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Vasculitis in acute cellular rejection early after heart transplantation

Short title: Vasculitis early after heart transplantation

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We present a case of 38-year-old male with cardiac graft rejection and concomitant vasculitis, admitted to our cardiological department for protocol monitoring of graft rejection. The patient underwent heart transplantation 10 weeks prior due to severe ischemic cardiomyopathy. The early post-operative period was complicated with primary graft dysfunction, detected based on 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.

At current admission, the patient complained about exertional intolerance and dyspnoe 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 the troponin I was between 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 under three months after heart transplantation.

In electrocardiogram regular sinus rhythm of 88 bpm, narrow QRS complexes and no significant ST-T changes were detected. Transthoracic echocardiogram revealed good systolic

and diastolic function of left ventricle and preserved right ventricular contractility, without any valvular defects.

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

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

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

Vasculitis, defined as an inflammatory process affecting intramyocardial arteries up to capillaries, was proved a negative predictor of both humoral and cellular rejection [1]. Moreover, presence of this histological feature, despite the grade and type of rejection, carries the poor prognosis in terms of mortality and persistence of rejection [2]. Although most available cases concerned mixed rejection (pathologic AMR + ACR) associated with the worst outcomes [3], vasculitis might also be observed in positive ACR without any sign of humoral rejection during the same EMB, as presented in our case. Especially as the frequency of ACR is approximately 45%, and both AMR and mixed rejection are detected in less than 5% of EMBs [4].

There lack specific guidelines concerning 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 these outcomes, meaning that enhanced corticosteroid therapy should reverse the lymphocytic infiltrate in myocardium and vessel wall.

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

Article information

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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.

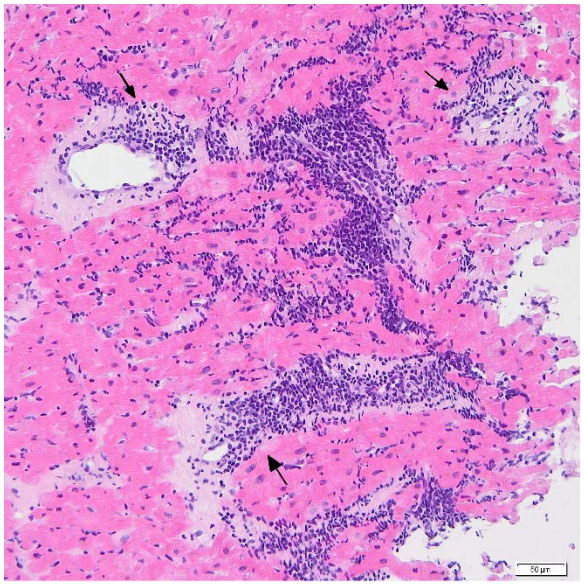

Figure 1. Interstitial, perivascular and endocardial lymphocytic infiltrate with prominent nucleoli associated with myocytolysis. Note the lymphocytic infiltrate of vascular walls (arrows). H&E, ×10