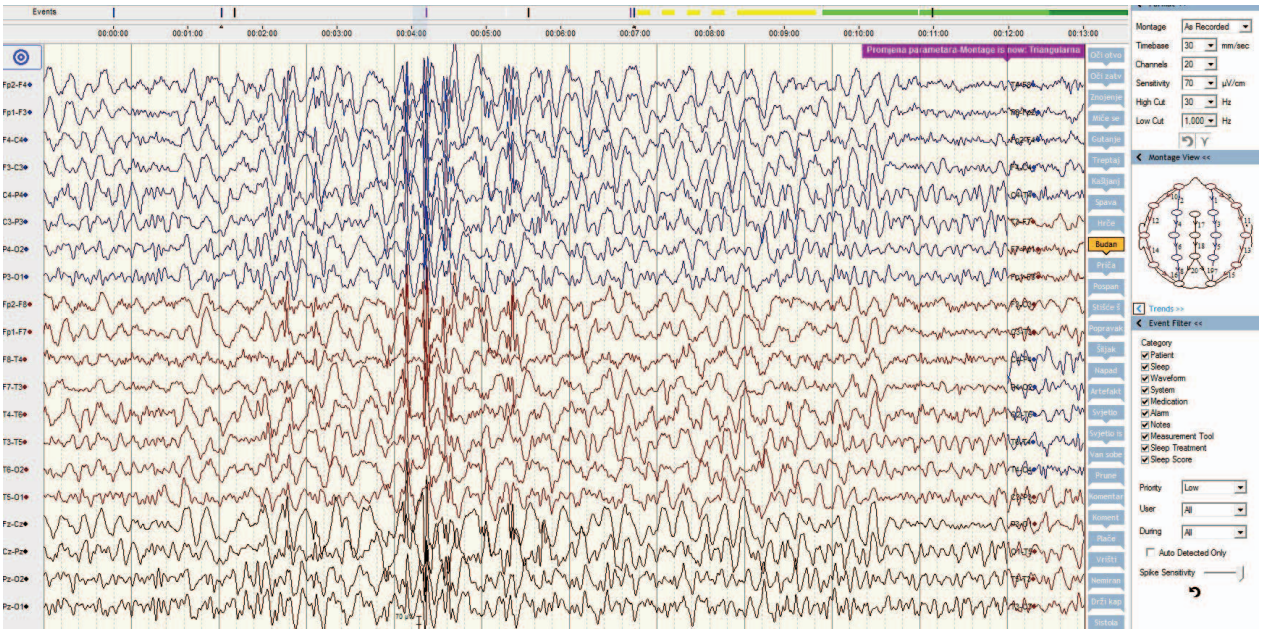

**Fig. 1**. *EEG of the patient showing generalized spike-wave (frequency 2-3 Hz, amplitude up to 200 uV) and polyspike-wave (frequency 3-4 Hz, amplitude up to 250 uV) discharges.*

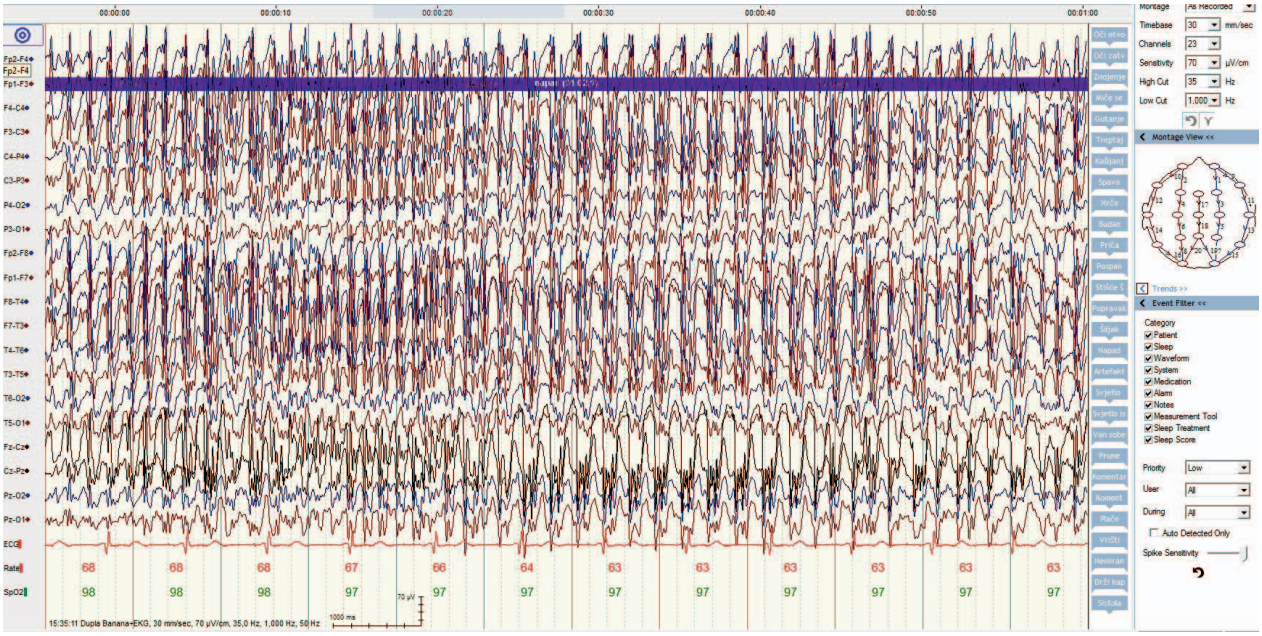

**Fig. 2.** *Showing absence seizure on a continuous video-EEG monitoring with typical generalized 3-5.5 Hz spike – wave discharges.*

aging MG symptoms likely contributed to the absence of complications. It has also been demonstrated that ASM, such as ESM, phenobarbital (PB), and phenytoin (PHT), have an impact on neuromuscular transmission in *in vitro* models (11). The patient in our case report is a rare example of a patient who, due to a good clinical response, had CBZ in antiepileptic therapy for many years following the diagnosis of MG, without worsening of MG symptoms. The patient's MG remained well-controlled following thymectomy, which likely contributed to disease stability (12). Thymectomy is known to reduce autoantibody production, particularly against acetylcholine receptors (AChR), potentially mitigating CBZ's adverse effects on neuromuscular transmission. Despite being seropositive, for both AChR-MG and MuSK-MG, the patient's MG symptoms were manageable without immunomodulatory therapy. This relatively mild MG phenotype may have reduced her susceptibility to CBZ-induced exacerbations.

We also wish to point out that clinical worsening of JAE, which can sometimes be caused by CBZ, did not happen in our patient. It is noteworthy that while CBZ was eventually replaced with levetiracetam (LEV) following a relapse linked to noncompliance, this shift demonstrated that alternative therapies could maintain control of both conditions without risking exacerbation. LEV is often introduced gradually to minimize side effects, particularly neuropsychiatric symptoms (13). Given the patient's history of stable epilepsy control on CBZ, careful overlap during the transition was necessary to avoid breakthrough seizures. The favourable response to LEV supports its use as a safer option for managing epilepsy in patients with coexisting MG. LEV is generally well-tolerated, though long-term use may be associated with mood disturbances or behavioural changes in some individuals (13). Regular follow-ups would be essential to monitor for such effects. More than 80% of JAE patients using the recommended ASM have well controlled epilepsy, with seizures occurring only due to the noncompliance to ASM. Our patient is an example of such case.

## CONCLUSION

This case highlights the necessity of prudent decision-making when managing patients with JAE and coexisting MG, given the potential adverse effects of ASM on MG symptoms. It is essential to select a treatment strategy that effectively addresses both conditions without compromising the management of either. Choosing an ASM with a favourable pharmacokinetic profile, low risk of drug interactions, and proven efficacy in controlling seizures is critical in such cases. As demonstrated in our case presentation, further well-designed longitudinal studies are needed to evaluate the impact of CBZ and other ASM on MG symptoms. Such research would provide valuable insights to guide clinical practice and optimize outcomes for patients with these coexisting conditions.



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