Steroid-Sparing Effect, Effectiveness, and Tolerability of Mepolizumab with EGPA in Real World Clinical Practice

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Abstract

Background

Eosinophilic polyangiitis/granulomatosa (EGPA) is a vasculitis syndrome that affects small and medium-sized blood vessels throughout the body. The mainstay of treatment is steroids, but there are no standardized doses or durations for steroids in combination with mepolizumab.

Methods

We investigated the efficacy, steroid administration, and course of steroid reduction in five patients who were diagnosed with EGPA and treated with mepolizumab for 1 year. Five patients who were diagnosed with EGPA using the American College of Rheumatology criteria and treated with mepolizumab for 1 year were included in our study from 2018–2020.

Results

Eosinophil levels as well as the Birmingham Vasculitis Activity Score (BVAS), remission rate, annual relapse rate, and steroid dosage were observed at 1 year after mepolizumab treatment. Fifty-two weeks after mepolizumab treatment, eosinophils, BVAS, and the steroid dosage showed a trend toward improvement in four out of five patients. In the one patient who received no dose reduction, there was no exacerbation of bronchial asthma that had previously occurred during the follow-up period. Although neurological symptoms often remain even in remission, all patients with neurological symptoms at diagnosis improved. There were no cases of relapse in this study, including two anti-neutrophil cytoplasmic antibody-positive cases.

Conclusions

Management that includes early administration of mepolizumab may improve patients' quality of life by alleviating lingering neurological symptoms that are caused by EGPA.

Background

Eosinophilic granulomatosis with polyangiitis (EGPA) is a vasculitis syndrome that affects small and medium-sized blood vessels throughout the body¹. Eosinophil-driven inflammation causes a variety of pathologies throughout the body². It is often preceded clinically by bronchial asthma or allergic rhinitis³.

Mepolizumab reduces the number of eosinophils in the blood and tissues by acting on the interleukin (IL)-5 receptor on eosinophils and inhibiting the IL-5 binding⁴. Since its approval by the US Food and Drug Administration, it has been available to treat patients with EGPA. Steroids are the mainstay of treatment. However, there is no standardized dose or duration of steroid administration in combination with mepolizumab. In addition, few reports have evaluated the efficacy of mepolizumab administration in

clinical practice. Therefore, we investigated the efficacy, steroid administration, and course of steroid reduction in five patients who were diagnosed with EGPA and treated with mepolizumab for 1 year.

Methods

From 2018 to 2020, five patients who were diagnosed with EGPA using the American College of Rheumatology criteria, received mepolizumab continuously for 1 year at our institution, and had a confirmed clinical course were included in the study. Clinical symptoms were assessed using the Birmingham Vasculitis Activity Score (BVAS), and eosinophils along with the BVAS, remission rates, annual relapse rates, and steroid doses were observed during the first year of mepolizumab administration. Written informed consent was obtained from all participants in this study. Approval for ethics and clinical trials registration was provided by the review board committees of Akashi Medical Center (18/06/2021; approval number: 2021-6) .

Results

Characteristics of the five patients who were treated with mepolizumab for 1 year are presented (Table 1). Their mean age at baseline was 60.4 years, and all patients were taking corticosteroids. At the time of diagnosis, peripheral neuropathy was present in four of the five patients, and their anti-neutrophil cytoplasmic antibody (ANCA) positivity rate was 40%. The eosinophil count, BVAS, and steroid dose reduction before and at 12, 24, and 52 weeks after starting treatment with mepolizumab are presented (Fig. 1, Table 2). Fifty-two weeks after treatment, the eosinophil count, BVAS, and steroid dose reduction all showed a trend toward improvement in all patients. The relapse rate was 0%. Steroid dose reductions at baseline and at 12, 24, and 52 weeks after treatment, immediately after mepolizumab administration, were 50%, 90%, 80%, 60%, and 0%, respectively. Two patients started with a BVAS of 0, one of whom had difficulty tapering off steroids before administration, but this patient maintained an eosinophil count reduction in response to 1 mg after starting mepolizumab. In the other patient who did not undergo a dose reduction, bronchial asthma exacerbation that had occurred previously and until mepolizumab treatment was started did not occur even once during the follow-up period.

Table 1. Patient characteristics at diagnosis (N = 5)

Characteristic	Result				
Mean age (years)	60.4 (41–82)				
ANCA-positive (%)	40				
Eosinophil count (/μL)	17915.8 (4369–41960)				
Mean BVAS	6.6 (0–14)				
Men/Women	1/4				
Asthma (%)	80				
Skin involvement (%)	40				
Pulmonary consolidation (%)	100				
Polyneuropathy (%)	80				
Sinus anomaly (%)	40				
Abbreviations: ANCA, anti-neutrophil cytoplasmic antibody; BVAS, Birmingham Vasculitis Activity Score.					

Table 2. Changes in symptoms and laboratory data results before and after starting mepolizumab

Pt. No		EGPA diagnosis	0 Weeks	12 Weeks	24 Weeks	52 Weeks	Steroid reduction rate
1	Corticosteroid administration (mg/day)	-	20	12.5	12	10	50%
	BVAS	10	10	0	0	0	
2	Corticosteroid administration (mg/day)	-	10	7	4	1	90%
	BVAS	0	0	0	0	0	
3	Corticosteroid administration (mg/day)	-	25	15	9	5	80%
	BVAS	9	9	0	0	0	
4	Corticosteroid administration (mg/day)	-	7.5	4	4	3	60%
	BVAS	14	14	0	0	0	
5	Corticosteroid administration (mg/day)	-	5	5	5	5	0%
	BVAS	0	0	0	0	0	

Abbreviations: BVAS, Birmingham Vasculitis Activity Score; EGPA, Eosinophilic granulomatosis with polyangiitis.

The EGPA remission rate (BVAS = 0 and an oral steroid dose of less than 7.5 mg/day) was 80% at 1 year. No significant side effects were reported. None of the patients relapsed.

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Discussion

EGPA is a systemic vasculitis that is associated with hypereosinophilia⁵. Mepolizumab acts on IL-5 and suppresses eosinophil production. Peripheral neuropathy is a frequent complication that is mainly due to polyneuritis, especially in patients with EGPA with positive ANCA⁶. In addition, neuropathy is more common in Japanese people⁷. Although oral prednisone is the first-line drug of choice for EGPA^{8,9,10}, extensive dose-dependent complications are known to occur with long-term use. Furthermore, most patients will experience recurrence^{1,11,12,13}. Therefore, administration of mepolizumab, which helps to reduce the steroid dose, may facilitate early dose reduction and reduce the risk of complications. In

addition, there were no relapses while tapering the prednisone dose until 12 months. There is no gold standard for steroid dose reduction. The observation that the patient went into remission without worsening of the BVAS and neurological symptoms was thought to be useful information.

The usefulness of early mepolizumab administration to treat EGPA has not been reported. In this study, two patients were clinically diagnosed and treated with mepolizumab within 6 months (Pt.1 and Pt.3). Because the neurological symptoms continued to improve while the steroid dose was reduced by 80%, we believe that early therapeutic intervention may have a positive impact.

EGPA is not homogeneous, and it is not known whether the distribution of organ damage or the response to treatment is reflected by an ANCA-positive result^{14,15}. In this study, no patient had a relapse including the two ANCA-positive patients. However, it is important to monitor for a relapse in patients with long-term mepolizumab use beyond 1 year.

There are currently no standardized criteria for the timing of mepolizumab administration. If mepolizumab administration facilitates steroid reduction and also improves neurological symptoms, further investigation into the significance of early intervention at the early stage of mepolizumab diagnosis may be required.

Conclusions

Early management, such as the administration of mepolizumab, may contribute to the management of side effects by ensuring a reduction in steroid dosage, as well as alleviating the prolonged neurological symptoms caused by EGPA and improving the patient's quality of life.

Abbreviations

EGPA, eosinophilic granulomatosis with polyangiitis

BVAS, Birmingham Vasculitis Activity Score

ANCA, anti-neutrophil cytoplasmic antibody

Declarations

Conflicts of interest

None to declare.

Consent for publication

All co-authors have consented to the publication of this study.

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Availability of data and materials

The datasets analyzed during the current study are available in the following repositories:

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Authors' contributions

RT, KM, SF, and RT have contributed to the concept of the study. MI, KO have contributed to the collection, analysis. HO have contributed to an integrative discussion based on the results. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Written informed consent was obtained from all participants in this study. Approval for ethics and clinical trials registration was provided by the review board committees of Akashi Medical Center (18/06/2021; approval number 2021-6) .

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Figures

Figure 1

Change in eosinophil levels before and after mepolizumab. Eosinophils were suppressed in all patients after initiation of mepolizumab, and eosinophil levels remained in the normal range after 52 weeks of treatment.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [EGPAdeatabase.xlsx](#)