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Case Report

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Successful Treatment of MuSK Antibody–Positive Myasthenia Gravis with Rituximab

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Abstract Muscle-specific tyrosine kinase antibody-associated myasthenia gravis (MuSK-MG) is a rare subtype of MG distinguished by recurring relapses and a clinical history unresponsive to conventional therapies. Rituximab, a monoclonal antibody that targets CD20+ B cells, has effectively induced long-term remission in adults. We report a pediatric MuSK-MG patient who exhibited a favourable response to rituximab following the ineffectiveness of steroid therapy and acetylcholinesterase inhibitor (AChEI) therapy.

Keywords Child · myasthenia gravis · MUSK

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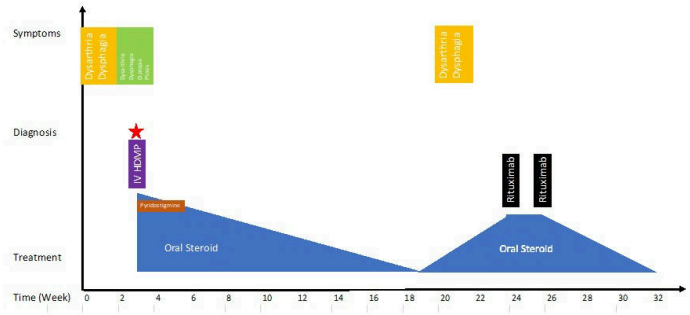
INTRODUCTION

Myasthenia gravis (MG) is a neuromuscular junction condition resulting from autoantibodies targeting proteins critical for synaptic transmission, chiefly the acetylcholine receptor (AChR) or, less frequently, muscle-specific tyrosine kinase (MuSK) [1]. Among the rarer subtypes of MG, MuSK-MG presents with more severe symptoms and often shows resistance to steroid and acetylcholinesterase inhibitor (AChEI) therapies, making it particularly challenging to manage [2]. While acetylcholinesterase inhibitors and corticosteroids are common therapeutic approaches, their efficacy is often limited, especially in MuSK-MG [3]. In recent years, rituximab, a monoclonal antibody targeting CD20+ B cells, has emerged as a promising treatment option, demonstrating success in inducing long-term remission in several adult cases [4]. However, pediatric cases remain underexplored, with limited data available on the optimal use and outcomes of rituximab in children. This case report presents the successful treatment of a pediatric MuSK-MG patient with rituximab, highlighting its potential as a first-line therapeutic option in children who are refractory to standard treatments.

CASE REPORT

A 16-year-old male patient exhibited speech and swallowing impairments, along with ptosis, which commenced two weeks prior. The patient had left semi-ptosis. The bilateral orbicularis oculi muscles exhibited weakness, while the strength of the neck extensor muscles was rated at 4/5. Nasal speech was evident. Muscle strength in both the upper and lower extremities was rated at 5/5. Deep tendon reflexes were normoactive. No pathological reflexes (e.g., Babinski, Hoffmann) were observed. The sensory assessment yielded typical results. Ice and tiredness assessments were conducted following an initial diagnosis of MG. No substantial response was elicited. A neostigmine test was conducted, revealing ophthalmoparesis and partial enhancement in speech. The patient received intravenous methylprednisolone at a dose of 1 g/day for 5 days. Improvement was noted in ptosis and dysarthria after intravenous methylprednisolone therapy. Single fiber electromyography (EMG) conducted on the left frontalis and extensor digitorum muscles of the patient revealed an elevation in the mean of consecutive differences (MCD) and conduction block in three pairings. The patient's acetylcholine receptor antibody test result was negative, and the anti-MuSK antibody test was positive (12.0 U/mL; normal <0.4 U/mL). The patient was diagnosed with Anti-MuSK antibody-positive MG, and pyridostigmine hydrobromide and oral methylprednisolone were started. Oral methylprednisolone was initiated at a dose of 1 mg/kg/day. Pyridostigmine treatment was stopped because there was no adequate response to the treatment. Ophthalmoparesis and speech completely improved in the first week of oral methylprednisolone treatment. Attack symptoms developed again during the drug tapering period 2 months later. Rituximab treatment was started in addition to low-dose steroid treatment. Rituximab was given two doses of 2x375mg/m²/day at 2-week intervals. Low-dose steroid treatment was completed in 6 months and stopped (Figure 1). At the time of initial presentation, the patient's MG-ADL (Myasthenia Gravis–Activities of Daily Living) score was 9, indicating significant functional impairment. Following rituximab treatment, the score improved to 0, reflecting complete resolution of daily functional limitations. No attacks were observed in the patient's 1-year outpatient clinic follow-ups. Rituximab was not repeated during this period, as the patient remained clinically stable. Side effects of steroid treatment included a moon face, widespread acne, weight gain and striae. No attack symptoms were observed. Written informed consent for the publication of this case report was obtained from the patient's parents.

Figure 1. Patient's Treatment Process



DISCUSSION

Muscle-specific tyrosine kinase antibody-associated myasthenia gravis is an uncommon and frequently more severe subtype of MG, characterized by unique aetiology and distinctive clinical manifestations. The prevalence varies among nations and ethnic groups, impacting 5-8% of all MG patients [5]. The condition is reported to be more prevalent among females [6]. This gender predominance may be attributed to hormonal factors or genetic predisposition, necessitating further investigation in pediatric situations. Unlike previously reported cases, our patient did not experience a respiratory crisis, despite presenting with bulbar symptoms. The presence of many clinical characteristics may postpone the diagnosis of MG and the identification of its subtype. Timely detection and subtype classification

are essential for customizing suitable therapy strategies and avoiding superfluous therapies.

The disease generally exhibits an abrupt onset and advances swiftly for weeks. Symptoms such as dysarthria and dysphagia are characteristic of bulbar involvement, whereas ptosis and diplopia reflect ocular symptoms. As many as 80% of individuals with MuSK-MG exhibit bulbar dysfunction, characterized by dysarthria, nasal dysphonia, dysphagia, and impaired mastication [7]. Our case commenced with clinical bulbar manifestations, as documented in the literature. Bulbar start typically correlates with swift decline and frequently results in a myasthenic crisis; however, no such crisis was noted in our case. The lack of myasthenic crises may indicate potential diversity in disease severity and progression across pediatric patients.

Prolonged pharmaceutical intervention is typically necessary to efficiently manage symptoms in MuSK-MG. Symptomatic treatment with acetylcholinesterase inhibitors, such as pyridostigmine, is often insufficient and may even worsen symptoms in MuSK-MG. In our case, pyridostigmine was poorly tolerated and ineffective, aligning with previous reports of limited efficacy in MuSK-positive patients. [8]. This discovery corresponds with prior research highlighting the restricted efficacy of acetylcholinesterase inhibitors in the therapy of MuSK-MG, hence necessitating alternate treatment strategies.

Immunosuppression continues to be the primary treatment for MuSK-MG. Steroids are recognized for delivering a swift and efficacious response; nevertheless, their long-term adverse effects must also be considered. Approximately 10 to 15% of individuals with MuSK-MG exhibit resistance to treatment, and relapses may arise with the reduction of immunosuppressive medications [5]. Anlar et al. documented the case of an 8-year-old kid diagnosed with generalized MG who achieved recovery within one month without the use of immunomodulatory treatment. His spontaneous recovery persisted for six years, concluding with a recurrence characterized by bulbar symptoms [9]. In our instance, like the literature, recurrence transpired following the reduction of immunosuppressive medication. The proportion of patients unresponsive to steroids is frequently challenging to handle. Research has advocated using monoclonal antibodies, including rituximab, a chimeric anti-CD20 monoclonal antibody, in patients with MuSK-MG [10]. A substantial percentage of MuSK-MG patients had enhanced and more prolonged symptom relief following rituximab treatment compared to those who did not get the medication. Immunosuppressant medicines may be decreased or even ceased. Topakian et al. validated the safety and efficacy of rituximab in a substantial cohort of AChR-MG and MuSK-MG patients; furthermore, they revealed a markedly greater remission rate in MuSK-MG patients relative to AChR-MG patients [11]. These data indicate that rituximab not only alleviates symptoms but also diminishes long-term reliance on steroids, potentially enhancing patients' quality of life.

The patient's symptoms ameliorated with rituximab treatment, steroid therapy was terminated, and no relapse occurred. This favourable result highlights the significance of prompt rituximab treatment in pediatric MuSK-MG patients, especially those refractory to standard treatments.

These findings are consistent with previous literature reporting that rituximab is particularly effective in treatment-refractory MuSK-MG cases, even in the pediatric population. O'Connell et al. [12] suggested that rituximab may be considered as a second-line immunosuppressive therapy in MuSK antibody-positive juvenile myasthenia gravis, especially due to the limited response to conventional treatments such as pyridostigmine and steroids. This case contributes to the limited pediatric literature by supporting rituximab's potential as an effective steroid-sparing agent in MuSK-MG.

Consequently, the therapy response in MuSK-MG patients frequently deviates from expectations, making symptom reduction somewhat challenging. Rituximab may serve as an initial therapeutic option in MuSK-MG and could function as a steroid-sparing agent from the outset of the disease.

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