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# Rescue treatment with add-on efgartigimod in a patient with impending myasthenic crisis: a case report

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***Abstract*:** Myasthenia gravis (MG) is an autoimmune disorder characterized by fluctuating muscle weakness. Severe patients may develop life-threatening respiratory failure and experience crisis. Plasma exchange or intravenous immunoglobulin (IVIg) is the first-line treatment option for myasthenia crisis, but some patients still poorly respond to them. Here, we first reported a generalized MG patient from China who was in a state of impending myasthenic crisis and did not respond effectively to IVIg but was successfully rescued by add-on efgartigimod. Especially, we also detected meaningful changes in T-cell and B-cell subsets after efgartigimod, promoting a potential role of efgartigimod in re-establishing immune homeostasis.

***Keywords:*** case report, efgartigimod, impending myasthenic crisis, myasthenia gravis

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## Introduction

Myasthenia gravis (MG) is an acquired autoimmune disorder caused by antibodies targeting the neuromuscular junction, leading to fluctuating muscle weakness.[1] The antibodies targeting acetylcholine receptor (AChR) were commonly detected in most MG patients.[1] The current therapeutic regime for MG includes cholinesterase inhibitors, immunosuppressive drugs, thymectomy, or plasma exchange (PLEX), and intravenous immunoglobulin (IVIg).[1,2] Severe patients develop impending myasthenic crisis (MC) or MC may experience a life-threatening rapid deterioration which presents with ventilatory and bulbar dysfunction.[3] Thus, it is very important to improve the patient's symptoms rapidly during the state of impending MC.

Efgartigimod, an Fc-fragment of human IgG1 antibody, is a natural ligand of neonatal Fc receptor (FcRn) and has a significantly higher affinity for FcRn compared with endogenous immunoglobulin G (IgG).[4] Efgartigimod competes with endogenous IgG binding to FcRn, thereby shortening the half-life of IgG and depleting pathogenic antibodies.[4] Due to the safety and efficacy of efgartigimod in the phase II and III trials in MG patients, it was approved by China's National Medical Products Administration in June 2023. Herein, for the first time to our knowledge, we report a generalized MG (gMG) patient from China who was in a state of impending MC and did not respond effectively to IVIg, was successfully rescued by add-on efgartigimod.

## Case report

The patient was a 35-year-old Chinese woman with initial symptoms of fluctuating left ptosis and slight dysarthria in mid-June 2023. Then she went to the local hospital for consultation and the chest computed tomography showed an anterior mediastinum mass. Based on the positive result of anti-AChR antibody (12.04 nmol/L, tested *via* radioimmunoassay, reference value <0.5 nmol/L), she was diagnosed as MG and initially treated with pyridostigmine (180 mg daily). Then she underwent thymectomy (histopathological diagnosis was thymoma, WHO B2 type) on June 30 and received adjuvant radiotherapy in the next 4 weeks.

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However, she gradually developed bilateral ptosis, diplopia, and weakness in swallowing, chewing, limbs, and neck from August 2023. Failed to be treated with pyridostigmine (360 mg daily) and prednisone (gradually increased from 15 to 35 mg daily), she was admitted to our hospital.

The patient was tested with a quantitative MG (QMG) score of 26 points and MG-specific activities of daily living scale (MG-ADL) score of 15 points (Myasthenia Gravis Foundation of America IVb, MGFA IVb) at admission. Her weakness of limbs and cervical muscle further worsened on the second day of hospitalization. She was promptly treated with IVIg (400 mg/kg daily, total 5 days), methylprednisolone (80 mg daily), and tacrolimus (3 mg daily), along with pyridostigmine (240 mg daily). No positive effects were observed, she developed dyspnea on 1 September, and she was treated with noninvasive ventilation (NIV). In addition, on 5 September, her bulbar symptoms further worsened, and she was unable to swallow, so a gastric tube was placed for feeding. The patient reached a 'worse' status after IVIg, methylprednisolone, as well as tacrolimus according to MGFA post-intervention status (MGFA-PIS). After communication, she was then treated with initial efgartigimod (400 mg weekly, total 4 weeks) on 7 September (QMG score was 27 points, and MG-ADL score was 19 points). Four days later, the weakness of swallowing and ptosis were first to improve, and she achieved clinically meaningful improvement (defined as MG-ADL score reduction of $\geqslant$2 points): MG-ADL reduced to 16 points. Symptoms improved further, and the MG-ADL score for the part of the limbs was reduced to 0 points on 24 September (18 days after initial treatment). She reached a mild subjective clinical manifestation with an MG-ADL score of 3 points from 29 September to 19 October, but her QMG score still fluctuated between 13 and 14 points. Her symptoms slightly worsened again on 20 October (MG-ADL score was 6 points and QMG score was 14 points). Importantly, though she was not treated with another cycle of efgartigimod, her MG-ADL score was stable from 4 to 6 points with prednisone (30 mg daily), tacrolimus (3 mg daily), and pyridostigmine (180 mg daily) after 3 months of initial efgartigimod. The treatment regimens after admission to our hospital and the changes in QMG score, MG-ADL score, and MG-ADL score in different muscle groups were presented in Figure 1.

The changes of laboratory examinations including total T cells (defined as CD45 + CD3+ cells), CD4+ T cells (defined as CD45 + CD3 + CD4+ cells), CD8+ T cells (defined as CD45 + CD3 + CD8+ cells), regulatory T cells (Treg) (defined as CD45 + CD3 + CD4 + CD25 + CD127 low cells), CD19+ B cells (defined as CD45 + CD3 − CD19+ cells), memory B cells (defined as CD45 + CD19 + CD27 + CD38− cells), plasmablasts (defined as CD45 + CD19 + CD27 + CD38+ cells), plasma cells (defined as CD45 + CD19 + CD27 + CD38 + CD138+ cells), and serum IgG, IgA, and IgM were summarized in Figures 1(c) and 2. Frequency of T-cell and B-cell subsets was measured by flow cytometry, and serum concentrations of IgG, IgA, and IgM were measured by immunonephelometry. The patient's level of IgG decreased rapidly after being treated with efgartigimod in the first 3 weeks and increased again after the seventh week, which was correlated with the severity of the disease [Figure 1(c)]. Remarkably, we detected a gradual decrease in the total T cells and CD4+ T cells from the second week [Figure 2(a) and (b)]. Besides, the frequency of Treg cells increased in the initial period of rapid improvement, and then decreased with symptoms rebounding, while Treg cells increased again on 6 December [Figure 2(d)]. Gradual decrease of CD19+ B cells from the first week after being treated with efgartigimod was detected in this patient, while CD19+ B cells increased 69 days after the last injection [Figure 2(e)]. Frequency of plasma cells, plasmablasts, and memory B cells fluctuated throughout the course, but on 1 November and 6 December, plasma cells and plasmablasts were still significantly lower than baseline [Figure 2(f)–(h)].

## Discussion

In recent years, new therapies targeting different pathogenetic process of MG has constantly emerged. Among them, the more downstream but more direct target of treatment is the depletion of antibodies. Traditionally, depleting antibodies by PLEX and IVIg was effective in MG.[2] However, PLEX was limited by availability and comorbidities, and nearly 30% of MG patients poorly responded to IVIg.[5,6] FcRn is a major histocompatibility complex class I-like molecular that specifically recycles and extends the half-life of circulation IgG, including pathogenic antibodies in autoimmune diseases like MG.[4] *FCGRT* gene encodes FcRn and has five different alleles

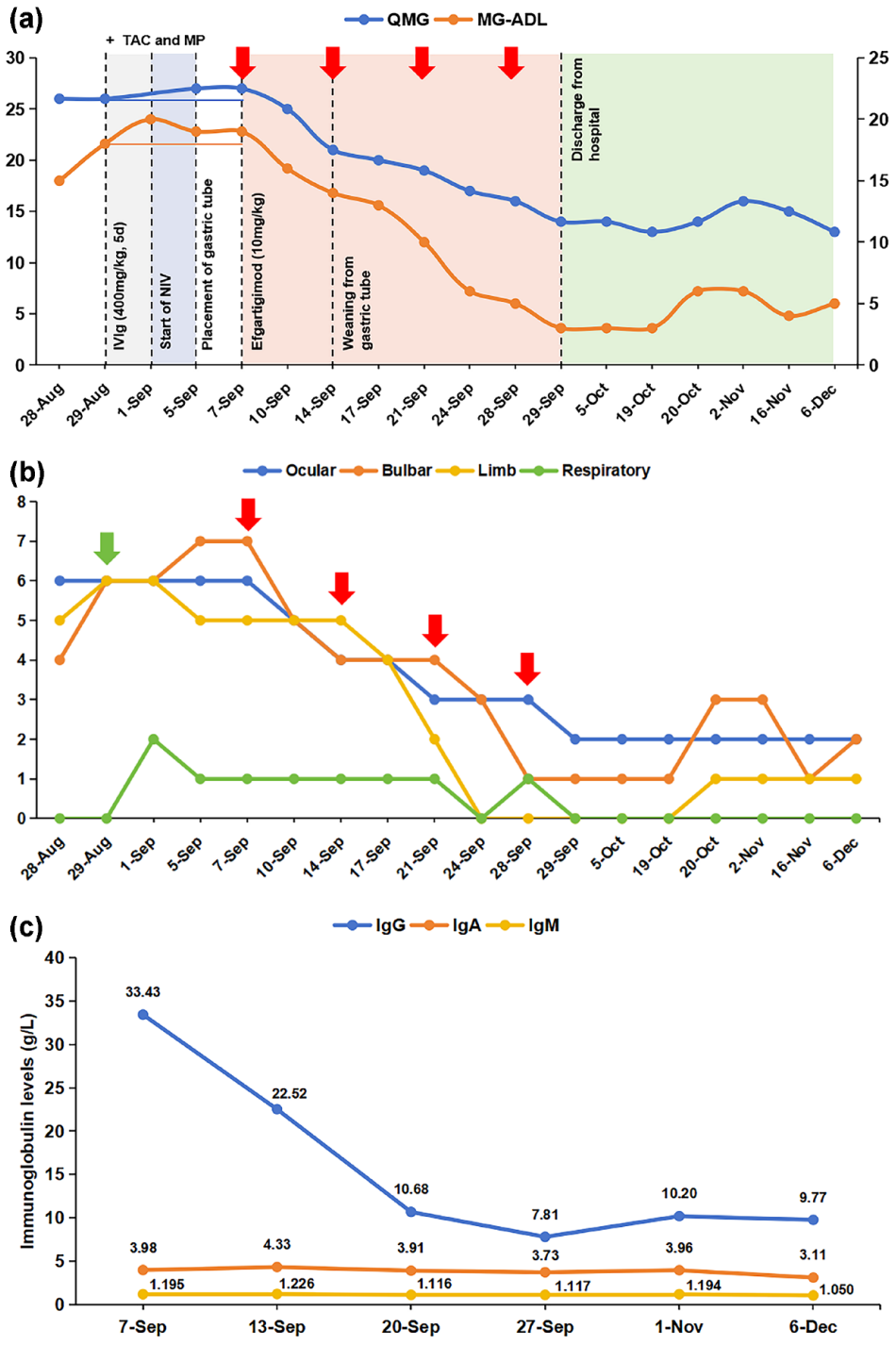


**Figure 1.** (a) The therapeutic timeline of the patient and changes of clinical severity of MG in the patient, assessed through QMG score and MG-ADL score (the red arrows represent the day of efgartigimod). (b) Changes of MG-ADL subdomains in the patient, assessed through QMG score and MG-ADL score (the green arrow represents the day of IVIg and the red arrows represent the day of efgartigimod). (c) The changes of serum IgG, IgM, and IgA levels in the patient.

Ig, immunoglobulin; IVIg, intravenous immunoglobulin; MG-ADL, myasthenia gravis-specific activities of daily living scale; MP, methylprednisolone; NIV, noninvasive ventilation; QMG, quantitative myasthenia gravis score; TAC, tacrolimus.

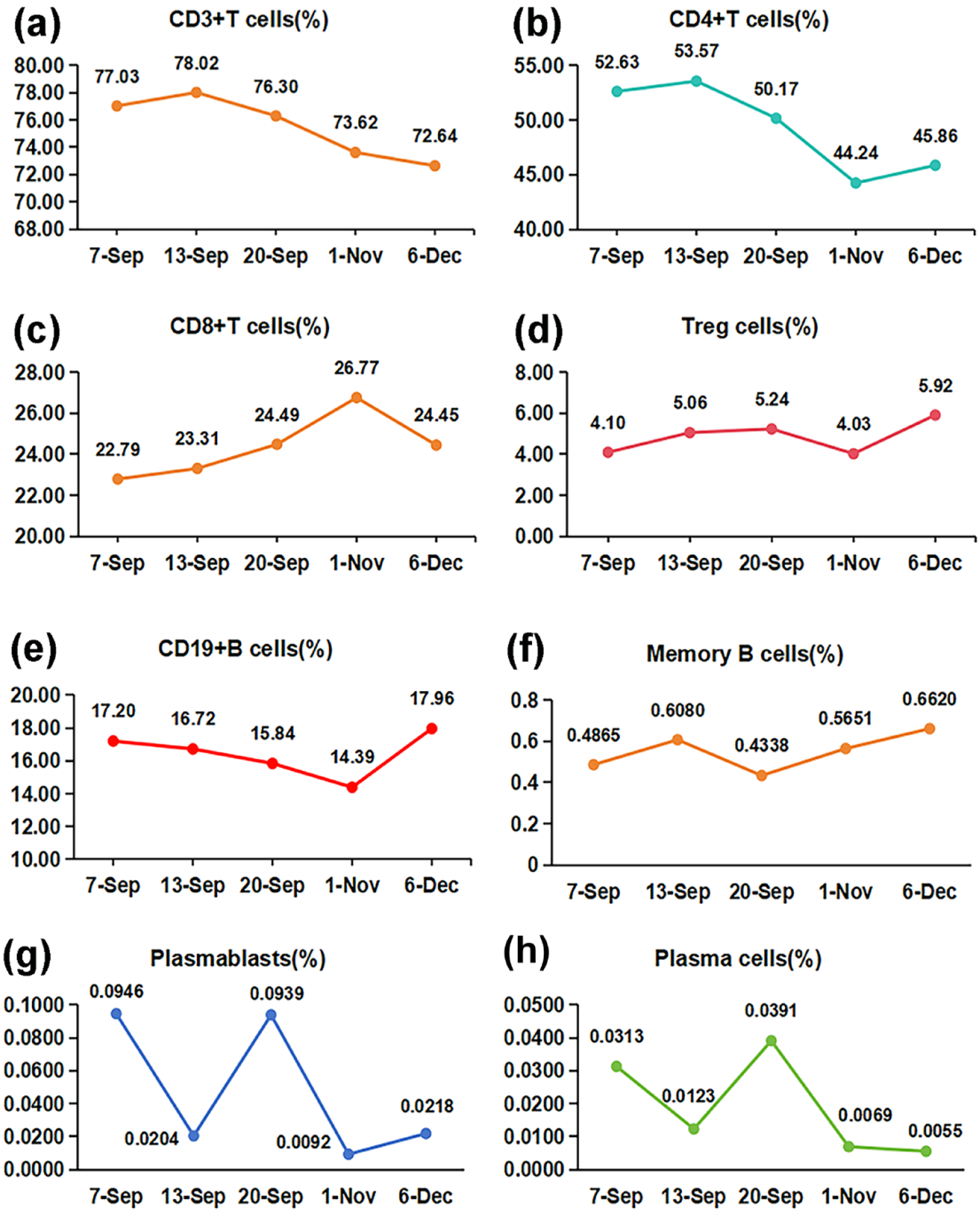


**Figure 2.** (a–d) The changes of frequency of T-cell subsets in the patient. (e–h) The changes of frequency of B-cell subsets in the patient.

with a variable number of tandem repeat (VNTR) polymorphisms, from VNTR1 to VNTR5, affecting the expression of FcRn mRNA and protein.[6] Competing with endogenous IgG for FcRn is an important mechanism of IVIg, but the efficacy of IVIg were influenced by VNTR polymorphisms.[6] Recently, Su *et al.*[5] found that MG patients with VNTR2/3 genotype expressed lower endogenous IgG and responded poorly to IVIg compared with patients with VNTR3/3 genotype. Dalakas and Spaeth[6] suggested that the efficacy of IgG biologics including IVIg varies due to the potential for

protective pathogenic antibody effects in heterozygous VNTR2/3 individuals. Generally, since VNTR genotype affects both endogenous and infused IgG, as well as potential influence on pathogenic antibodies, it may explain the heterogeneity of therapeutic effect of IVIg to some extent. Further VNTR polymorphisms detection is expected to guide the administration of IVIg.

Efgartigimod is a novel FcRn inhibitor and was known as PLEX in a glass bottle. Rapid onset is one of the advantages of efgartigimod in treating gMG; however, very few studies have explored whether it can be used as an effective rescue treatment. Recently, a study by Watanabe *et al.*[7] showed that a late-onset MG patient from Japan who suffered from a severe MC did poorly in response to both PLEX and IVIg and was rescued by add-on efgartigimod. However, there were differences between their case and ours. Firstly, the MG patient in their report underwent increased dyspnea after efgartigimod, and the weakness of limbs was first to improve 18 days after infusion of efgartigimod. Besides, significant improvement occurred after the second cycle of efgartigimod, another infusion of IVIg, and a cycle of large-dosage intravenous methylprednisolone. However, our patient's symptoms improved as early as 4 days after efgartigimod treatment and presented persistent improvement, with remaining mild symptoms (MG-ADL score was 5 points, MGFA classification was IIb, and MGFA-PIS was 'improved'). Bulbar muscle weakness was the first to improve in our case. So, our patient's symptoms improved more rapidly. Furthermore, our patient only accepted one cycle of efgartigimod and achieved significant improvement. Overall, both two cases suggested that efgartigimod may be a rescue therapy in MG patients. But it indicated that early applications, that is, using it in the pre-crisis state is more effective than using it during the crisis phase.

In addition, we detected a gradual decline in the frequency of CD19+ B cells and CD4+ T cells. Plasma cells and plasmablasts also decreased after treatment in our case. The frequency of Treg cells, which participate in suppressing the activation and proliferation of autoreactive cells and play an important role in immune homeostasis, was detected to increase after treatment. In the phase II study of efgartigimod in pemphigus vulgaris and foliaceus, total CD19+ B cells also revealed declining but no changes in CD4+ T cells.[8] Although not statistically significant, Treg cells in their study increased at the end of efgartigimod treatment.[8] Research has demonstrated that FcRn could mediate antigen presentation and activate T cell immunity, but whether treatment target FcRn affects autoreactive T cells and pathological B cells remains further investigated.[9] The changes of T cells and B cells in our case suggest that efgartigimod may have a role in re-establishing immune homeostasis in MG, except for rapid depletion of antibodies.

It is worth noting that as the improvement of the patient's condition is still within the duration of IVIg and other treatments, including methylprednisolone and tacrolimus, it is indeed difficult to interpret it as the effect of taking efgartigimod alone. However, our patient received oral prednisone treatment for nearly 1 month before admission, which failed to prevent disease progression and she worsened again 10 days after infusion of IVIg and methylprednisolone in our center. Therefore, considering that most patients gain benefits from IVIg within 4–5 days and glucocorticoid often has an effect within 2–4 weeks in 75% of patient,[10,11] we believe that the rapid therapeutic effect of efgartigimod was an important reason for the significant improvement in this case.

In summary, the rapid effect of efgartigimod observed in our patient was better to be an 'add-on' effect to other conventional therapies. In addition, it is only a single-center case report, and a larger cohort of patients was needed to further explore the application of efgartigimod in impending MC and underlying mechanisms of efgartigimod in immune homeostasis.

## Declarations

### *Ethics approval and consent to participate*

Ethical approval to report this case was obtained from the Ethics Committee of Affiliated Hospital of Xuzhou Medical University (XYFY2023-KL471-01) and it complied with the Declaration of Helsinki.

### *Consent for publication*

The patient has provided a written informed consent for publication of this article.

### *Author contributions*

**Zhouao Zhang:** Data curation; Formal analysis; Visualization; Writing – original draft.

**Mingjin Yang:** Data curation; Formal analysis; Investigation; Methodology.

**Tiancheng Luo:** Data curation; Formal analysis; Investigation; Methodology; Software.

**Xue Du:** Data curation; Methodology; Visualization.

**Zhouyi Wang:** Investigation; Methodology; Software.

**Xiaoyu Huang:** Conceptualization; Visualization; Writing – review & editing.

**Yong Zhang:** Conceptualization; Funding acquisition; Supervision; Writing – review & editing.

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### *Competing interests*

The authors declare that there is no conflict of interest.

### *Availability of data and materials*

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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