Acute Orthotopic Heart Transplantation Rejection With ST-Segment Elevation in Leads I and aVL

Peter Vlismas, MD; Pedro Villablancas, MD; Andrew Krumerman, MD; Snehal Patel, MD; J. Julia Shin, MD; Ulrich P. Jorde, MD; Daniel B. Sims, MD

Acute allograft rejection is a prominent cause of graft failure in heart transplant recipients. Graft infiltration with immune-mediated cells is associated with changes in electric conduction. ECG patterns in heart transplant rejection generally include changes in the electric activity of the atria. ST-segment elevation is an uncommon presentation in acute rejection. We describe a case of mixed cellular and humoral rejection in a 74-year-old man 5 years after orthotopic heart transplantation presenting with lateral ST-segment elevations on ECG and normal coronary arteries on coronary angiography. Endomyocardial biopsy revealed International Society for Heart and Lung Transplantation grade 3R severe acute cellular rejection with associated pAMR1 (I+) antibody–mediated rejection.

Case Presentation
A 74-year-old man with chronic heart failure caused by an ischemic cardiomyopathy who underwent heart transplantation 5 years previously presented with left-sided chest pain of 4 days duration. Associated symptoms included dyspnea on exertion, fatigue, orthopnea, paroxysmal nocturnal dyspnea, and nausea. The past medical history was notable for an episode of acute cellular rejection 4 years before admission. The patient’s medications included aspirin, rosuvastatin, clonidine, and a 2-drug immunosuppression regimen consisting of tacrolimus and mycophenolate mofetil.

On presentation, the patient’s blood pressure was 150/86 mm Hg, heart rate 106 beats per minute, and respiratory rate 30 breaths per minute. He was afebrile. Physical examination was remarkable for jugular venous distension, bibasilar crackles, and 1+ bilateral lower extremity edema. ECG revealed sinus tachycardia with ST-segment elevations in leads I and aVL with reciprocal changes in the inferior leads consistent with a lateral myocardial infarction (Figure 1). The patient was taken for emergent coronary angiography that revealed no obstructive coronary lesions. Echocardiogram obtained in the cardiac catheterization laboratory revealed a left ventricular ejection fraction of 25% and severe right ventricular dysfunction. A right heart catheterization performed while the patient was receiving dobutamine infusion showed severely elevated biventricular filling pressures and low cardiac index. An endomyocardial biopsy was performed. Laboratory analysis sent off in the emergency department returned a creatine phosphokinase of 983 U/L, troponin T of 1.28 ng/mL, pro-brain natriuretic peptide of 146 128 pg/mL, potassium of 5.0 mEq/L, creatinine of 5.0 mg/dL, aspartate aminotransferase of 2676 U/L, and alanine aminotransferase of 1911 U/L. The patient was diagnosed with cardiogenic shock resulting in renal and hepatic failure. He was empirically started on intravenous methylprednisolone because of suspicion for acute allograft rejection. Blood pressure declined, and he required vasopressor support in addition to inotropic support. Tacrolimus level returned undetectable. The endomyocardial biopsy revealed both severe acute cellular (Figures 2 and 3) and antibody-mediated rejection (Figure 4). The patient was started on cytolytic therapy with thymoglobulin for cellular rejection. He received intravenous immunoglobulin and plasmapheresis to treat the antibody-mediated rejection. ST-segment elevation resolved on hospital day 5 (Figure 1). Repeat endomyocardial biopsy on hospital day 12 showed resolved cellular rejection with minimal evidence of antibody-mediated rejection (Figure 5).

Echocardiogram that day showed minimal improvement in function. Repeat echocardiogram on hospital day 23 showed normalized biventricular function.

Discussion
Acute allograft rejection is a major cause of early mortality after heart transplantation. Cellular rejection, mediated by a T-lymphocyte response to the allograft tissue, is the most common form of rejection in heart transplant recipients. Antibody-mediated (humoral) rejection occurs because of antibody fixation and activation of the complement cascade resulting in tissue injury. Mixed cellular and humoral rejection is uncommon and has been associated more often with International Society for Heart and Lung Transplantation grade 3R rejection. Although acute rejection is a common complication post heart transplantation, ST-segment elevation has not been associated with rejection. Review of the literature reveals only 1 case report of a patient 2 weeks post heart transplantation that developed ST-segment elevation on the ECG. Autopsy revealed acute cellular rejection.

ECG findings commonly seen with rejection are low QRS voltage and atrial flutter or atrial fibrillation. Although low

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From the Division of Cardiology (P. Villablanca, A.K., S.P. J.J.S., U.P.J, D.B.S.), Department of Medicine (P. Vlismas), Montefiore Medical Center, Bronx, NY.
Correspondence to Peter Vlismas, MD, Montefiore Medical Center, 111 E 210 St, N W 3 Room 351, Bronx, NY 10467. E-mail pvlismas@montefiore.org
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QRS voltage during severe rejection has been explained by edema between the myocytes, the mechanism of ST-segment elevation has not been elucidated. We surmise that intense inflammation caused by the combined cellular and antibody-mediated rejection led to an injury current and ST-segment elevation manifest on the ECG. Heart transplant patients can develop ST-segment elevation; however, this often occurs in the setting of a myocardial infarction because of coronary allograft vasculopathy, also called transplant coronary artery disease. Coronary allograft vasculopathy is an immune-mediated process involving smooth muscle hyperplasia characterized by diffuse, concentric proliferation rather than the focal, eccentric lesions of coronary atherosclerosis.

Conclusions

In conclusion, this is the first case to our knowledge of mixed cellular and antibody-mediated rejection presenting with ST-segment elevation. It exemplifies the difficulty of rapid and accurate diagnosis of the cause of acute ST-segment elevation. Our case highlights the need for awareness of this rare ECG manifestation in transplant recipients and the importance of recognizing imitators of acute myocardial infarction presenting with ST-segment elevation.

Disclosures

None.

References


Key Words: allograft ■ antibodies ■ cardiac catheterization ■ electrocardiography ■ heart transplantation
Figure 4. Same endomyocardial biopsy with C4d staining, showing capillary deposition of complement degradation product C4d, an immune-pathological finding in antibody-mediated rejection.

Figure 5. Repeat endomyocardial biopsy on hospital day 12 showing minimal inflammation.
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