Case Report

Acute necrotizing eosinophilic myocarditis presenting with cardiogenic shock after mRNA booster dose for COVID-19: Case report and review of literature

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Abstract

Eosinophilic myocarditis is a rare subtype of myocarditis characterized by myocardial eosinophilic infiltration, and it is potentially lethal if untreated. In its severest form, acute eosinophilic necrotizing myocarditis may lead to cardiac dysfunction and cardiogenic shock. Several cases have been reported after coronavirus disease 2019 (COVID-19) vaccination, but the pathophysiology is still unclear. We describe a case of acute necrotizing eosinophilic myocarditis complicated by cardiogenic shock in a 33-year-old man after booster dose of mRNA COVID-19 vaccine. The patient was diagnosed with endomyocardial biopsy, successfully treated with steroids, and discharged on Day 20 after admission in stable condition. In short term follow-up, he was asymptomatic with normal left and right ventricular ejection fraction.

Learning objectives: Eosinophilic myocarditis (EM) still has a high morbidity and mortality, so it is crucial to promptly diagnose it and treat as appropriate. Endomyocardial biopsy is the gold standard for the diagnosis of EM. This case highlights the diagnostic work-up, differential diagnosis of hypereosinophilia, and the management of this life-threatening condition.

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Keywords:
Eosinophilic myocarditis
Hypersensitivity myocarditis
Myocarditis
Coronavirus disease 2019
Severe acute respiratory syndrome coronavirus-2 vaccine
Endomyocardial biopsy

Introduction

Eosinophilic myocarditis (EM) is a potentially lethal disease characterized by eosinophil infiltration of the myocardium. It may arise from several etiologies, such as hypersensitivity or autoimmune diseases, infections, or neoplasms. In some cases, the etiology remains unknown, and it is defined as idiopathic hypereosinophilic syndrome [1]. Clinical manifestations range from mild symptoms to severe syndromes and its severest form, the acute necrotizing EM, may lead to cardiogenic shock [1]. The definitive diagnosis is made through endomyocardial biopsy, while cardiac magnetic resonance may be helpful after the acute phase to identify the structural changes caused by myocarditis. Treatment includes corticosteroids and, in some cases, anticoagulation together with heart failure therapy and management of cardiac complications [2]. Recently, myocarditis has increasingly emerged as an adverse effect of coronavirus disease 2019 (COVID-19) vaccinations [3]. We present the case of a patient who developed cardiogenic shock due to acute necrotizing EM after mRNA booster dose for COVID-19.

Case report

A 33-year-old man was admitted to a peripheral hospital for dyspnea, chest, and abdominal pain. The patient had a history of juvenile epilepsy in pharmacological treatment with valproic acid 500 mg b.i. d.; no history of cardiac disease or cardiovascular risk factors; he received Pfizer-BioNTech COVID-19 booster vaccination 10 days before hospital admission. Recent medical history did not reveal fever and/or recent infections, no overseas travel in the last months, and no history of known allergic diathesis. The clinical examination showed increased jugular pressure, bilateral lung rales, quiet heart sounds, gallop rhythm without peripheral edema. Blood pressure was 90/60 mmHg, heart rate...
around 100 bpm. Electrocardiogram (ECG) showed sinus tachycardia and diffuse ST-segment elevation with no reciprocal changes (Online Fig. 1); laboratory tests revealed eosinophilic leucocytosis at complete blood count with elevated high-sensitivity troponin I (hs-TnI, 4748 pg/ml) and C-reactive protein levels (CRP, 8.5 mg/dl, upper limit <0.05 mg/dl). The nasopharyngeal swab tested negative for severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). Echocardiography showed global hypokinesia with reduced left ventricular ejection fraction (LVEF 35%), normal right heart size and function, no significant valvular diseases, and pericardial effusion with signs of tamponade. Urgent pericardiocentesis was performed draining around 250 ml of citrine fluid and the patient was admitted to the cardiology ward. On the next day, due to the progression of LV dysfunction with haemodynamic instability, the patient was referred to our intensive care unit (ICU).

The differential diagnosis included acute coronary syndrome, fulminant myocarditis, and septic shock. COVID-19 was excluded through the SARS-CoV-2 polymerase chain reaction (PCR) test. ECG showed non-

![Fig. 1.](image)

Light (A and B) and electron microscopy (C-E) views of endomyocardial biopsy samples. Massive interstitial inflammatory infiltration, burdened by eosinophilic granulocytes (A: hematoxylin and eosin; B: Giemsa stain). Panel (C) shows a partially degranulated eosinophilic granulocyte close to a myocyte that shows non-specific myofibrillar lysis. Although the inflammatory cells were mixed (D), most infiltrates were constituted of eosinophilic granulocytes (E).

![Fig. 2.](image)

Short-axis late gadolinium enhancement imaging demonstrated intramyocardial fibrosis at middle inferior septum (red arrows); at the same level, T1 mapping showed an increased native T1 value (yellow arrows).
ischemic abnormalities, troponin was elevated, and echocardiogram findings together with leukocytosis and elevated CRP oriented to differential diagnosis between peri-myocarditis or septic shock. Blood and urine cultures were unrevealing and chest X-ray showed bilateral pleural effusion, ruling out the infective status hypothesis. Pericardial exudate demonstrated inflammatory cells but was negative for malignant cells, acid-fast bacilli stain, and tuberculosis PCR. Moreover, the presence of remarkable eosinophilia at presentation and the recent vaccination raised concern for possible drug-induced eosinophilia versus hypersensitivity reaction.

Myocarditis is one of the major recognized adverse reactions to the COVID-19 mRNA vaccine. EM is a hypersensitivity syndrome with cardiac involvement and, about in 20 % of cases, persistent eosinophilia [4]. Myocarditis is a major cause of morbidity and mortality. Eosinophil-mediated cardiac damage evolves through 3 phases and many cases are fatal in the first stage: acute necrotic phase, an intermediate stage with hypercoagulability and risk of thrombotic development, and, if not promptly diagnosed and treated, a fibrotic stage that may result in restrictive cardiomyopathy [5]. The histological findings obtained by EM were characterized by prevalent eosinophil infiltrates associated with the degranulation of crystalloids (Fig. 1). Early diagnosis and treatment with high-dose steroids have however resulted in complete cardiac recovery in the majority of individuals [2]: our patient, immediately treated with systemic steroids, demonstrated a fast recovery, thus not requiring any mechanical support. In a systematic revision of all published histologically proven cases of EM [2,3], 6% of cases were not attributed to an underlying heart disease but to eosinophilic cardiomyopathy, and, if not promptly diagnosed and treated, a fibrotic stage that may result in restrictive cardiomyopathy [5].

**Table 1**

| Infections | Urine cultures | Negative |
| Blood cultures | Negative |
| Pericardial fluid | Negative |
| HCV, HBV, HAV, HDS, CMV, HHV-6, EBV, parvovirus B19, adenovirus, Cossackie virus, HTLV1–2 | Negative |
| Toxoplasmosis, Toxocara spp., Entamoeba histolytica, Strongyloides stercoralis; parasitological stool test | Negative |
| Immunology | Total IgE | 30 μg/l (n.v. 0–87) |
| Total IgA | 1.15 g/dl (n.v. 0.80–3.50) |
| Total Ig M | 2.38 g/dl (n.v. 0.50–2.00) |
| IgG | 270.7 mg/l (n.v. 29.2–864.0) |
| Complement C3 | 1.10 g/dl (n.v. 0.79–1.52) |
| Complement C4 | 0.13 g/dl (n.v. 0.16–0.38) |
| Autoimmunity | c-ANCA; p-ANCA, ANA, AMA, ENA, nDNA-Ab | Negative |
| Coronavirus | SARS-CoV2 PCR testing | Negative |
| RBD–SARS–CoV2 Ab | Positive (28,925 U/ml) |
| Total SARS–CoV2–Ab | Positive |
| Hematology | BCR/ABL, PDGFR/TEL; FIPIL1/PDGFR | Negative |
| HCV, hepatitis C virus; HBV, hepatitis B virus; HAV, herpes simplex virus; VZV, varicella-zoster virus; HHV-6, human herpesvirus 6; EBV, Epstein-Barr virus; HTLV1–2, human T-lymphotropic virus type 1–2; IgG, immunoglobulin G; IgA, immunoglobulin A; IgM, immunoglobulin M; IgG4, immunoglobulin G4; c-ANCA, p-ANCA, anti-neutrophil cytoplasmic antibodies targeting proteinase 3 and myeloperoxidase respectively; ANA, anti-nuclear antibody; AMA, anti-mitochondrial antibody; ENA, extractable nuclear antigen; nDNA-Ab, anti-native DNA antibody; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; RBD-SARS-CoV-2 Ab, anti-SARS-CoV-2 spike protein receptor binding domain. BCR/ABL, PDGFR/TEL; FIPIL1/PDGFR gene transcripts. |
significantly differ between people who received COVID-19 vaccines and those who received non-COVID-19 vaccines. However, among people who received COVID-19 vaccines, the incidence of myopericarditis was significantly higher in males, in people younger than 30 years, after receiving an mRNA vaccine, and after the second dose of vaccine (vs. a first or a third dose) [3]. More recently, EM has been described as a possible adverse reaction to the mRNA COVID-19 vaccine, suggesting a possible hypersensitivity to some component of the vaccine that may act as a hapten: the first case has been reported in a previously well 57-year-old woman after the first Pfizer-BioNTech vaccine [8], and three cases were described within a period of two weeks after the second dose of the same vaccine in patients with known allergic disorders [9]. Furthermore, the presence of eosinophils in myocardial infiltrates has already been described in previous reports of post-COVID-19 vaccine myocarditis undergoing EMB or autopsy studies [10]. In conclusion, in our case, EMB was essential to make the diagnosis and start immunosuppressive treatment. Although a definite cause was not identified, the recent vaccination supports the hypothesis of a possible role of mRNA vaccine in the pathogenic mechanisms. Myocarditis is increasingly being reported in young adults after vaccination for COVID-19, predominantly in young males after their second dose of vaccination [3]. Temporal association does not prove causation, but the brief timespan between vaccination and myocarditis onset together with recent evidence lend support to a possible relationship that deserves further investigations.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jccase.2022.10.001.

Funding

Not funded.

Declaration of competing interest

The authors declare that there is no conflict of interest.

Acknowledgments

NA.

References