ESC European Society of Cardiology

European Heart Journal - Case Reports (2021) **5**(6), 1–8
doi:10.1093/ehjcr/ytab075

CASE REPORT
Arrhythmias/electrophysiology

Necrotizing myopathy presenting as congestive heart failure and life-threatening ventricular arrhythmias: a case report

Kyunghee Lim [1], Jong Sung Park [1]*, Byeol-A Yoon [2], and Song-Hee Han [3]

[1]Department of Cardiology, Dong-A University Hospital, 32 Daesingongwon-ro, Seo-gu, Busan 49202, Korea; [2]Department of Neurology, Dong-A University Hospital, 32 Daesingongwon-ro, Seo-gu, Busan 49202, Korea; and [3]Department of Pathology, Dong-A University Hospital, 32 Daesingongwon-ro, Seo-gu, Busan 49202, Korea

Received 5 October 2020; first decision 22 October 2021; accepted 10 February 2021

Background Necrotizing autoimmune myopathy is a rare subtype of idiopathic inflammatory myopathy; however, it can be associated with fatal cardiac manifestations.

Case summary A 58-year-old female patient was referred for congestive heart failure with dysrhythmia. Electrocardiograms showed ventricular arrhythmias of various QRS complex morphologies and coupling intervals with beat-to-beat differences. Despite optimal medical therapy for heart failure, the patient was admitted for the progression of dyspnoea and generalized motor weakness. The burden of non-sustained ventricular tachycardia gradually increased, and ventricular fibrillation eventually occurred. In view of a differential diagnosis of an inflammatory myocardial diseases such as sarcoidosis, a cardiac biopsy was performed. However, pathologic examinations revealed only necrotic muscle fibres without granuloma. Further examinations revealed proximal dominant motor weakness, an elevated serum creatinine-phosphokinase level, myogenic potentials on needle electromyography, and biceps muscle biopsy findings that were compatible with necrotizing autoimmune myopathy. High-dose steroid therapy improved the patient's motor weakness, including her respiratory impairment, and successfully suppressed ventricular arrhythmias.

Discussion This case suggests that intensive immunosuppressive therapy with high-dose steroid could be useful in the necrotizing autoimmune myopathy manifested as congestive heart failure and life-threatening ventricular arrhythmias.

Keywords Case report • Necrotizing myopathy • Cardiac arrhythmia • Heart failure

Learning points

- Cardiac involvement of necrotizing autoimmune myopathy should be considered as a possible cause of congestive heart failure and life-threatening ventricular arrhythmias.
- Complications of necrotizing autoimmune myopathy including arrhythmias may be successfully controlled by aggressive immune suppressive therapy, such as high-dose steroid.

* Corresponding author. Tel: +82 51 240 5040, Fax: +82 51 242 5852, Email: thinkmed@dau.ac.kr
Handling Editor: David Duncker
Peer-reviewers: Markus Bettin and Rafael Vidal-Perez
Compliance Editor: Max Sayers
Supplementary Material Editor: Mariame Chakir

Introduction

Necrotizing autoimmune myopathy is a rare subtype of idiopathic inflammatory myopathy comprising polymyositis and dermatomyositis. Although mild arrhythmias, such as premature ventricular contractions or non-specific conduction abnormalities, have been the most common electrocardiographic findings observed in approximately 30% of affected patients, cases of life-threatening ventricular arrhythmias have been rarely reported.[1] We report a case of necrotizing autoimmune myopathy manifesting as congestive heart failure and life-threatening ventricular arrhythmias which were controlled with high-dose steroid therapy.

Case presentation

A 58-year-old woman was referred to our institution for the evaluation of progressive dyspnoea, dizziness, and general weakness. Initial standard 12-lead electrocardiogram (ECG) showed diffuse intracardiac conduction abnormalities (*Figure 1A*). The patient's medical history was unremarkable. A chest X-ray image showed marked cardiomegaly with bilateral pleural effusions. Echocardiography demonstrated a dilated left ventricle with preserved ejection fraction [left ventricular (LV) end-diastolic volume 160 mL; LV end-systolic volume 71 mL; LV ejection fraction 55%] and grade II diastolic dysfunction with elevated left atrial pressure [ratio of peak early to late diastolic filling velocity (*E*/*A* ratio) 1.5; ratio of mitral peak velocity of early filling (*E*) to early diastolic mitral annular velocity (*E*′) (*E*/*E*′ ratio) 18.9; left atrial volume index 47.5 mL/m^2]. Twenty-four-hour

Timeline

Time	Events
4 months prior to admission	Dyspnoea on exertion, dizziness, and general weakness.
3 months prior to admission	First visit to medical centre, angiotensin II receptor blocker, beta blocker, diuretics, and spironolactone treatment were initiated under the impression of heart failure. Twenty-four hour ambulatory electrocardiogram (ECG) monitoring: daily burden of ventricular arrhythmia 20–30%.
2 months prior to admission	Atrial fibrillation observed.
First day of admission	Acute decompensated heart failure with pleural effusion observed and treated with additional diuretics. Creatine kinase level 919 U/L (normal range: 0–145 U/L).
Second admission (day of admission)	After 1 month, patient was readmitted for aggravated dyspnoea and general weakness.
Day 5 of admission	Mechanical ventilator used due to respiratory acidosis and drowsiness.
	Observed polymorphic ventricular tachycardia degenerated into ventricular fibrillation, requiring defibrillated.
	Echocardiography revealed a decreased ejection fraction of 37% with an akinetic basal septum. Patient administered with pulse intravenous methylprednisolone 125 mg once. Because of high fever over 38.3°C, high-dose steroid treatment was discontinued.
	N-terminal pro-brain natriuretic peptide 10 140.0 pg/ml (normal range: <287 pg/ml)
2 weeks after admission	Endomyocardial biopsy performed.
3 weeks after admission	Tracheostomy performed.
10 weeks after admission	^{18}F-Fluorodeoxyglucose positron-emission tomography/computed tomography scan performed and did not show abnormal myocardial uptake.
11 weeks after admission	Needle electromyography and nerve conduction study suggestive of myopathy.
	Low-dose hydrocortisone treatment initiated.
15 weeks after admission	Bicep muscle biopsy confirmed autoimmune necrotizing myopathy.
	Gradual improvement in motor power and respiratory muscle weakness.
	Patient weaned off mechanical ventilator support.
22 weeks after admission	Intravenous immunoglobulin G, methotrexate treatment initiated.
31 weeks after admission	Patient administered with daily pulse intravenous dexamethasone for 1 week followed by tapering doses of oral prednisolone.
38 weeks after admission	Gradual return of cardiac rhythm and improvement in daily burden of ventricular arrhythmia in 24-h ambulatory ECG monitoring (<10%).
	Patient discharged from hospital.

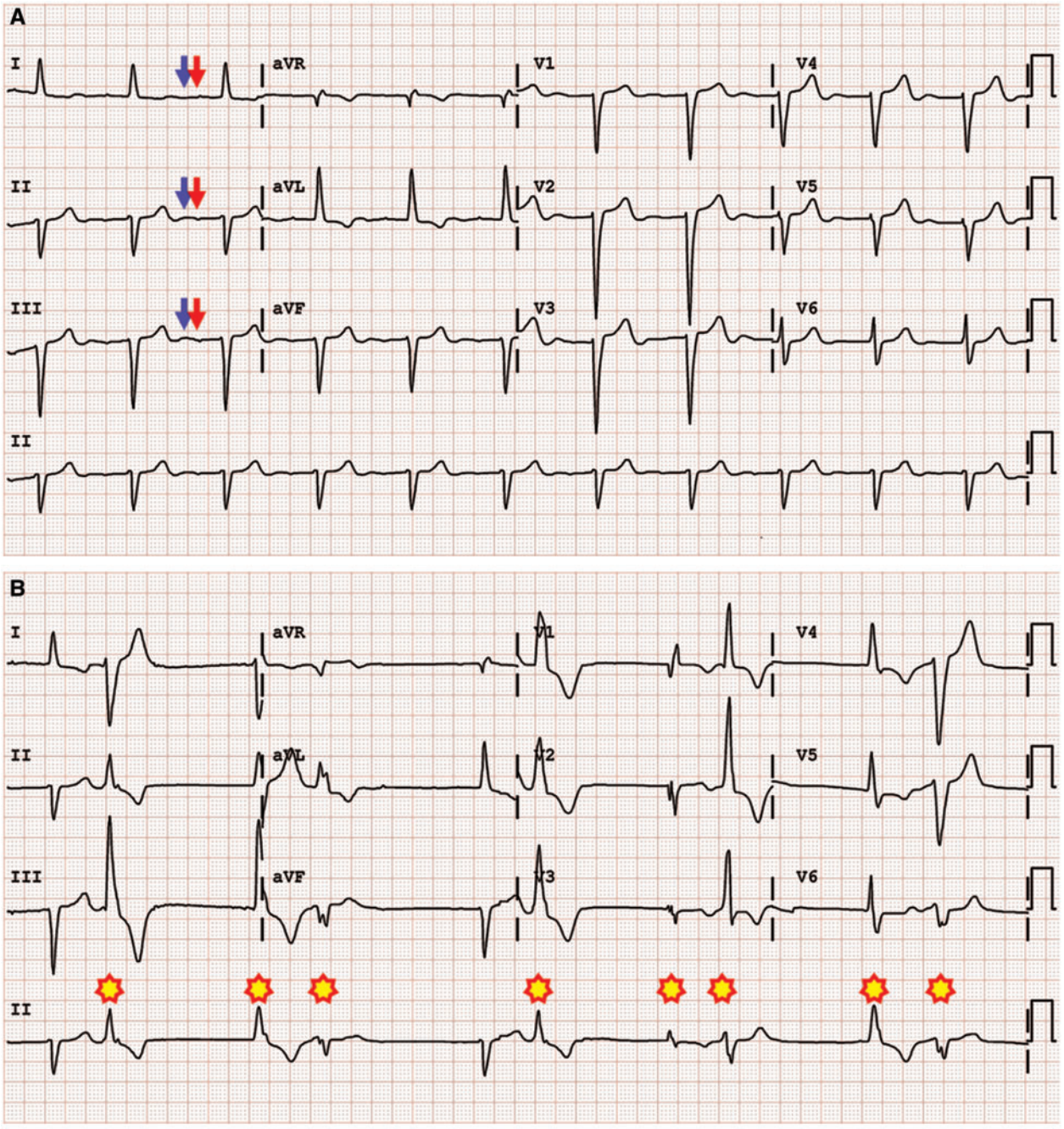


Figure 1 Electrocardiographic findings. (*A*) Initial standard 12-lead ECG showed small P waves (red arrows) less than 0.1 mV and prolonged PR intervals of 220 ms. Diffuse intraventricular conduction delay with left bundle branch block-like QRS complex morphology, QRS complex duration of 140 ms, and left axis deviation were noted. Broad U waves (blue arrow) of 200 ms and prolongation of QT intervals were also noted. Initial ECG findings suggested the presence of a diffuse conduction disorder involving both atriums and ventricles. (*B*) Follow-up standard 12-lead ECG recorded after aggravation of congestive heart failure showed abnormal ventricular depolarizations (stars) of left bundle branch configurations in the V1 lead, suggestive of a left ventricular origin. Abnormal depolarizations had various QRS complex morphologies and coupling intervals with beat-to-beat differences reflecting their multifocal origins due to increased automaticity. Abnormal ventricular depolarizations raised the suspicion of myocardial disease. (*C*) Telemetry recordings revealed the onset of R-on-T phenomenon in atrial fibrillation at the ventricular rates of 70–90 beat per minute (b.p.m.) followed by polymorphic VT. Polymorphic VT degenerated into VF which was terminated by external defibrillation (empty arrow). Although no inotropic agent was administered after termination of VF, VT with various QRS complex morphologies was sustained for 1 min, suggestive of increased automaticity as its electrophysiologic mechanism. (*D*) A 24-h ambulatory ECG monitoring before high-dose steroid therapy showed frequent episodes of non-sustained VT of 150 b.p.m. The daily burden of ventricular arrhythmia was 30–40%. b.p.m., beat per minute; ECG, electrocardiogram; VF, ventricular fibrillation; VT, ventricular tachycardia.

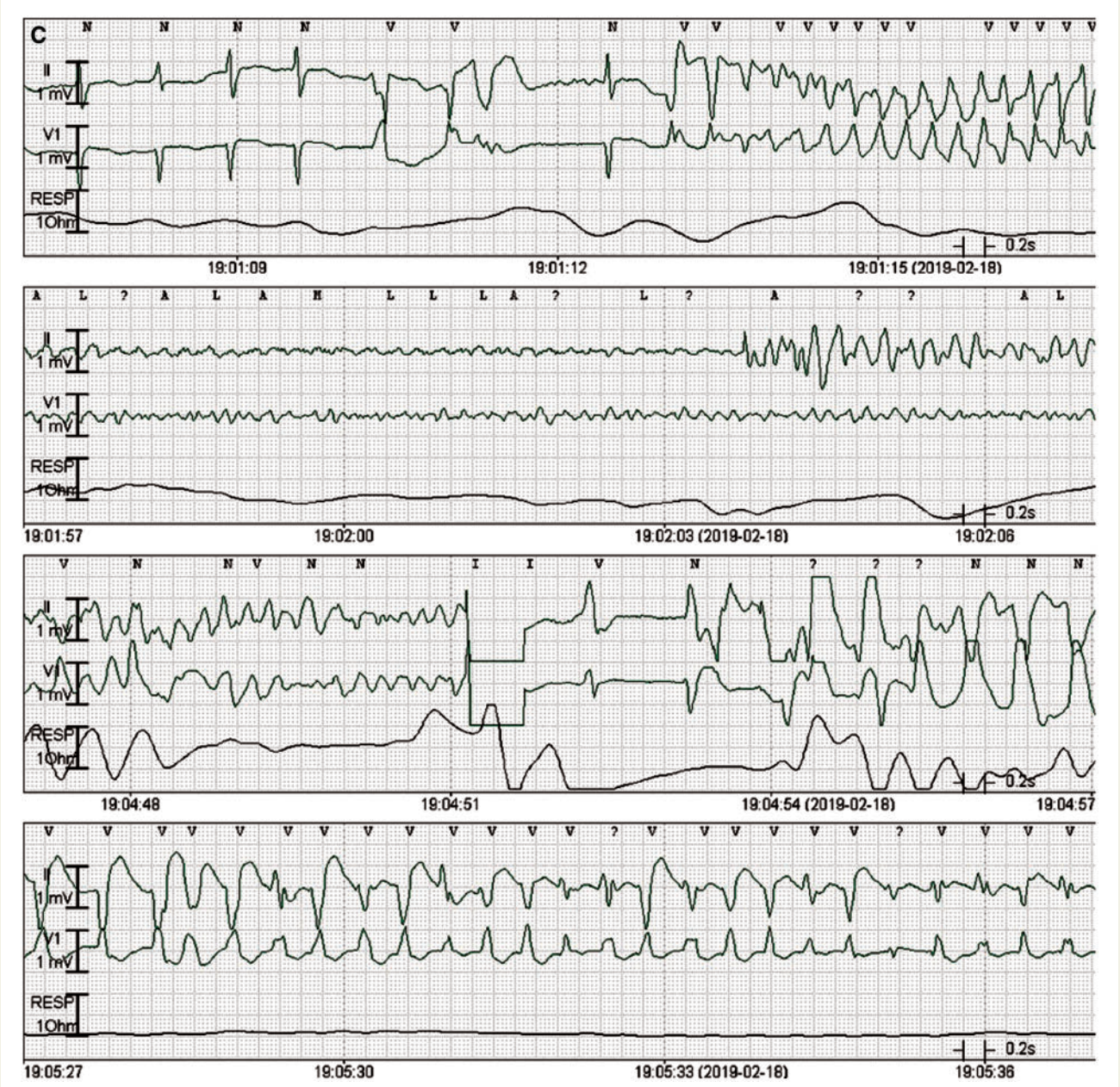


Figure 1 Continued

ambulatory ECG monitoring revealed the recurrence of sustained atrial fibrillation. Under the impression of heart failure with a preserved ejection fraction and paroxysmal atrial fibrillation, the patient was treated with losartan 50 mg/day, furosemide 40 mg/day, and spironolactone 25 mg/day for over 5 months. However, her symptoms gradually aggravated, and multifocal ventricular arrhythmias were observed on follow-up ECGs (*Figure 1B*). Bisoprolol 2.5 mg/day or amiodarone 200 mg/day maintenance therapy failed to suppress the recurrence of ventricular premature beats or atrial fibrillation and was discontinued due to the development of severe sinus bradycardia with dizziness. Finally, the patient was admitted for aggravation of dyspnoea and a sensation of general weakness.

The patient complained of New York Heart Association class IV dyspnoea. Although minimal lower extremity pitting oedema was noted on physical examination, typical signs of heart failure such as pulmonary crackles and internal jugular vein distention were not prominent. Cardiac biomarker studies revealed marked increases in N-terminal pro-brain natriuretic peptide of 10 140 (reference: 0–287) pg/mL, troponin-I of 0.2035 (reference: 0–0.0156) ng/mL, and creatinine phosphokinase of 437 (reference: 0–145) U/L. Antinuclear antibody titer was 1:160 (reference: negative). Although the patient received high-dose furosemide for pulmonary decongestion over a period of 4 days, she required intubation for respiratory acidosis and drowsiness. One day after the initiation of mechanical ventilation, the

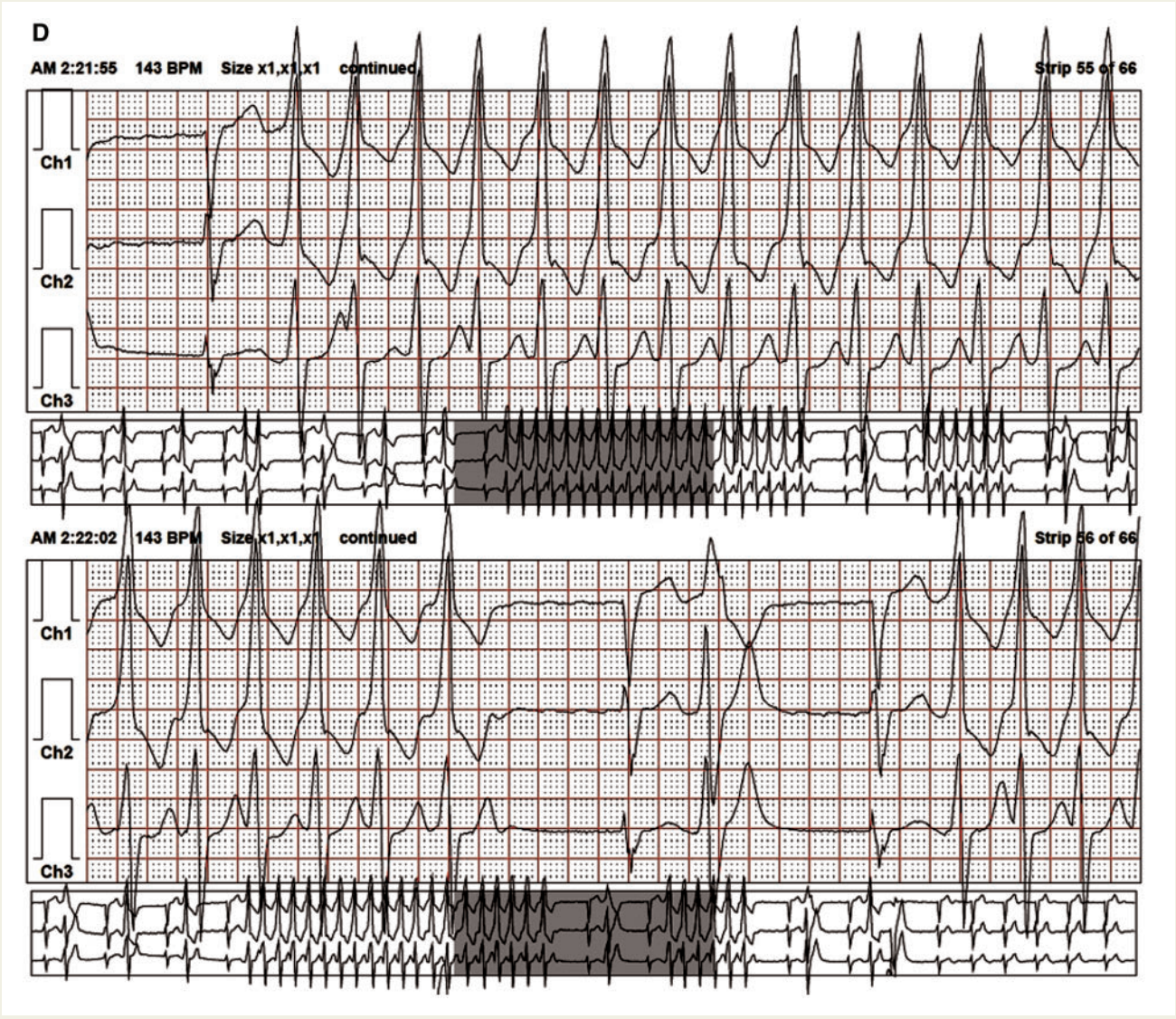


Figure 1 Continued

R-on-T phenomenon began to appear on ECG monitoring at a serum potassium concentration of 3.9 (3.5–5.1) mEq/L in atrial fibrillation at a rate of 70–90 beats per minute. Eventually, polymorphic ventricular tachycardia (VT) degenerated into ventricular fibrillation (VF), and the patient was defibrillated (*Figure 1C*). Unlike conventional acquired long QT syndrome induced by hypokalaemia, non-sustained VTs with various QRS complex morphologies with beat-to-beat differences recurred, frequently, even after the correction of serum potassium concentrations to over 5.3 mEq/L (*Figure 1C*). Echocardiography showed a decreased ejection fraction of 37% with an akinetic basal septum (*Figure 2A* and *B*, *Videos 1* and 2). However, coronary angiography showed no stenotic lesions. Under the impression of inflammatory myocardial disease such as sarcoidosis, methyl-prednisolone 125 mg was infused once to prevent the recurrence of polymorphic VT or VF. However, 1 day after methyl-prednisolone administration, a high fever of over 38°C developed and persisted for a total of 2 weeks, although all subsequent laboratory test findings were unremarkable. Broad spectrum empirical antibiotics were administered considering the possibility of infection. Because the recurrence of non-sustained VTs was remarkably reduced after a single infusion of high-dose methyl-prednisolone, endomyocardial biopsy was performed to confirm the diagnosis of inflammatory myocardial disease. However, pathologic examinations showed non-specific inflammatory changes with regeneration (*Figure 3A*). Tracheostomy was performed to maintain mechanical ventilation. Cardiac magnetic resonance imaging study has been attempted several times, but it could not be performed due to severe respiratory muscle weakness. ^{18}F-fluorodeoxyglucose positron-emission tomography/computed tomography scan did not show abnormal myocardial uptake (*Figure 2C*). We could not make a clinical diagnosis to explain the occurrence of polymorphic VT and pleomorphic non-sustained VT for more than 4 weeks.

Fortuitously, prolonged ventilator weaning failure with unexplained respiratory muscle weakness in the absence of pulmonary

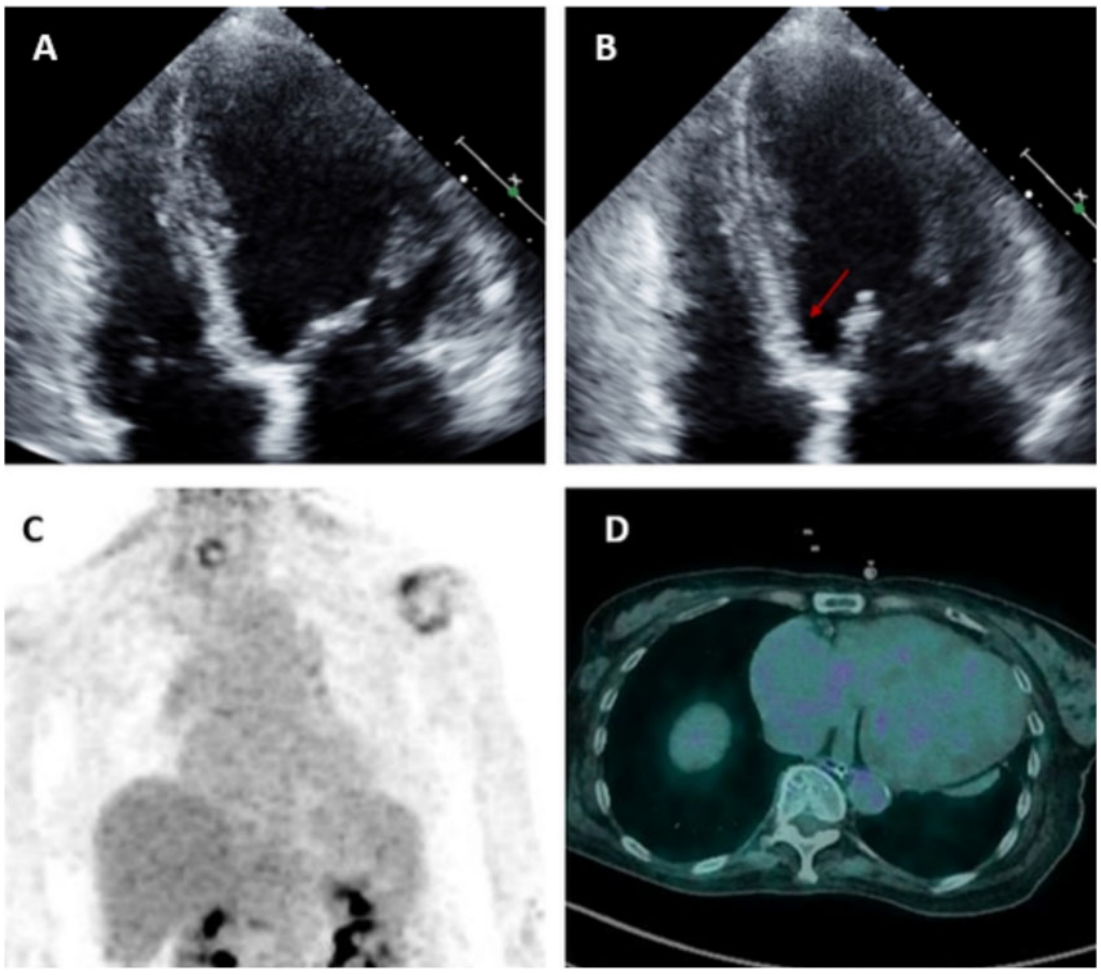
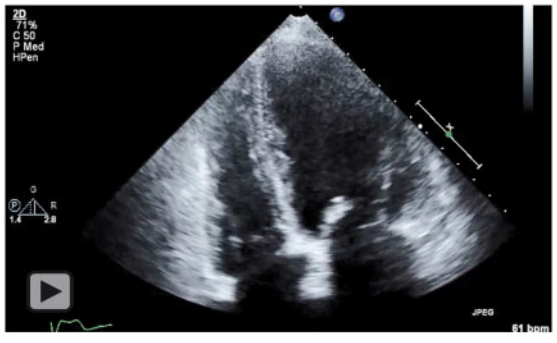
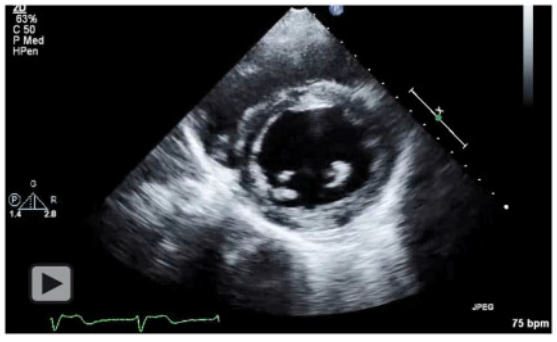


Figure 2 Findings of multimodality cardiac imaging studies. Echocardiograms taken 1 day after cardiac arrest in the apical four-chamber view of the end-diastole (*A*) and end-systole (*B*) showed a decreased LV ejection fraction of 37% with an akinetic basal septum (arrow) and dilated LV. Maximum-intensity projection image (*C*) and fused ^{8}F-FDG positron-emission tomography/computed tomography image (*D*) showed no abnormal FDG uptake in the LV myocardium. FDG, fluorodeoxyglucose; LV, left ventricular.



Video 1 Apical four-chamber view showing moderately reduced LV systolic function with an akinetic basal septum (arrow).



Video 2 Parasternal short-axis view at the base level.

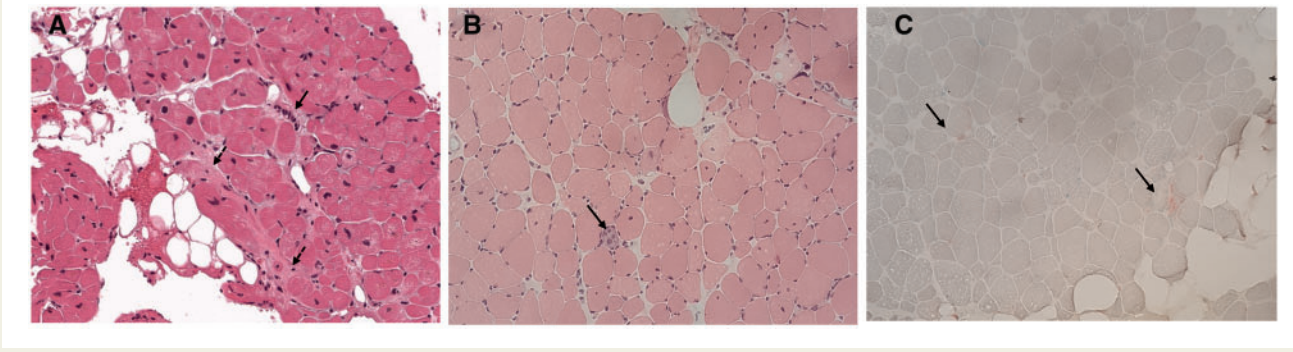


Figure 3 Pathologic findings of cardiac and biceps muscle biopsy specimens. (*A*) Haematoxylin and eosin staining of the cardiac biopsy specimen showed focal infiltrates of inflammatory cells (solid arrow), the formation of fibrosis, and myocardial regenerative changes (dotted arrows), suggesting the possibility of myocardial inflammation. (*B*) Haematoxylin and eosin staining of the specimen from the biceps muscle biopsy showed various-sized muscle fibres, reflecting skeletal muscle atrophy, and a necrotic muscle fibre (black arrow) without remarkable infiltration of inflammatory cells. (*C*) Acid phosphatase stained section of the specimen from the biceps muscle biopsy showed mild phosphatase activation, reflecting necrotized muscle fibres (black arrows).

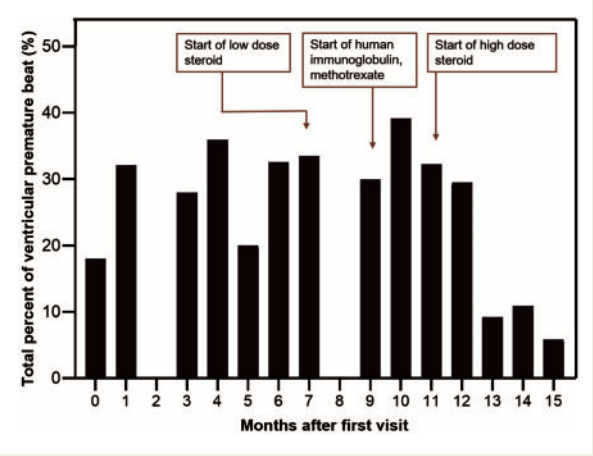


Figure 4 Ventricular premature beat burden with immunotherapy. Bar graph represents the change in daily ventricular premature beat burden recorded by monthly 24-h ambulatory electrocardiographic monitoring after the patient's first visit.

oedema or other active lung disease on chest imaging studies raised a clinical suspicion of systemic myopathy. During a bedside swallowing study, dysphagia was observed. Aggravation of dysphagia and progressive weakness of the upper and lower extremities along with a Medical Research Council score of 3/5 also supported the possibility of systemic myopathy. Needle electromyography demonstrated fibrillation potentials and small-amplitude, short-duration motor unit action potentials as well as increased recruitment in the upper and lower extremity muscles. Nerve conduction study findings were unremarkable. Biceps muscle biopsy revealed necrotic muscle fibres without significant inflammatory infiltrates, findings consistent with necrotizing autoimmune myopathy (*Figure 3B*). We therefore administered immune suppressive therapy. The patient received oral prednisolone 10–20 mg/day for 2 months in combination with human immunoglobulin G (2 g/kg for 3 days, 2 cycles) or methotrexate (2.5–12.5 mg/week) therapy, and maintenance therapy allowed improvement of her respiratory muscle power until she was completely weaned off the ventilator. However, non-sustained monomorphic VT frequently recurred (*Figure 1D*). Although low-dose amiodarone or sotalol maintenance therapy was considered, due to a prior history of severe bradycardia and risk of polymorphic VT recurrence, we decided to continue immune suppressive therapy. Fortunately, high-dose steroid therapy (dexamethasone 10 mg/day infusion for 7 days followed by oral prednisolone 20 mg/day) successfully suppressed the recurrence of non-sustained monomorphic VT with a marked reduction in the daily burden of ventricular premature beat (*Figure 4*). Because the patient strongly refused implantable cardioverter-defibrillator implantation to prevent sudden arrhythmic death against medical recommendation, we continued prolonged ECG monitoring for the recurrence of polymorphic or sustained pleomorphic VT until discharge. The patient was discharged on methotrexate and oral prednisolone combination therapy after improvements in dyspnoea and general weakness at 38 weeks after admission. During the follow-up duration over 1 year, the patient's functional status was well preserved with New York Heart Association class II dyspnoea and Medical Research Council score 5/5 motor power. Although occasional recurrences of slow monomorphic VT of 1–2 s were observed on repeated ambulatory ECG monitoring, there were no further recurrences of polymorphic or sustained pleomorphic VTs.

Discussion

Necrotizing autoimmune myopathy is a rare subtype of idiopathic inflammatory myopathy with the unique features of subacute proximal limb weakness, increased serum creatinine phosphokinase levels, myopathic electromyographic findings, and a muscle biopsy demonstrating necrotic muscle fibres with minimal inflammatory infiltration.[2–7] Although cardiac arrhythmias associated with idiopathic inflammatory myopathies have been reported in up to 2.4–13.8% of cases,[1] most have been reported as benign conduction disorders.

According to a systematic review of inflammatory myopathies with cardiac involvement, complete heart block has been suggested as the cause of cardiac deaths in approximately 10% of cases. Non-specific arrhythmias were also reported as the cause of cardiac death in approximately 8% of cases.[1] It appears that cardiac arrhythmia complicating inflammatory myopathies often results in fatal clinical outcomes. Interestingly, in the present case, various arrhythmias from a diffuse conduction disorder through atrial fibrillation to monomorphic and polymorphic VTs appeared in accordance with the disease progression. Morphologic features of ventricular premature beats and VTs suggested increased automaticity as their electrophysiologic mechanism and raised a clinical suspicion of inflammatory myocardial diseases, such as isolated cardiac sarcoidosis. However, a cardiac biopsy did not show any specific findings. Systemic myopathies were not considered until the patient suffered a prolonged ventilator weaning failure. Clinical manifestations of the patient emphasize that necrotizing autoimmune myopathy may present as various atrial and ventricular arrhythmias that cannot be explained by known arrhythmic or structural heart diseases, which can present as heart failure.

Necrotizing autoimmune myopathy is known to be refractory to conventional immunotherapy.[5] Although a standard therapy protocol has not yet been established, an aggressive combination immunesuppressive therapy has been recommended, especially in cases with cardiac complications.[8–10] In the present case, although low-dose steroid or human immunoglobulin and methotrexate combination therapy failed, high-dose steroid therapy successfully suppressed the recurrence of VTs and the daily burden of ventricular premature beat. Although clinical evidence is limited, our case suggests that aggressive immune suppressive therapy may, at least partially, elicit antiarrhythmic effects in patients with necrotizing autoimmune myopathy. In this patient, we considered defibrillator implantation before discharge for the secondary prevention of sudden arrhythmic death. However, the patient strongly refused any further invasive procedures, including defibrillator implantation. We were also unsure whether defibrillator therapy would impart a survival benefit because the risk of non-cardiac death by respiratory failure or infection was expected to be high at the time of admission. Defibrillator therapy is now under consideration as a therapeutic option because the clinical response to steroid therapy has been satisfactory and the patient's functional status has been well preserved.

Lead author biography

Kyunghee Lim is currently an Assistant Professor of Cardiology at Dong-A University Hospital. She graduated from Dong-A University in 2012. She became resident in Samsung Medical Center from 2013 to 2017 in internal medicine, and then a fellow in cardiology, Samsung Medical Center from 2018 to 2019. She is interested in clinical cardiology and echocardiography.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The authors confirm that written informed consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: None declared.

Funding: None declared.

References

1. Gupta R, Wayangankar SA, Targoff IN, Hennebry TA. Clinical cardiac involvement in idiopathic inflammatory myopathies: a systematic review. *Int J Cardiol* 2011;**148**:261–270.
2. De Bleecker JL, De Paepe B, Aronica E, De Visser M, Amato A, Aronica E *et al.*; ENMC Myositis Muscle Biopsy Study Group. 205th ENMC International Workshop: Pathology diagnosis of idiopathic inflammatory myopathies part II 28-30 March 2014, Naarden, The Netherlands. *Neuromuscul Disord* 2015;**25**:268–272.
3. Hoogendijk JE, Amato AA, Lecky BR, Choy EH, Lundberg IE, Rose MR *et al.* 119th ENMC international workshop: trial design in adult idiopathic inflammatory myopathies, with the exception of inclusion body myositis, 10-12 October 2003, Naarden, The Netherlands. *Neuromuscul Disord* 2004;**14**:337–345.
4. Kassardjian CD, Lennon VA, Alfugham NB, Mahler M, Milone M. Clinical features and treatment outcomes of necrotizing autoimmune myopathy. *JAMA Neurol* 2015;**72**:996–1003.
5. Milone M. Diagnosis and management of immune-mediated myopathies. *Mayo Clin Proc* 2017;**92**:826–837.
6. Selva-O'Callaghan A, Pinal-Fernandez I, Trallero-Araguás E, Milisenda JC, Grau-Junyent JM, Mammen AL. Classification and management of adult inflammatory myopathies. *Lancet Neurol* 2018;**17**:816–828.
7. Lundberg IE, Tjärnlund A, Bottai M, Werth VP, Pilkington C, Visser M *et al.*; the International Myositis Classification Criteria Project Consortium, the Euromyositis Register, and the Juvenile Dermatomyositis Cohort Biomarker Study and Repository (UK and Ireland). European League Against Rheumatism/American College of Rheumatology Classification Criteria for adult and juvenile idiopathic inflammatory myopathies and their major subgroups. *Arthritis Rheumatol* 2017;**69**:2271–2282.
8. Valiyil R, Casciola-Rosen L, Hong G, Mammen A, Christopher-Stine L. Rituximab therapy for myopathy associated with anti-signal recognition particle antibodies: a case series. *Arthritis Care Res* 2010;**62**:1328–1334.
9. Christopher-Stine L, Casciola-Rosen LA, Hong G, Chung T, Corse AM, Mammen A. A novel autoantibody recognizing 200-kd and 100-kd proteins is associated with an immune-mediated necrotizing myopathy. *Arthritis Rheum* 2010;**62**:2757–2766.
10. Allenbach Y, Drouot L, Rigolet A, Charuel JL, Jouen F, Romero NB *et al.* Anti-HMGCR autoantibodies in European patients with autoimmune necrotizing myopathies: inconstant exposure to statin. *Medicine (Baltimore)* 2014;**93**:150–157.