Vasculitis in acute cellular rejection early after heart transplantation

Zofia Lasocka[1], Rafał Pęksa[2], Jerzy Bellwon[1], Marcin Gruchała[1]

[1]1st Department of Cardiology, Medical University of Gdansk, Gdańsk, Poland
[2]Department of Pathomorphology, Medical University of Gdansk, Gdańsk, Poland

Correspondence to:
Zofia Lasocka, MD,
1st Department of Cardiology,
Medical University of Gdańsk,
Smoluchowskiego 17,
80–214 Gdańsk, Poland,
phone: +48 58 584 47 10,
e-mail:
zofia.lasocka@gumed.edu.pl

DOI: 10.33963/KP.a2023.0148

Received:
February 27, 2023

Accepted:
June 11, 2023

Early publication date:
July 2, 2023

We present a case of a 38-year-old male with cardiac graft rejection and concomitant vasculitis, admitted to our Department of Cardiology for protocol monitoring of graft rejection. The patient underwent heart transplantation 10 weeks earlier due to severe ischemic cardiomyopathy. The early postoperative period was complicated with primary graft dysfunction, diagnosed on the basis of the current guidelines. Due to low output syndrome and, consequently, kidney and liver failure, the patient required temporary venoarterial extracorporeal membrane oxygenation, renal replacement therapy, and albumin dialysis. First endomyocardial biopsies (EMBs) showed no signs of rejection.

On current admission, the patient reported exertional intolerance and dyspnea, NYHA (New York Heart Association) class II. Physical examination revealed no abnormalities. Blood tests demonstrated elevated B-type natriuretic peptide level — 253 pmol/l (normal <21 pmol/l), while troponin I was in the normal range — 0.023 µg/l (normal <0.036 µg/l). The immunosuppressive drugs taken by the patient included tacrolimus 4 mg b.i.d., mycophenolate mofetil 500 mg b.i.d., and prednisone 20 mg daily. Tacrolimus serum level was 15.5 µg/l, within the target range three months after heart transplantation.

On the electrocardiogram, regular sinus rhythm of 88 bpm, narrow QRS complexes, and no significant ST-T-wave changes were detected. A transthoracic echocardiogram revealed good systolic and diastolic function of the left ventricle and preserved right ventricular contractility, without any valvular defects.

Coronary angiography showed no significant stenosis in any of the epicardial arteries, while EMBs indicated infiltration of multiple inflammatory cells with myocyte injury, corresponding with acute cellular rejection (ACR) grade 2R. Additionally, lymphocyte infiltration was detected in the wall of intramyocardial arterial vessels, defined as vasculitis (Figure 1). The antibody-mediated rejection (AMR) was C4d-negative.

To treat the biopsy-proven graft rejection, a 3-day course of intravenous methylprednisolone 1000 mg/day was used. Then, oral prednisone at an increased dose of 1 mg/kg/day was introduced and then gradually reduced. The dosage of tacrolimus and mycophenolate mofetil did not change. After two weeks of enhanced immunosuppression, a repeat EMB revealed no evidence of lymphocyte infiltration in either myocardium or vessel walls (ACR grade 0R).

This is the first example of rejection-induced vasculitis in over 100 cardiac transplant recipients in our Heart Transplantation Center, successfully reversed with increased immunosuppression.

Vasculitis, defined as an inflammatory process affecting intramyocardial arteries up to capillaries, was demonstrated to be a negative predictor of both humoral and cellular rejection [1]. Moreover, the presence of this histological feature, despite the grade and type of rejection, carries a poor prognosis in terms of mortality and rejection persistence [2]. Although most described cases concerned mixed rejection (pathological AMR plus ACR) associated with the worst outcomes [3], vasculitis might also be observed in positive ACR without any sign of humoral rejection in the same EMBs, as presented in our case. This is especially worth noting as the frequency

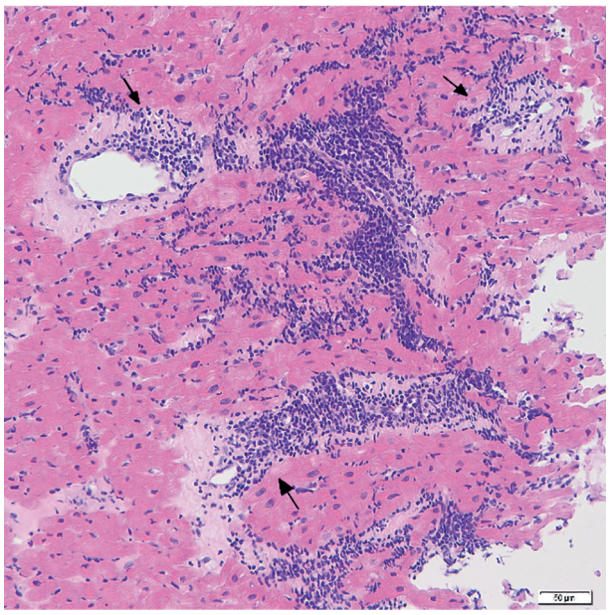

Figure 1. Interstitial, perivascular, and endocardial lymphocyte infiltration with prominent nucleoli associated with myocytolysis. Note the lymphocyte infiltration of the vascular walls (arrows). H&E, ×10

of ACR is approximately 45%, and both AMR and mixed rejection are detected in less than 5% of EMBs [4].

There are no specific guidelines concerning the management of heart transplant recipients with rejection-induced vascular damage. Only a few reports illustrated successful treatment of vasculitis with increased immunosuppression [5]. Our case corresponds with those outcomes, meaning that enhanced corticosteroid therapy should reverse lymphocyte infiltration in the myocardium and vessel wall.

Identification of cardiac recipients with rejection-induced vasculitis that need temporally enhanced immunosuppression is of great clinical importance to avoid further immunological aggression against the graft.

Article information

Conflict of interest: None declared.

Funding: None.

References

1. Fedrigo M, Romano A, Bottio T, et al. Vasculitis in post-heart transplant endomyocardial biopsy: possible relationship with mixed rejection, circulating donor specific antibodies and worse outcome. J Heart Lung Transplant. 2018; 37(4): S302, doi: 10.1016/j.healun.2018.01.767.
2. Cipullo R, Finger MA, Rossi Neto JM, et al. Vasculitides and eosinophils in endomyocardial biopsies as rejection predictors in heart transplantation. Arq Bras Cardiol. 2011; 97(2): 163–170, doi: 10.1590/s0066-782x2011005000069, indexed in Pubmed: 21655876.
3. Fedrigo M, Bottigliengo D, Romano A, et al. Clinical relevance of vasculitis in heart transplant. J Heart Lung Transplant. 2020; 39(4): S59–S60, doi: 10.1016/j.healun.2020.01.1252.
4. Fedrigo M, Bottigliengo D, Romano A, et al. Clinical relevance of vasculitis in mild form of rejections in heart transplant patients. J Pulm Med. 2021; 5: 1–6.
5. Ballester M, Obrador D, Carrió I, et al. Reversal of rejection-induced coronary vasculitis detected early after heart transplantation with increased immunosuppression. J Heart Transplant. 1989; 8(5): 413–417, indexed in Pubmed: 2795284.