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LETTER TO THE EDITOR

Mepolizumab therapy improves endomyocarditis in seropositive eosinophilic granulomatosis with polyangiitis

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Heart involvement with cardiac insufficiency is a cause of early death and is associated with poor prognosis in eosinophilic granulomatosis with polyangiitis (EGPA),[1] a disease classified as antineutrophil cytoplasmic antibody-associated vasculitis. Although cyclophosphamide (CYC) is required to induce disease remission in the presence of cardiac insufficiency,[2] there is well-known dosage-related cardiotoxicity in addition to increased risks of infertility, infection, and malignancy.[3] Limited efficacy with significant adverse effects of CYC therapy has prompted the search for effective and secure alternative therapeutics in EGPA. Eosinophils play a central role in the pathogenesis, and the activation and recruitment of these cells are mainly mediated by interleukin (IL)-5, a key therapeutic target in EGPA.[4] Nevertheless, mepolizumab (MEP), an anti-IL-5 monoclonal antibody, has been suggested in the induction treatment of EGPA with nonsevere diseases, such as asthma and sinonasal manifestations.[5] Herein, we report a case of EGPA endomyocarditis with cardiac insufficiency under MEP induction therapy, leading to normalized cardiac dysfunction and disease remission with sparing use of glucocorticoids (GCs).

A 36-year-old female presented to our hospital with dyspnea and palpitation that had lasted for one month. Based on bronchial asthma, mononeuritis multiplex, and blood eosinophilia with extravascular infiltration,[6] the patient had received an EGPA diagnosis a year ago. She was in remission under combined CYC/GC induction therapy. At admission, laboratory tests revealed positive antimyeloperoxidase and increased levels of eosinophils (7,140/μL) and cardiac biomarkers. Echocardiography and magnetic resonance imaging demonstrated impaired left ventricular ejection fraction, myocardial edema, and diffuse mid-wall and endocardial enhancement, indicating endomyocarditis with cardiac insufficiency (Figure 1a, b). Holter monitoring revealed paroxysmal atrial tachycardia and atrial/ventricular premature contractions. Glucocorticoid and cardiac supporting agents were prescribed for the disease relapse with heart involvement. The patient refused CYC induction therapy due to the

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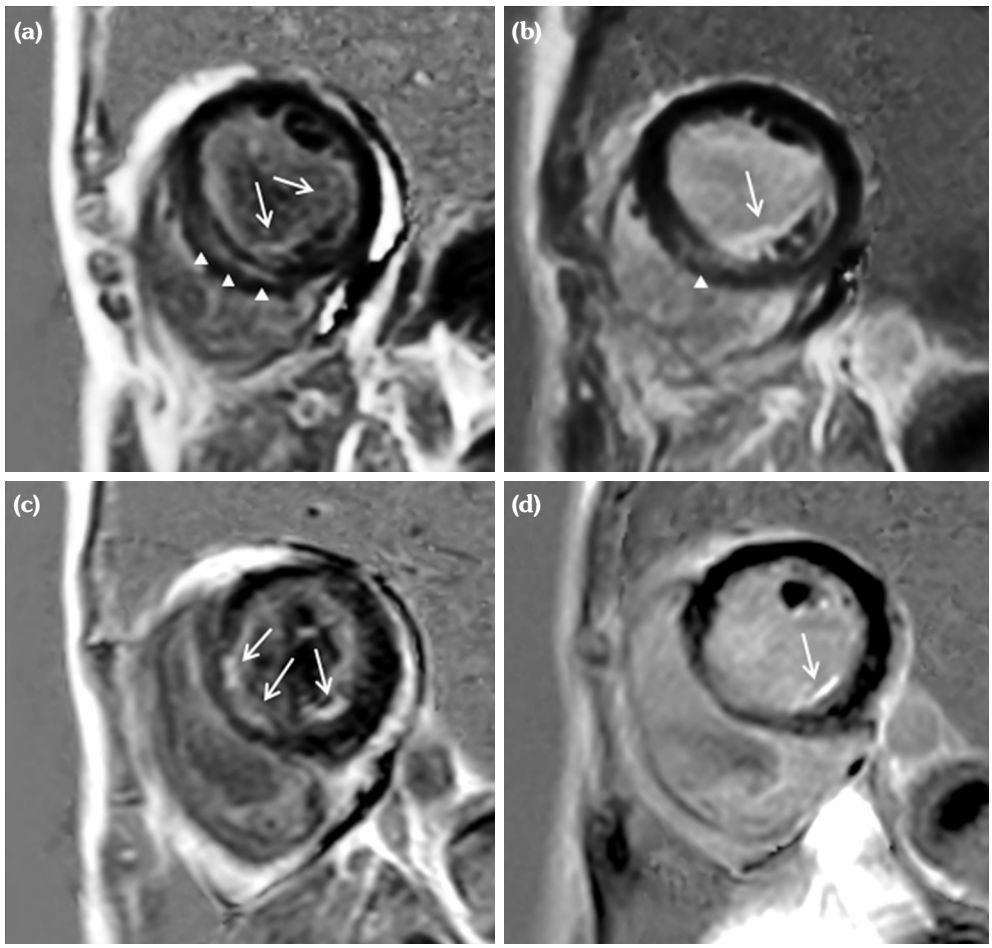

Figure 1. Serial magnetic resonance imaging sequences in the EGPA patient before and after MEP therapy. **(a, b)** Before MEP therapy, short-axis postgadolinium delayed enhancement images show acute edema (white arrowheads) at the mid-wall of the left ventricular septal wall, and endocarditis at the left ventricular septal and inferior walls (white arrows). **(c, d)** After MEP induction treatment, short-axis postgadolinium delayed enhancement images demonstrate septal mid-wall fibrosis (white arrowhead) and residual endocarditis (white arrows) with improvement at the left ventricular septal and inferior walls.
EGPA: Eosinophilic granulomatosis with polyangiitis; MEP: Mepolizumab.

side effects from earlier exposure. There was a more than 90% decrease in blood eosinophilia with stationary follow-up counts less than 150/μL following subcutaneous injection of 100 mg MEP quadriweekly (i.e. one time every four weeks). Twelve months after therapy, in addition to absent clinical symptoms and normalized biomarker levels, cardiac examinations showed normalized rhythm and left ventricular ejection fraction, resolved myocardial edema, and reduced mid-wall and endocardial delayed gadolinium enhancement (Figure 1c, d). No adverse effects were observed. The patient had a complete remission with sparing daily use of GCs.

Persistent blood and tissue eosinophilia can damage the myocardium and endocardium, causing eosinophilic myocarditis/endomyocarditis in EGPA.[3,7] In our patient, the improvement in endomyocarditis appeared to be mediated by an action mechanism of reduced eosinophilia under anti-IL-5 therapy. Mepolizumab injection has indications for eosinophilic asthma and hypereosinophilic syndrome quadriweekly (i.e. one time every four weeks) at 100 and 300 mg, respectively. This medication was approved in EGPA based on a phase III trial comparing a 300 mg regimen with a placebo.[8] Since there were no available dose-escalation

studies, it remains to be determined whether 100 mg is inferior to the 300 mg regimen. Nevertheless, in practice, most patients with EGPA receive a 100 mg regimen.[9,10] A recent European retrospective study has demonstrated similar efficacy and higher safety of 100 mg dose compared to 300 mg for EGPA therapy.[10]

Ethics Approval: The Institutional Review Board of our hospital approved this study (IRB number B-ER-105-108, human study amendment approval on 2022 March 16 with research term extending till 2025 April 30).

Patient Consent for Publication: A written informed consent was obtained from patient.

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

Author Contributions: Study conception and design: W.C.R.; Acquisition of data: W.C.R., T.Y.S., L.C.H.; Analysis and interpretation of data: W.C.R., T.Y.S., L.C.H.: All authors were involved in drafting the article and approved the final version to be published.

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