

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

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To the Editor,

We read with interest the recent publication by Trefond and colleagues on the efficacy of mepolizumab for the treatment of eosinophilic cystitis: a report of two cases [1]. The authors first reported two patients with idiopathic eosinophilic cystitis who successfully improved with off-label treatment with mepolizumab [1]. We support and appreciate the authors' work and agree with their conclusions, and we would like to share here a case of successful treatment of eosinophilic cystitis using mepolizumab in China.

A 77-year-old man presented to the rheumatology and immunology department with a history of difficulty in urination for over 2 years. Upon examination, his symptoms included frequent urination and difficulty in urination. There was no tenderness in the kidney area, and he did not have any allergic rash. Two years ago, he underwent a bladder biopsy in the urology department, which showed infiltration of eosinophils. He was diagnosed with eosinophilic cystitis and was discharged after a week of treatment with antibiotics and hemostasis. Subsequently, he received long-term treatment with 4mg of methylprednisolone once daily and 20mg of Tripterygium

wilfordii twice daily. During this period, he did not use any biological agents. Over the past month, his symptoms of difficulty in urination and frequent urination worsened. He experienced nocturia 3-4 times a night but did not have a fever or significant weight changes. Laboratory tests 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), white blood cell count in the urine of 53/ μ l (0-28), red blood cell count in the urine of 20/ μ l (0-17), 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. Tumor markers, prostate-specific antigen (PSA), and tuberculosis T cell spot test (T-SPOT) were within normal ranges. Urinary system ultrasound and abdominal CT did not reveal any tumors. After excluding urinary tract infections, tuberculosis, and tumors, based on the patient's bladder biopsy results, he was finally diagnosed with eosinophilic cystitis. Treatment was initiated with methylprednisolone (4mg) combined with *Tripterygium wilfordii* twice daily, but the symptoms of difficulty in urination, frequent urination, and nocturia did not improve, and IgE levels remained persistently elevated. Subsequently, the patient received mepolizumab (a humanized monoclonal antibody against interleukin-5) and after one course of injection (100mg), there was an improvement in laboratory test results and symptoms. One month later, the repeated tests showed decreased indicators compared to previous ones (supplementary material 1-SM1). The patient was followed up for six months, and similar urinary tract irritation symptoms greatly improved, with all laboratory indicators gradually returning to normal.

Eosinophilic cystitis is a rare inflammatory disease characterized by eosinophil infiltration of the bladder wall [2]. Eosinophilic cystitis is associated with infections, drug therapies, bladder cancer, trauma, and allergies, but its exact cause is still unclear [2]. Bladder irritative symptoms are the main manifestations in most eosinophilic cystitis patients, including frequency (67%), dysuria (62%), gross/microscopic hematuria (68%), suprapubic pain (49%) and urinary retention (10%) [2]. Approximately 43% of cases show peripheral eosinophilia, while more than half of the cases do not have significantly elevated peripheral eosinophil counts [2]. There is no consensus on the treatment of eosinophilic cystitis, but initial treatment typically involves medications such as glucocorticoids, antihistamines, and antibiotics. The medication-based treatment has a recurrence rate of 17%, while surgical treatment has 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 interleukin-5, a cytokine, is capable of attracting and activating eosinophils [3]. Mepolizumab, a humanized monoclonal antibody against interleukin-5, blocks the binding of interleukin-5 to its receptor, thereby inhibiting eosinophil proliferation, differentiation, and activation [4]. In the case of our patient who has a history of refractory eosinophilic cystitis for two years, his symptoms include urinary frequency and difficulty urinating. Despite antibiotic treatment, his symptoms persisted. Subsequently, she underwent a systemic treatment trial including prednisolone, but the results were not satisfactory. In the follow-up after starting low-dose mepolizumab,

there was a good response in both his symptoms and laboratory indicators. Mepolizumab could be an effective treatment for eosinophilic cystitis, but formal clinical trials are needed to standardize the treatment.

In summary, we thank the authors and their colleagues for their great contribution to the treatment of eosinophilic cystitis.

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Competing interests

The authors declare that they have no conflicts of interest.

Patient and other consents

The patient in this manuscript has given written informed consent to the publication of her case details.

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