Off-label Use of Mepolizumab: A Potential Therapeutic Option for Eosinophilic Cystitis

Wang G[1], Zhuo N[2], Liu Z[1]
[1]*Department of Rheumatology and Immunology, The Second Affiliated Hospital of Soochow University, Suzhou, China*
[2]*Department of Nephrology, The Affiliated Suzhou Hospital of Nanjing Medical University, Suzhou Municipal Hospital, Suzhou, China*

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To the Editor:

We read with interest the recent publication by Trefond et al [1] on the efficacy of mepolizumab for the treatment of eosinophilic cystitis. The authors first reported 2 patients with idiopathic eosinophilic cystitis whose condition improved after off-label treatment with mepolizumab [1]. We support and appreciate the authors' work and agree with their conclusions. Here, we would like to share a case of successful treatment of eosinophilic cystitis using mepolizumab in China. The patient gave his written informed consent for the publication of his case details.

A 77-year-old man came to the rheumatology and immunology department with a >2-year history of difficulty urinating. Questioning during the physical examination also revealed frequent urination. There was no tenderness in the kidney area, and he did not have an allergic rash. Two years previously, he had undergone a bladder biopsy in the urology department, which showed eosinophilic infiltration. He was diagnosed with eosinophilic cystitis and discharged after a week of treatment with antibiotics and hemostasis. Subsequently, he received long-term treatment with methylprednisolone 4 mg once daily and *Tripterygium wilfordii* 20 mg twice daily. During this period, he did not take any biological agents. Over a period of 1 month, his symptoms of difficulty urinating and frequent urination worsened. He experienced nocturia (3-4 times a night) but not fever or significant weight changes. Laboratory tests (reference values in parenthesis) showed an erythrocyte sedimentation rate of 25 mm/h (0-15 mm/h), C-reactive protein level of 40.3 mg/L (0-10 mg/L), urine white blood cell count of 53/μL (0-28/μL), urine red blood cell count of 20/μL (0-17/μL), white blood cell count of 9.8 × 10^9/L (3.5-9.5 × 10^9/L), eosinophil count of 0.85 × 10^9/L (0.02-0.52 × 10^9/L), and IgE level of 175 IU/mL. Values for tumor markers, prostate-specific antigen, and the tuberculosis T-cell spot test were within normal ranges. Urinary system ultrasound and abdominal CT did not reveal tumors. After excluding urinary tract infections, tuberculosis, and tumors based on the bladder biopsy results, we eventually diagnosed the patient with eosinophilic cystitis. Treatment was initiated with methylprednisolone 4 mg combined with *Tripterygium wilfordii* twice daily, although the symptoms of difficulty urinating, frequent urination, and nocturia did not improve, and IgE levels remained persistently elevated. Subsequently, the patient received mepolizumab (a humanized monoclonal antibody against interleukin [IL] 5), and after 1 course of injections (100 mg), both laboratory test results and symptoms improved. The results of tests repeated 1 month later revealed lower values than the previous ones (supplementary material 1-SM1). The patient was followed up for 6 months, and his irritative urinary tract symptoms improved considerably, with all laboratory indicators gradually returning to normal.

Eosinophilic cystitis is a rare inflammatory disease characterized by eosinophilic infiltration of the bladder wall [2]. It is associated with infections, drug therapy, bladder cancer, trauma, and allergy, although its exact cause remains unclear [2]. Irritative bladder symptoms are the main manifestations in most cases of eosinophilic cystitis and include frequency (67%), dysuria (62%), gross/microscopic hematuria (68%), suprapubic pain (49%), and urinary retention (10%) [2]. Approximately 43% of cases involve peripheral eosinophilia, while more than half do not have significantly elevated peripheral eosinophil counts [2]. There is no consensus on the treatment of eosinophilic cystitis, although initial treatment typically involves corticosteroids, antihistamines, and antibiotics. Medication-based treatment is associated with a recurrence rate of 17%; surgical treatment is associated with a recurrence rate of 2.6% [2]. Recent studies have shown that activated eosinophils release cytotoxic cationic proteins, which can induce tissue damage. In vitro studies have demonstrated that IL-5, a cytokine, can attract and activate eosinophils [3]. Mepolizumab blocks the binding of interleukin-5 to its receptor, thereby inhibiting eosinophil proliferation, differentiation, and activation [4]. In the case we report, the patient had a >2-year history of refractory eosinophilic cystitis, and his symptoms included frequent urination and difficulty urinating. Despite antibiotic treatment, his symptoms persisted. Subsequently, he underwent systemic treatment including prednisolone, although the results were not satisfactory. After starting low-dose mepolizumab, the patient responded well in terms of symptoms and laboratory indicators. Mepolizumab could be an effective treatment for eosinophilic cystitis. However, formal clinical trials are needed to standardize the treatment.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Zhichun Liu

https://orcid.org/0000-0001-6170-9601
Department of Rheumatology and Immunology
The Second Affiliated Hospital of Soochow University,
Suzhou, China.
E-mail: zcliurheu@suda.edu.cn

