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Case Report

Variable Cardiac Responses to Immunosuppressive Therapy in Anti-Mitochondrial Antibody-Positive Myositis

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ABSTRACT

We describe a case of anti-mitochondrial antibody-positive myositis associated with cardiovascular involvement. An electrophysiological study (EPS) showed binodal dysfunction, and cardiac magnetic resonance (CMR) imaging revealed left ventricular dysfunction with diffuse, patchy T2 high-intensity areas and late gadolinium enhancement indicative of inflammation and fibrosis. The left ventricular dysfunction was successfully treated with immunosuppressive therapy as documented by CMR. Persistence of conduction system dysfunction was confirmed by EPS, and a pacemaker was implanted. CMR and EPS concisely documented the variable cardiac response to treatment in anti-mitochondrial antibody-positive myositis. We demonstrate the utility of cardiac investigations in this rare disorder.

RÉSUMÉ

Nous décrivons un cas de myosite à anticorps anti-mitochondries positifs associée à une atteinte cardiovasculaire. Une étude électrophysiologique (EEP) montrait une dysfonction binodale, et l'imagerie cardiaque par résonance magnétique (IRM cardiaque) révélait une dysfonction du ventricule gauche associé à des zones irrégulières diffuses d'intensité élevée en T2 et un rehaussement tardif après injection de gadolinium révélateur d'une inflammation et d'une fibrose. La thérapie immunosuppressive comme l'a montrée l'IRM cardiaque a permis de traiter efficacement la dysfonction du ventricule gauche. À la suite de la confirmation de la persistance de la dysfonction du système de conduction par l'EEP, un stimulateur cardiaque a été implanté. L'IRM cardiaque et l'EEP ont permis d'expliquer de manière concise la réponse cardiaque variable au traitement de la myosite à anticorps anti-mitochondries positifs. Nous démontrons l'utilité des examens du cœur pour cette atteinte rare.

Anti-mitochondrial antibody (AMA)-positive myositis is an atypical inflammatory myopathy characterized by chronic progressions of muscle atrophy and cardiac involvement. Cardiac involvement includes arrhythmias and left ventricular dysfunction. The first-line treatment is steroid therapy, and in most cases, it is effective for muscle weakness. By contrast, the effectiveness of immunosuppressive therapy for the various cardiac involvements is yet to be elucidated.[1,2] We present the case of a young woman with AMA-positive myositis associated with binodal and left ventricular dysfunction.

Case Report

A 38-year-old woman without specific medical history was evaluated for chronic fatigue that persisted for 4 years and an abnormal electrocardiogram (ECG) finding at the annual medical checkup. Physical examination revealed muscle weakness in her neck and proximal limbs. ECG revealed sinus nodal dysfunction and complete atrioventricular (AV) block (Fig. 1A). Blood tests revealed markedly elevated levels of creatine kinase (CK) and high-sensitivity troponin I (TnI) (Fig. 1B, Supplementary Material). Anti-nuclear antibodies were positive, and the levels of M2 antibodies were significantly high. Muscle biopsy of the deltoid muscle demonstrated a myositis pattern (Supplementary Material). Echocardiogram revealed an inferior wall motion abnormality

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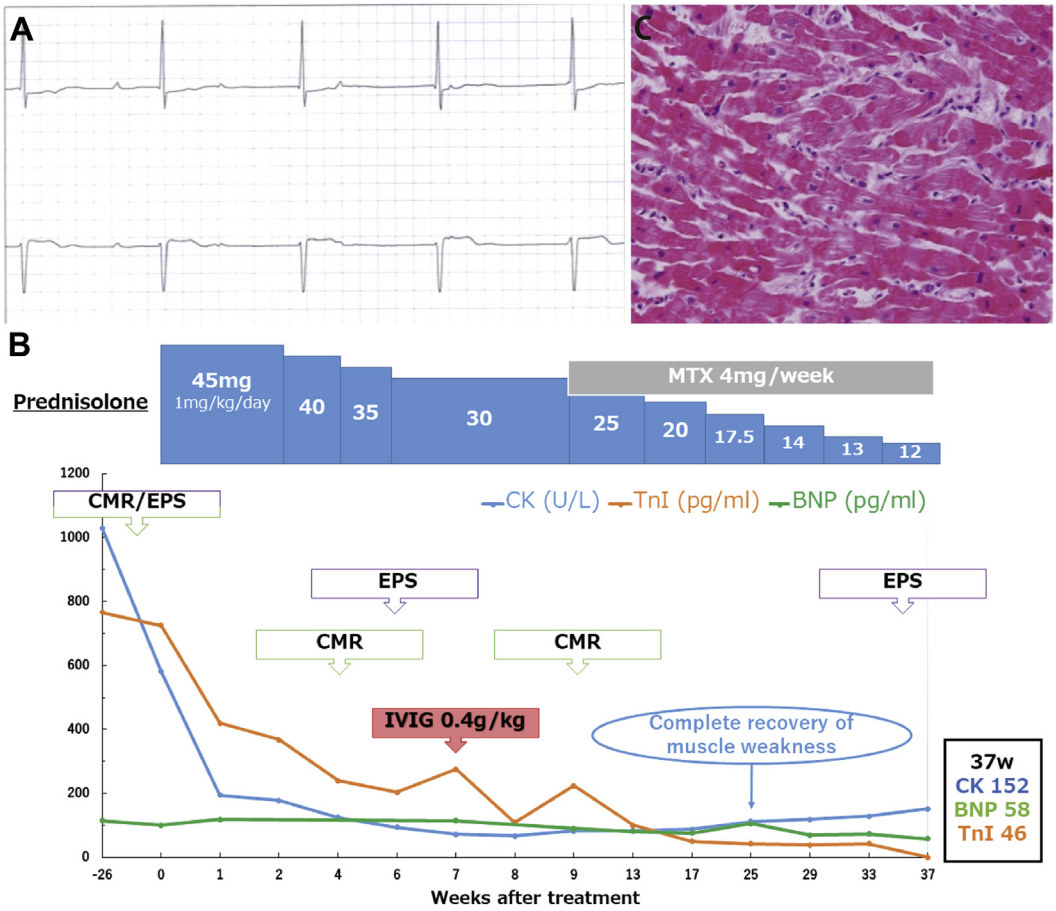

Figure 1. (**A**) Electrocardiogram (ECG) demonstrating complete atrioventricular (AV) block before admission. (**B**) Time courses of the levels of CK, high-sensitivity TnI, and brain natriuretic peptide. (**C**) Endomyocardial biopsy of the right ventricle, hematoxylin–eosin stain. BNP, brain natriuretic peptide; CK, creatine kinase; CMR, cardiac magnetic resonance; EPS, electrophysiologic study; IVIG, intravenous immunoglobulin; MTX, methotrexate; TnI, troponin I.

in the left ventricle without dilation or decreased left ventricular ejection fraction (LVEF). Endomyocardial biopsy of the right ventricle demonstrated a mild interstitial fibrosis with mild inflammatory cell invasion (Fig. 1C). Cardiac magnetic resonance (CMR) imaging revealed a patchy T2 high-intensity area, indicating inflammation and widespread late gadolinium enhancement with a mild decrease in LVEF (47%; Fig. 2A). On the basis of these findings, a diagnosis of AMA-positive myositis associated with myocarditis was made. For the evaluation of conduction system disturbance, an electrophysiological study (EPS) was performed (Fig. 2D). It showed a complete AV block, an extended sinus node recovery time (50 seconds), and broad low-voltage and scar areas in the right atrium. We did not implant a pacemaker at that time because of the absence of symptoms and possibilities for recovery of the conduction system. She was treated with oral prednisolone 1 mg/kg/d (45 mg) according to the polymyositis treatment protocol, which starts with high-dose prednisolone. Her muscle weakness improved within 1 week, and the CK and TnI levels remarkably decreased (Fig. 1B, Supplementary Material). After 1 month, CMR revealed drastically decreased T2 high-intensity areas (Fig. 2B). Also, EPS showed slight improvement of sinus node function and AV conduction (Fig. 2E). When the prednisolone dose was decreased to 30 mg/d, the TnI level increased again, and intravenous immunoglobulin 0.4 mg/kg for 5 days and methotrexate 4 mg/wk were administered for the resistant polymyositis. The TnI level decreased and the CK levels normalized 2 months later. Repeated CMR (Figs. 1B and 2C) confirmed the disappearance of the T2 high-intensity areas and LVEF recovery, whereas the binodal dysfunction, exemplified in an EPS (Fig. 2F), did not improve. The symptom of the bradycardia worsened, so a pacemaker was implanted 1 year after treatment initiation.

Discussion

AMA-positive myositis is an uncommon condition, and 20% to 30% of patients had a cardiac involvement, including arrhythmias and decreased LVEF.[1,3] The influence of immunosuppressive therapy on cardiac symptoms is unknown.[1,2] This case showed an improvement in TnI levels, T2 high-intensity areas, and LVEF on CMR, whereas the EPS demonstrated limited treatment efficacy for the binodal dysfunction that could be explained by the residual late gadolinium enhancement observed on CMR. The long duration after symptom onset may be related to the irreversibility of cardiac dysfunction, and steroid therapy is more likely to be

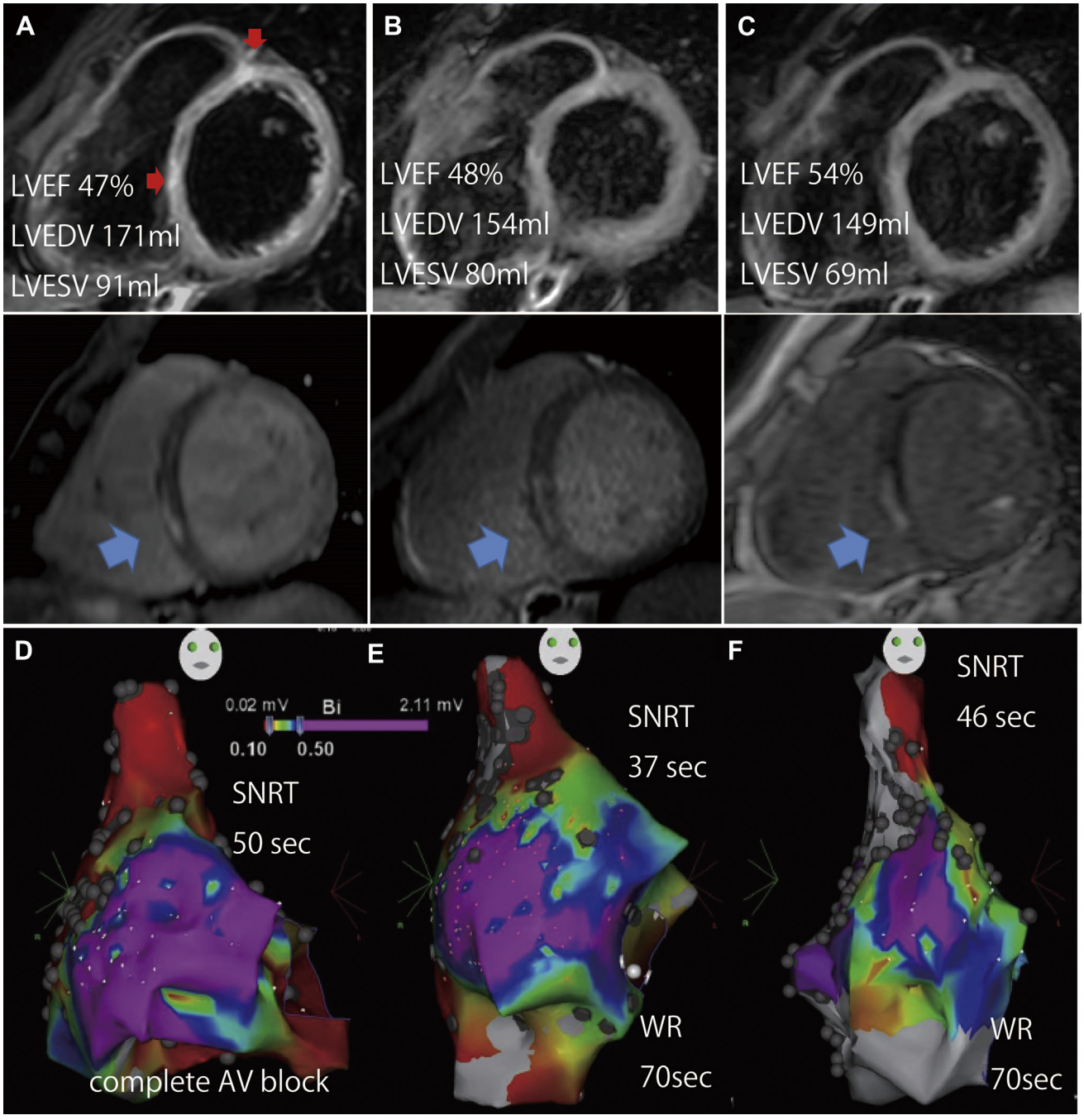

Figure 2. Cardiac magnetic resonance imaging before treatment (**A**) and 4 weeks (**B**) and 9 weeks (**C**) after immunosuppressive therapy. Improvement of diffuse patchy T2 high-intensity areas (**red arrow**s) (**upper row**) and remaining late gadolinium enhancement (**blue arrow**) (**lower row**). CMR also confirmed the recovery of LVEF and volume (end-diastolic volume/end-systolic volume). Electrophysiologic study before treatment (**D**), 6 weeks (**E**), and 35 weeks (**F**) after immunosuppressive therapy. The voltage region with more than 0.5 mV (**purple**) gradually decreased, whereas sinus node recovery time was still extended. AV conduction improved slightly at first, but was unchanged later. LVEF, left ventricular ejection fraction; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; SNRT, sinus node recovery time; WR, Wenckebach rate.

effective in the early phase of inflammation. Therefore, early diagnosis of myocarditis is important and CMR is a potentially useful method. However, conduction system abnormalities cannot be visualized because of the minute size of the affected lesions. It is evaluated functionally by conducting an EPS and can identify the injured area of the right atrium. Patients with AMA-positive myositis should be considered to undergo CMR for myocarditis screening. Moreover, CMR and EPS could be used to evaluate the detailed response to immunosuppressive therapy in the presence of conduction disturbance. In this case, ECG and echocardiogram did not reveal any change during the treatment, whereas CMR

revealed an improvement of myocardial inflammation. In addition, the findings of conduction disturbance showed only slight improvement, which supported our decision to implant a pacemaker.

Conclusion

Myocarditis-associated AMA-positive myositis is a rare disease. This is the first case report to describe CMR and EPS appearances before and after immunosuppressive therapy for cardiac involvements. These modalities might be useful for defining the extent of the disease and evaluating treatment outcomes.

Disclosures

The authors have no conflicts of interest to disclose.

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Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Cardiology* at www.onlinecjc.ca and at https://doi.org/10.1016/j.cjca.2019.07.002.