Early introduction of mepolizumab for refractory coronary vasospasm and severe acute coronary syndrome secondary to eosinophilic granulomatosis with polyangiitis: a case report

Sirs,

We report on a 40-year-old man, of Iraqi ethnicity, with a 5-year history of not allergic asthma, who was admitted in April 2023, to our hospital for asthma exacerbation, followed by atrial fibrillation and chest pain with normal troponin and ECG. Four days later the patient underwent a cardiac arrest with pulseless electrical activity converted with adrenalin, into ventricular fibrillation, refractory to multiple DC shocks with the need for mechanical support with extracorporeal membrane oxygenation. Coronary angiography revealed diffuse vasospasm in the left arteries; he was treated with intracoronary nitrates with rescue of the normal flow except for the 2° marginal branch of the circumflex, which required angioplasty with stent implantation for an atherosclerotic stenosis. After revascularisation there was a restoration of heart activity. The patient remained one month in Intensive Care Unit for several infections.

When he was admitted to our Internal Medicine Unit, he presented, during corticosteroids tapering, several asthma exa-cerbations and episodes of chest pain with normal troponin and ECG. Laboratory analysis revealed a progressive increase of eosinophilic count (peak 7.950/mmc) (Fig. 1) and p-ANCA positivity (anti-MPO). A cardiac MRI showed a diffuse left ventricular (LV) hypokinesia with a moderate ventricular dysfunction (LVEF 37%), diffuse subendocardial fibrosis, high native T1-mapping (1365msec) and extracellular volume (ECV36%) values, evocative of myocardial involvement. A craniofacial MRI and a HRCT scan reveal nasal sinus mucosal thickening and diffuse consolidation areas, respectively. Electroneurography was negative. EGPA was diagnosed and therapy with 6-methyl-prednisolone pulses, followed by oral prednisolone and cyclophosphamide, was started. One week after, eosinophilic count was still high (3040/mmc); the patient presented a new episode of chest pain with troponin elevation (4430 ng/l) and an inferior NSTEMI at ECG. A new coronarography showed a severe vasospasm of the right coronary artery, that required intracoronary nitrates. After 2 weeks from intravenous 6-methyl-prednisolone, an elevation of transaminases (2.5 times ULN) occurred and cyclophosphamide was stopped (cumulative dose 1.2gr). The patient still presented episodes of chest pain and asthma exacerbations requiring high doses of prednisone. Therefore, after 18 days from corticosteroid pulses, mepolizumab 300mg/4weeks was introduced, as corticosteroid-sparing therapy. Due to the transaminases' elevation and the history of infections no immunosuppressant was associated. After 6 months from mepolizumab introduction, remission (BVAS=0 and prednisone<5mg/day) was achieved (Fig. 1).

However, after 7 month the patient developed a sensitive neuropathy of the left peroneal nerve. Prednisone was increased (25mg/day tapered to 5mg/day within 1 month) and mycophenolate mofetil 2g/day was introduced with quick resolution of symptoms. A cardiac MRI after 10 months from mepolizumab introduction showed a stable subendocardial fibrosis with mild LV dysfunction (LVEF 52%, ECV30%).

Cardiac involvement represents the main cause of death in EGPA (1), especially in patients ANCA-negative with high eosinophil levels (2). Guidelines recommend corticosteroids as initial therapy for organ-threatening manifestations, as cardiomyopathy, together with cyclophosphamide or rituximab (3).

Recent studies described in hypereosinophilic disorders an eosinophilia-associated coronary vasospasm (CV), a condition presenting with vasospastic angina or repetitive ACS, that might be life-threatening (4). Huang *et al*. reported that anti-IL5 agents seem promising in the long-term control of eosinophilia-associated CV (5).

Our patient presented a severe CV at EGPA onset, resulting in cardiac arrest and ACS. Due to hepatotoxicity, he could not be treated with cyclophosphamide. The history of multiple infections before EGPA diagnosis, made rituximab inadvisable. Given his severe hypereosinophilia, resistant to prednisolone pulses, mepolizumab was introduced early, alongside with corticosteroids and remission was achieved in six months.

Eosinophilia significantly contributes to cardiac damage in EGPA (1, 6) through several mechanisms, as direct cardiomyocytes cytotoxicity, fibrogenesis and thrombosis. Postmortem studies indicate that eosinophilic infiltration of coronary arteries may trigger vasospasm (7). At cardiac MRI our patient exhibited a characteristic non-ischaemic LGE pattern (8), suggesting that vasospasm and eosinophilic damage were primary contributors to cardiac injury. Mepolizumab successfully controlled eosinophil levels, prevented vasospasm and chest pain recurrences, indicating that the early inhibition of

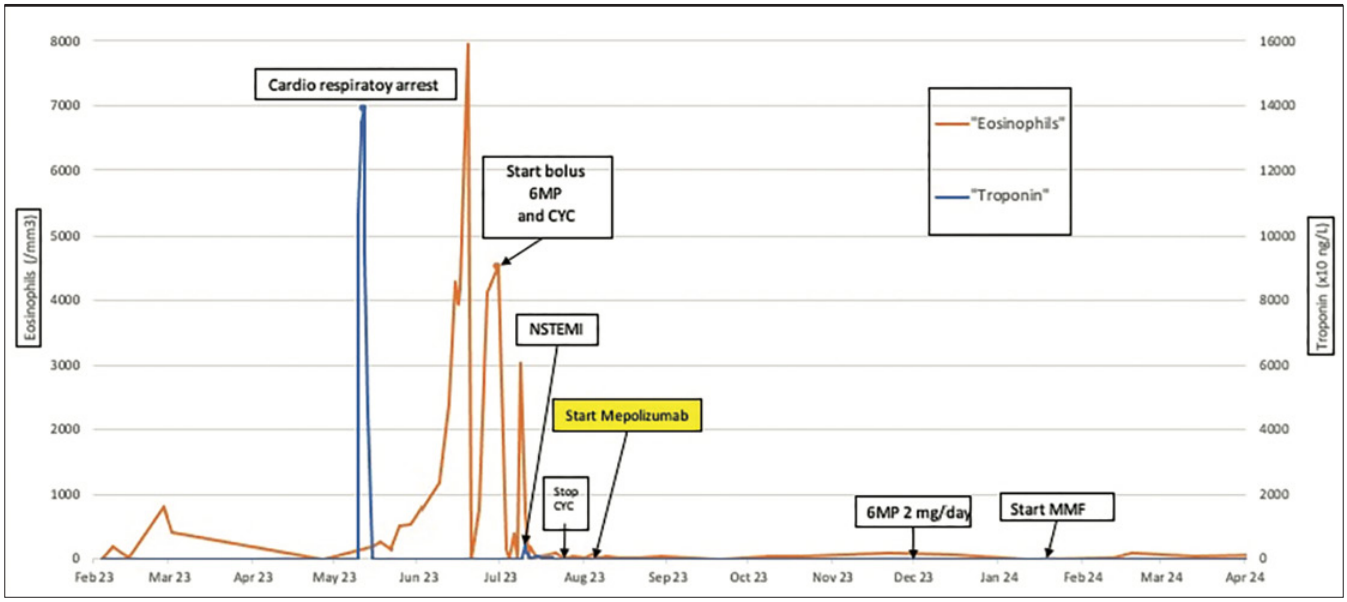

Fig 1. The graph shows the trend of serum troponin values and eosinophil count of the patient during hospitalisation and in the following months.
CYC: cyclophosphamide; MMF: mofetil mychophenolate.

eosinophils is crucial for managing cardiac damage.

Interestingly, the patient developed after 7 months a left peroneal neuropathy, which resolved with a short course of corticosteroids and the introduction of mycophenolate mofetil. This suggests caution when using mepolizumab in monotherapy in ANCA-positive patients, who may present vasculitic manifestations. The ongoing randomised controlled trial (E-MERGE) aims to address this issue (9).

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