Relapsing Leukemia Infiltrating the Heart

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Large granular lymphocyte (LGL) leukemia is a chronic indolent leukemia. Microscopic evidence of cardiac involvement by leukemia is found in 30% to 40% of patients who have died of the disease. Most of the times it is diagnosed because of cardiac complications, such as pericardial effusion.

Case Report

A 21-year-old woman with history of lymphoproliferative T-cell disease (LGL leukemia CD4+) while on therapy with low dose methotrexate and corticosteroid was admitted to the Emergency Department with anasarca. LGL leukemia had been previously diagnosed by morphological, immunophenotypic, and molecular analysis of blood and bone marrow biopsy. An electrocardiogram showed sinus tachycardia with infero-lateral T-wave inversions. High-sensitivity troponin I was normal. Physical examination was notable for bilateral pleural effusions, hepatosplenomegaly, and ascites. Pulmonary embolism was ruled out by computed tomographic angiography. An echocardiogram was remarkable for biventricular dilatation with severe systolic dysfunction (ejection fraction, 24%). Cardiac catheterization revealed coronary arteries. Cardiac magnetic resonance (CMR) showed left ventricular dilatation, no myocardial edema, but a focal area of subendocardial delayed enhancement involving the basal infero-lateral wall (Figure 1A and 1C; Movie I in the Data Supplement).

Endomyocardial biopsy was notable for diffuse monomorphic infiltration of lymphocytes with focal myocardial necrosis. The immunophenotype of the infiltrating cells was identical to that of leukemic T cells. Human Leucocytes Antigen - DR positivity of most of T lymphocytes and negativity of endothelial cells made autoimmune myocarditis less likely. Molecular analysis confirmed the monoclonal nature of the infiltrating cells (Figure 2). The latter findings, coupled with no evidence by polymerase chain reaction analysis for the most common cardiotropic viruses, ruled out active viral myocarditis. The patient was treated with high-dose corticosteroids and diuretics achieving a complete clinical recovery in a week. The following echocardiograms and serial CMR confirmed persistent subendocardial delayed enhancement without edema and full restoration of the kinetic and function of the heart, with no sequelae (Figure 1B; Movie II in the Data Supplement).

Discussion

The sudden occurrence of severe heart failure in this young patient with LGL leukemia and a previously normal heart suggested acute myocarditis or relapsing leukemia. The CMR findings detected a limited area of previous ischemic pattern necrosis that was not in proportion to the severe diffuse myocardial systolic dysfunction. The endomyocardial biopsy was consistent with myocarditis that was characterized by the prevalent infiltration of lymphocytes morphologically, immunophenotypically, and molecularly identical to LGL leukemia lymphocytes. The most probable morphological/immunophenotypic diagnosis, therefore, was infiltration of myocardium by monoclonal CD4+ lymphocytes with cytotoxic properties. Also, the rapid recovery after lymphocytotoxic corticosteroid therapy supported this hypothesis.

The mechanism(s) whereby myocardial cell necrosis/dysfunction has been produced remains to be elucidated. However, a cytotoxic potential by CD4+ lymphocyte in the context of Major Histocompatibility Complex II restricted fashion is presently under investigation. This report represents the first case where diffuse myocardial involvement leading to heart failure was the first manifestation of relapsing leukemia and exemplifies how challenging the diagnosis could be with minimal findings by CMR. In fact, the endomyocardial biopsy was essential to obtain the final diagnosis. However, CMR was able to provide information on prognosis predicting myocardial recovery because there was no evidence of scar or significant acute myocardial necrosis.

Disclosures

None.

References


Key Words: heart failure □ cardiac MRI □ immunology □ cardiac leukemia □ endomyocardial biopsy

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Figure 1. Cardiac magnetic resonance (CMR) findings. Diastolic image during acute phases CMR (A) and in follow-up CMR (B), showing a reduction of left ventricular dilatation and pleural effusion restoration. Postcontrast CMR image (C), note the presence of a limited sub-endocardial necrosis identified by the delayed enhancement (white arrow head).

Figure 2. Histological findings. The endomyocardial biopsy showed the lymphocytic infiltrate associated with myocardial necrosis (A, magnification ×20). Infiltrating cells were strongly positive for CD3+ CD4+ (B and C, magnification ×20) and for HLA-DR (D, magnification ×20). The box in the right showed the monoclonality of the T lymphocytes. H&E indicates hematoxylin and eosin stain.
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SUPPLEMENTAL MATERIAL

Video 1. CMR finding during acute phase. A 4 chamber long axis view showing the impaired heart function and the presence of pleural effusion.

Video 2. CMR finding during follow up. A 4 chamber long axis view showing the recovery of the systolic function and the pleural effusion restoration.