## Successful treatment of eosinophilic granulomatosis with polyangiitis and Crohn's disease with combined mepolizumab and adalimumab

Sirs,

Hypereosinophilia (HE), defined as a peripheral eosinophil count >1,500/μL, can result from various conditions, making differential diagnosis challenging (1). We report the case of a 25-year-old male presenting with non-specific symptoms, including fatigue, cough and respiratory discomfort. Blood tests revealed severe HE (eosinophil count of 23,000/μL), along with elevated levels of IgE, C-reactive protein, and troponin. Cardiac MRI confirmed myopericarditis (Fig.1 a,b), initially treated with NSAIDs and colchicine.

The patient developed diarrhoea with negative faecal calprotectin, a marker of intestinal inflammation, leading to the suspicion of colchicine-induced diarrhoea. Given the presence of fever, an extensive infectious workup was performed which yielded negative results. PET-CT scan revealed hypermetabolism in multiple deep lymphadenopathies and in a focal area of the small intestine. Bone marrow biopsy and genetic testing for primary hypereosinophilic syndromes (FIP1L1/PDGFRalpha, PDGFRbeta, FGFR1) and systemic mastocytosis (D816V c-kit) were negative.

Further evaluation detected mildly elevated anti-proteinase 3 (anti-PR3) IgG antibodies (12 IU/mL; normal <2 IU/mL), high rheumatoid factor (RF) titres (918 IU/mL; normal <15 IU/mL), and mild bronchial hyperreactivity on spirometry. These findings supported a diagnosis of eosinophilic granulomatosis with polyangiitis (EGPA) and the patient was started on mepolizumab (300 mg/month), an anti–IL-5 monoclonal antibody. This therapy led to prompt clinical and laboratory improvement, including normalisation of eosinophil count and resolution of fever, without requiring corticosteroids.

A colonoscopy was performed to investigate persistent diarrhoea, revealing mildly hyperaemic mucosa with areas of lymphoid hyperplasia. Histology was consistent with a reactive process. A biopsy of a PET-positive hypermetabolic lymph node showed reactive follicular lymphoid hyperplasia.

Despite overall clinical improvement, diarrhoea persisted and coincided with a rise in faecal calprotectin, anti-PR3 antibody titres, and systemic inflammatory markers. At this stage, eosinophil counts had normalised, and RF levels had decreased. A repeat colonoscopy showed macroscopic (Fig.1 c-d) and histological (Fig.1 e-g) findings consistent with Crohn's disease (CD).

Ultimately, the patient was diagnosed with two concurrent conditions: EGPA (based on eosinophilia, anti-PR3 positivity and high RF) with constitutional (fever), cardiac (myopericarditis), and respiratory (bronchial hyperreactivity) involvement, and CD. He continued on mepolizumab, which effectively controlled vasculitis, and was started on adalimumab (40 mg every 2 weeks), an anti-TNF-α agent, approved for CD. This led to resolution of diarrhoea and systemic inflammation.

This is the first reported case in which two rare autoimmune diseases with distinct pathogenetic mechanisms were successfully treated using a combination of two tar-

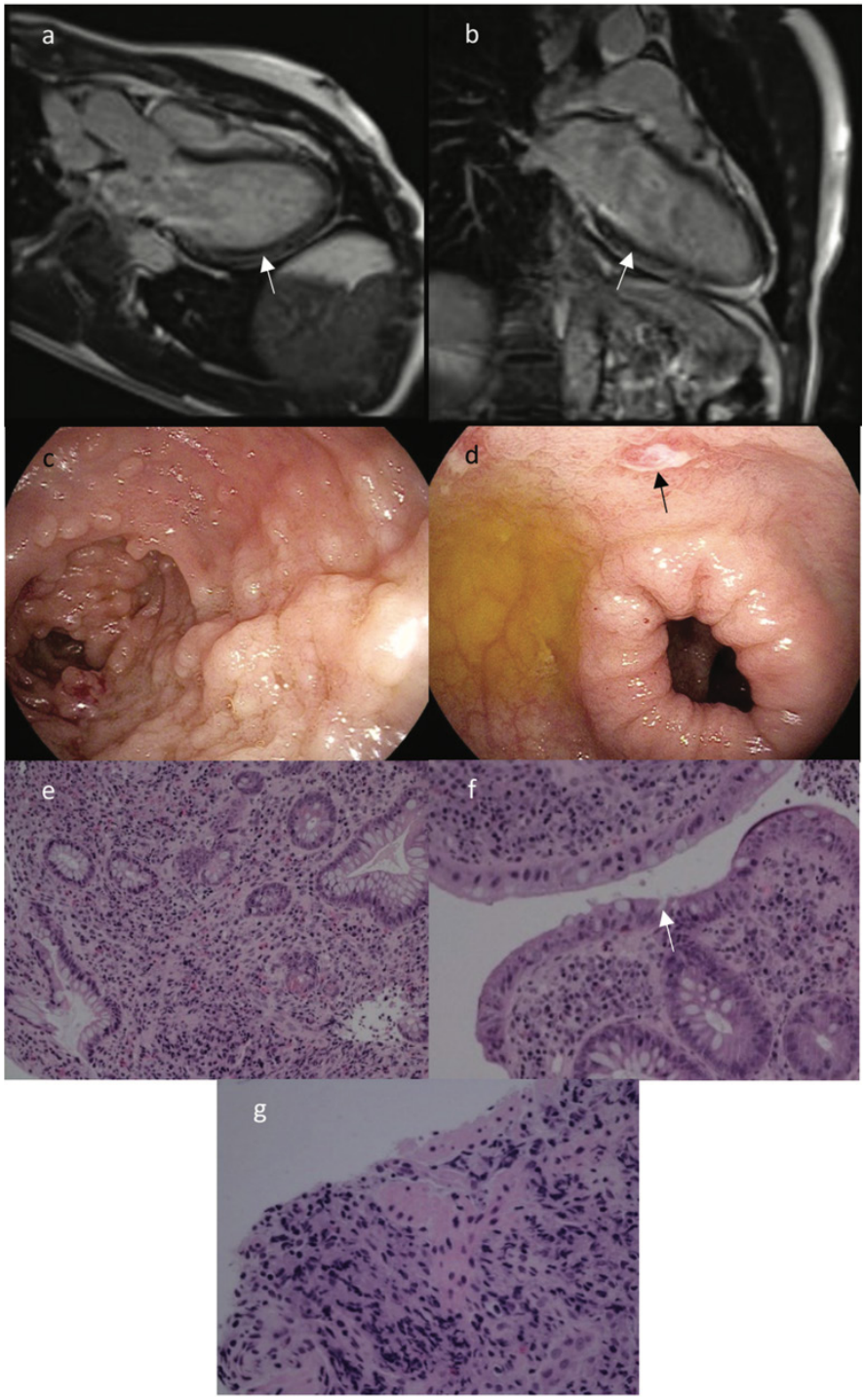


**Fig. 1.** a-b) Myopericarditis: detailed cardiac MRI images. Late enhancement areas are observed in the delayed post-contrast sequences, with a subepicardial localisation, involving the inferior (a) and inferolateral (b) mid-basal wall. c, d) Colonoscopy: macroscopic findings diagnostic of Crohn's disease. c) Inflammatory pseudo-polyps of the colon. d) Superficial colonic ulcer. e, f, g) Histopathological detail of colonoscopy sections stained with haematoxylin and eosin. e) Cryptitis, representative image of chronic and active inflammatory infiltrate, with presence of neutrophilic granulocytes (20 x). f) Superficial erosion (20 x). g) Transmural inflammation (40 x).

geted monoclonal antibodies: mepolizumab and adalimumab.

The key challenge was to determine whether the presentation reflected one atypical disease or two separate immune-mediated conditions (2). Eosinophilia, while a hallmark of EGPA, has also been associated with more severe forms of Inflammatory Bowel Disease (IBD) (3). In addition, anti-PR3 antibodies, typically linked to ANCA-associated vasculitis, can occasionally be found in IBD (4). RF elevation, commonly observed in vasculitis, has also been correlated with eosinophilia (5).

Given the concomitant diagnosis of EGPA and CD, combination therapy was initiated. Mepolizumab, which effectively reduces eosinophilia and related symptoms in EGPA, particularly in ANCA-negative or non-vasculitic forms, helped control systemic and respiratory manifestations and prevented myopericarditis relapse (6). Adalimumab, which induces and maintains remission in CD, was subsequently added to the treatment regimen (7). Notably, the initial decision to withhold corticosteroids allowed the full clinical picture to emerge, leading to a timely and accurate diagnosis of CD. Although the combination of biologics carries distinct infection risks, with TNF inhibitors associated with bacterial and tuberculosis infections (8) and mepolizumab with parasitic infections (9), no adverse effects were observed during treatment.

This case highlights the feasibility and potential clinical value of combining biologics with distinct mechanisms of action and safety profiles to personalise treatment and avoid corticosteroids in complex autoimmune overlap syndromes (10).

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