BMC Cardiovascular Disorders

CASE REPORT

Open Access

Rapid progression of right ventricular dysfunction: a case report

Guoliang Li[1†], Changying Zhao[2†], Lingmin Wu[3] and Yang Yan[2*]

Abstract

Background Arrhythmogenic cardiomyopathy (ACM) is a genetic myocardial disease characterized by progressive myocyte loss and fibrofatty (fibrous and adipose) tissue replacement to predispose these patients to fatal ventricular arrhythmias and impairment of ventricular systolic function. The relationship of ACM and myocarditis has gained significant attention.

Case presentation This case presented a 28-year-old female who was admitted to the hospital with complaints of recurrent lower limb edema and palpitations for 6 months. Her electrocardiogram revealed a typical manifestation of an advanced form of biventricular arrhythmogenic cardiomyopathy (ACM). Despite systematic medical management, her right ventricle (RV) function deteriorated rapidly, necessitating heart transplantation. Postoperative histopathological examinations confirmed the RV involvement as reflected in the electrocardiogram. Especially, multiple foci of lymphocytic infiltration were observed throughout the heart, with the RV being the most severe.

Conclusion When a rapid progression of ACM occurs, a concomitant myocarditis should be considered. ACM may be an inflammation-mediated transformation from myocardial tissue to fibrofatty tissue, and myocarditis may be a part of the natural history in some ACM cases.

Keywords Arrhythmogenic cardiomyopathy, Myocarditis, Arrhythmogenic right ventricular cardiomyopathy

Background

Arrhythmogenic cardiomyopathy (ACM) is a genetic myocardial disease characterized by progressive myocyte loss and fibrofatty (fibrous and adipose) tissue replacement to predispose these patients to life-threatening ventricular arrhythmia and impairment of ventricular systolic function [1]. The typical pathological manifestation of ACM is the progressive replacement of ventricular myocardial tissue by fibro-fatty tissue [1, 2]. Pathological examination remains the gold standard for diagnosing ACM. However, due to the challenges and invasiveness associated with myocardial biopsy, the diagnosis of ACM mainly relies on clinical evaluation. Early studies indicated that fibrofatty replacement was confined to the right ventricle (RV). In 1994, the European Task Force first established diagnostic criteria for arrhythmogenic

†Guoliang Li and Changying Zhao contributed equally to this work and shared the first authorship.

*Correspondence:
Yang Yan
yangyan3@xjtu.edu.cn
[1]Department of Cardiovascular Medicine, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China
[2]Department of Cardiovascular Surgery, The First Affiliated Hospital of Xi'an Jiaotong University, No. 277 Yanta West Road, Xi'an 710061, China
[3]Arrhythmia Center, Peking Union Medical College, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences, Fuwai Hospital, Beijing, China

right ventricular cardiomyopathy (ARVC), which serves as a precursor to ACM, and subsequently revised these criteria in 2010 [3, 4]. As research has advanced, it has been observed that some ACM patients exhibit left ventricular (LV) involvement or even isolated LV involvement, leading to diagnoses of biventricular or left-sided phenotype [5]. In 2023, the European Task Force published updated clinical diagnostic criteria for ACM [6]. Recently, there has been growing interest in exploring the relationship between myocardial inflammation and ACM [7].

Case presentation

A 28-year-old woman was admitted to our hospital with complaints of recurrent lower limb edema and palpitations over 6 months.

Six months prior to admission, she experienced unexplained lower limb edema along with abdominal distension, which did not raise her concern. During this period, she also had an episode of unheralded syncope. Four months ago, her edema worsened and was accompanied by chest tightness and shortness of breath that were unrelieved by rest. Subsequently, she was hospitalized locally where suspicion for ACM. Despite receiving systematic medication after discharge last month, she continued to experience frequent palpitations upon readmission. Physical examination at admission revealed facial edema (notably around the eyelids) as well as an enlarged heart borders downward on percussion. Laboratory tests showed troponin I at 0.11 ng/mL (reference range: 0.01–0.02 ng/mL), troponin T at 0.12 ng/mL (reference range: 0.010–0.017 ng/mL), NT-pro BNP at 1390 ng/mL (reference range for healthy populations: 0-125 ng/mL; diagnosis range for acute heart failure in people less than 50 years old: >450 ng/mL; diagnosis range for chronic heart failure: >2000 ng/mL). Neutrophil percentage was 80.2% (reference range: 40–75%), but C-reaction protein (CRP) and high-sensitive CRP were in normal range. She did not have a family history of ACM or any cardiomyopathy.

Electrocardiogram revealed a typical manifestation of an advanced form of biventricular ACM (Fig. 1). The patient exhibited ventricular extrasystoles with two different morphologies: one with left bundle branch block morphology with inferior axis suggestive of RV involvement; and the other with right bundle branch block pattern and positive concordance in precordial leads suggestive of l LV involvement as well. Additionally, in the precordial leads, there was a QRS delay resembling a right bundle branch block, which was also typical for forms involving the RV. Low QRS voltages could be observed in the peripheral lead, which might be a risk predictor for heart failure death, or heart transplantation for ACM patients [8]. Finally, T-wave inversion in all precordial leads was also present, which was a typical manifestation of the electrocardiogram in advanced ACM. Echocardiography showed major dilatation of the RV and right atrium associated with regional wall motion abnormalities (Fig. 2 and Supplementary Video) and normal LV size and ejection fraction, which was further confirmed by cardiac magnetic resonance (CMR, Fig. 3). Furthermore, the myocardial fibrosis detected in delayed phase of CMR imaging was strong evidences of end-stage ACM, showing great diagnostic value of CMR in the

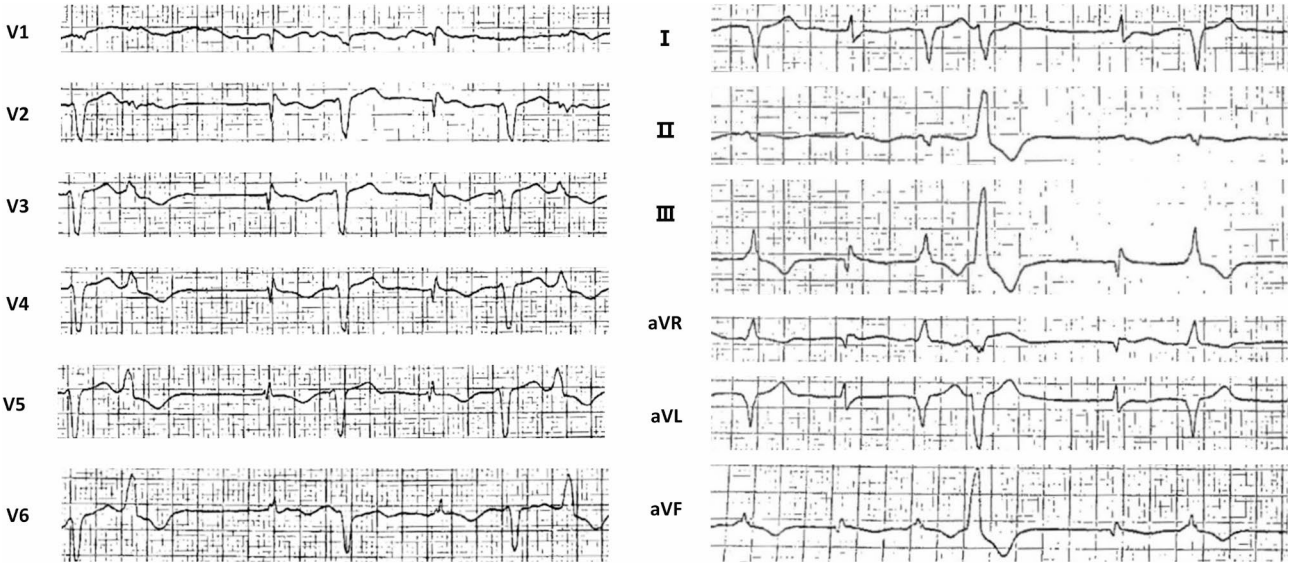

Fig. 1 ECG results before 4-month, revealing a typical manifestation of an advanced form of biventricular arrhythmogenic cardiomyopathy (25 mm/s 10 mm/mV)
ECG: electrocardiogram

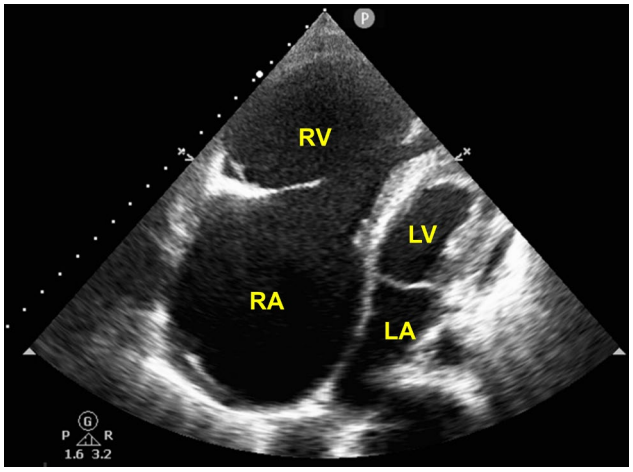

Fig. 2 Echocardiography showed major dilatation of the right ventricle and atrium associated with regional wall motion abnormalities. Parasternal long-axis right ventricular outflow tract at end diastole: 60 mm; tricuspid annular plane systolic excursion: 8 mm; tricuspid regurgitation area: 10cm^2; left ventricle ejection fraction: 52%

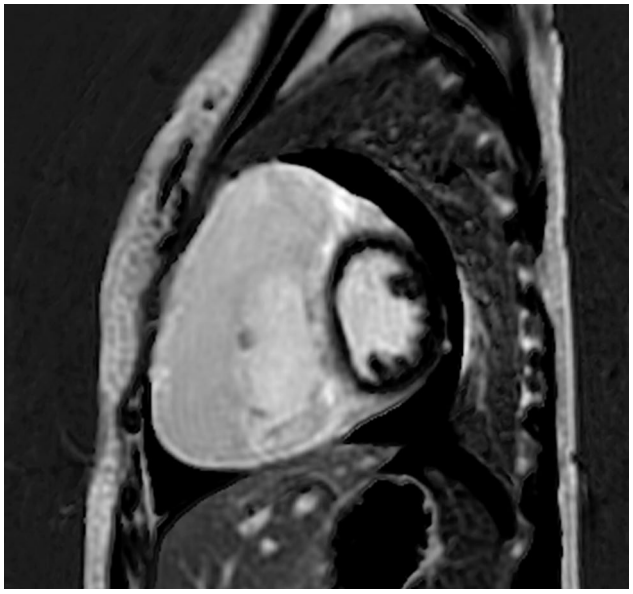

Fig. 3 Delayed phase imaging of CMR indicated the presence of myocardial fibrosis in right ventricle. Fatty infiltration of the free wall of the left ventricle may be present
CMR: cardiac magnetic resonance
Right ventricle: ejection fraction, 16.7%; end-diastolic volume: 286 mL; end-systolic volume: 238 mL; stroke volume: 48 mL
Left ventricle: ejection fraction: 52%; end-diastolic volume: 79 mL; end-systolic volume: 37 mL; stroke volume: 42 mL

diagnosis. Despite guideline–directed systematic medical management, including beta-blockers, antiarrhythmics and diuretics, her RV function deteriorated rapidly. Consequently, she underwent heart transplantation.

From a morpho-functional perspective, the disease predominantly affected the RV. The postoperative histopathology also demonstrated evidences of RV involvement: myocyte loss and the presence of massive fibrofatty tissue in Masson's trichrome and HE staining (Fig. 4A, B). Though viral PCR tests before the operation did not indicate the presence of a viral infection. Autoimmune serology tests also yielded negative results. Multiple foci of lymphocytic infiltration were observed throughout the heart, with the RV being the most severe (Fig. 4C). The results were further confirmed immunohistochemistry CD3 and CD8 staining (Fig. 5). Infiltrative lymphocyte aggregates were observed, interspersed among the remaining myocardium, without any evident necrosis. The epicardium exhibited the most pronounced infiltration, while a decreasing number of infiltrates was noted as one approached the endocardium. Masson's trichrome and HE staining of LV were basically normal, with slight fatty tissue infiltration and fibrosis (Fig. 6). Overall, a diagnosis of concomitant ACM and myocarditis was made though all known pathogenic mutations about ARVC were not found.

At present, this patient is two years post-surgery and has successfully resumed normal work and daily activities, with regular follow-up in our outpatient department.

Discussion

This case report was about a female adult who was diagnosed with ACM and exhibited rapid progression of RV dysfunction. The histopathological examinations after heart transplantation indicated a combination of ACM and myocarditis. It can be hypothesized that the elevated troponin I and T were attributable to concomitant myocarditis. This patient exhibited characteristics more akin to a biventricular phenotype of ACM, with involvement of the RV and progressive changes in the LV. As the LV was reported to be normal in echocardiography and CMR, the inverted T-waves in V1-V6 may be due to the enlargement of the RV, which diminishes the representation of the LV on the ECG.

The pathology underlying ACM is not fully understood. Current perspectives suggest that ACM is an inherited cardiomyopathy primarily resulting from variants in desmosomal genes. The revised 2010 Task Force criteria identified seven genes associated with ARVC, none of which were found in our patient [4]. However, next-generation sequencing of whole-exome sequencing in this patient indicated mutations in *MYH6*, *MYPN* and *OBSCN*, which are associated with dilated cardiomyopathy or hypertrophic cardiomyopathy [9–11]. We hypothesized that various types of cardiomyopathy may share some concurrent pathways. The 2023 diagnostic criteria proposed a novel phenotypic classification for cardiomyopathies based on end-diastolic LV volume: the dilated cardiomyopathy or non-dilated LV cardiomyopathy. The potential role of mutations related to dilated

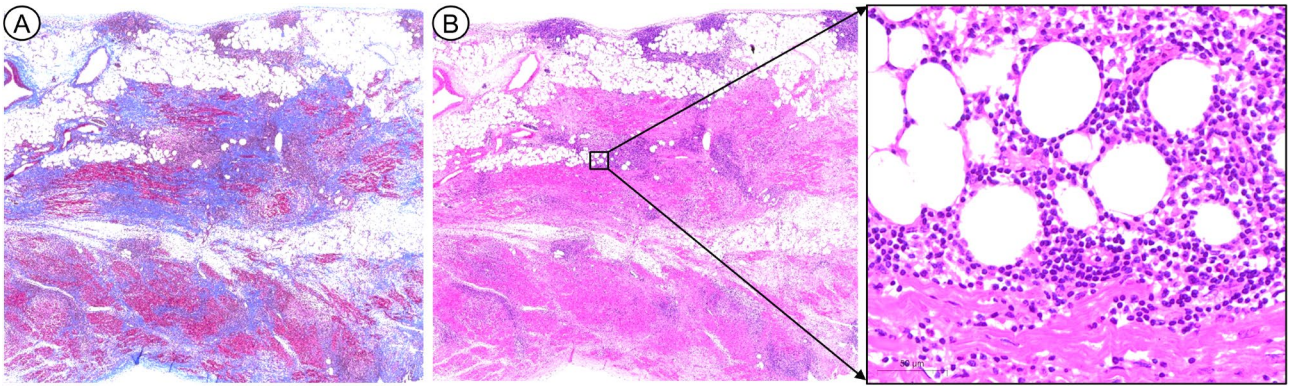

Fig. 4 Masson's trichrome staining (**A**) and HE staining (**B**) of RV showed typical presence of ACM (both magnification 2×). The black box was amplified (**C**, magnification 40×), indicating multiple foci of lymphocytic infiltration. RV: right ventricle, ACM: arrhythmogenic cardiomyopathy

cardiomyopathy in prompting the progression of ACM warrants further investigation.

The relationship between ACM and myocarditis has garnered significant attention. Some ACM patients may present clinical signs of myocarditis at an early stage or may even initially manifest with myocarditis, who are predominantly woman, have LV involvement or have desmoplakin mutations [12]. Fewer patients may display subclinical myocarditis during the advanced stages of ACM, potentially persisting for some time without overt symptoms. A case report described a female ARVC patient who was found to have subclinical chronic myocarditis four years after her initial diagnosis of ARVC with a desmoglein-2 mutation. The examinations found RV infiltration of CD3-positive T lymphocyte in endomyocardial biopsy, elevated troponin T levels and negative virus genome [7]. One possible explanation posits that myocarditis could serve as an inciting factor for ACM. Specifically, a trigger stimulates the innate inflammation response in myocardium, and the replacement of myocardial tissue with fibro-fatty deposits may be a consequence of this inflammatory response [13]. One study found that mutations within the cardiomyocyte desmosomal complex lead to the release of desmoglein-2 into circulation, subsequently stimulating an autoimmune response. The released desmoglein-2 proteins may activate T-cells to produce anti-desmoglein-2 antibodies, which can bind to the cardiomyocyte desmosomal complex in myocardial tissue and attract immune cell infiltration [14]. It suggests that heart failure resulting from myocardial fibro-fatty replacement may induce cytokine release from cardiomyocytes, thereby facilitating inflammatory cell infiltration. Another study indicated that in severe phenotypic forms of ARVC, characterized by biventricular involvement and right auricular fatty accumulation accompanied by RV dilation, 50% of the 16 patients displayed inflammatory infiltrates [15]. Overall, inflammation is considered to play a significant role in the progression of ACM, rendering ACM patients particularly susceptible to myocarditis.

Due to the unclear pathogenesis, the treatment of ACM remains focusing on symptomatic treatment, including the management of arrhythmia and heart failure, including pharmacological therapy (heart failure, antiarrhythmic and antithrombotic therapy), catheter ablation, cardiac sympathetic denervation and cardiac sympathetic denervation). The beta-blockers and antiarrhythmic medications are recommended for patients, though none of which offer protection against sudden cardiac death. Heart transplantation continues to be the definitive therapy for patients with untreatable arrhythmias or congestive heart failure [16]. However, the systematic medications were ineffective in this patient, potentially due to the presence of concomitant myocarditis. Given that the European Task Force consensus for myocarditis recommend the use of immunosuppressive therapy, we hypothesized that steroid treatment and immunotherapy might be viable therapeutic options for ACM patients [17]. Nonetheless, the case report mentioned above reported limited efficacy of corticosteroid therapy when oral prednisolone was administered [7]. Whether treating myocarditis can slow disease progression and improve outcomes for ACM patients awaiting transplantation warrants further investigation.

In summary, this finding of ACM superimposed with myocarditis may elucidate the rapid disease progression leading to necessary heart transplantation and support the hypothesis that: ACM may be an inflammation-mediated transformation from myocardial tissue to fibrofatty tissue, and myocarditis may be a part of the natural history in some ACM cases. Whether steroid treatment and immunotherapy for myocarditis may represent as a potential approach to prevent accelerated RV dysfunction remains to be evaluated.

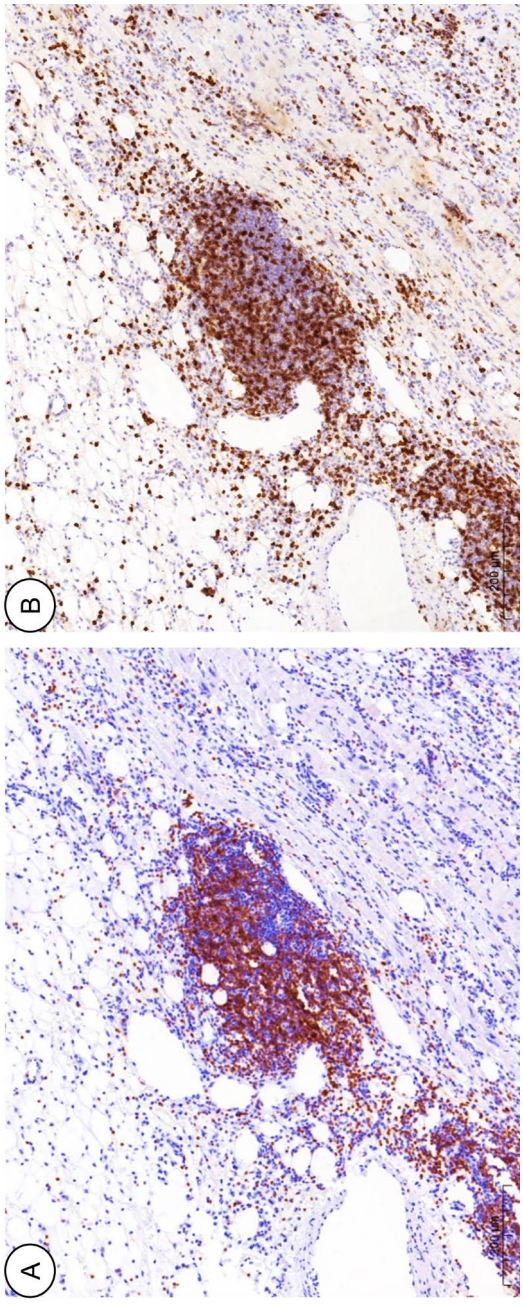

Fig. 5 Immunohistochemistry CD3 (**A**) and CD8 (**B**) staining results (both magnification 10x) of RV.

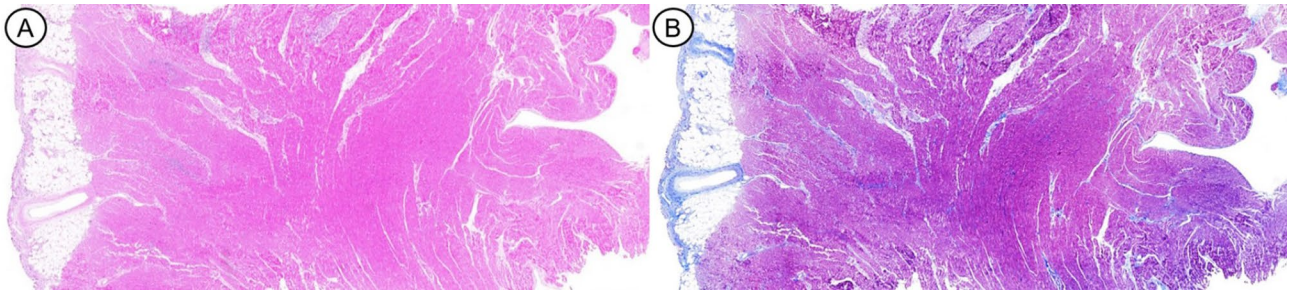

Fig. 6 Masson's trichrome staining (**A**) and HE staining (**B**) of LV (both magnification 2×)

Conclusions

When a rapid progression of arrhythmogenic cardiomyopathy occurs, a concomitant myocarditis may be considered. Whether steroid treatment and immunotherapy for myocarditis may represent as a potential approach to prevent accelerated RV dysfunction remains to be evaluated.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12872-025-04601-2.

Supplementary Material 1: The video showed echocardiography of the patient at admission

Acknowledgements

We would like to thank our patient for allowing us to present this case.

Author contributions

Conceptualization, all named authors; writing - original draft, Guoliang Li and Changying Zhao; writing - review and editing, all named authors; supervision, Yang Yan.

Funding

This study was supported by the National Natural Science Foundation of China [No. 82070353].

Data availability

All the data supporting this case report were included within the article and its additional file.

Declarations

Consent to participate

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

Competing interests

The authors declare no competing interests.

Received: 4 December 2024 / Accepted: 24 February 2025
Published online: 07 March 2025

References

1. Corrado D, Basso C, Judge DP. Arrhythmogenic cardiomyopathy. Circ Res. 2017;121(7):784–802.
2. Pilichou K, Thiene G, Bauce B, Rigato I, Lazzarini E, Migliore F, Perazzolo Marra M, Rizzo S, Zorzi A, Daliento L, et al. Arrhythmogenic cardiomyopathy. Orphanet J Rare Dis. 2016;11:33.
3. McKenna WJ, Thiene G, Nava A, Fontaliran F, Blomstrom-Lundqvist C, Fontaine G, Camerini F. Diagnosis of arrhythmogenic right ventricular dysplasia/cardiomyopathy. Task force of the working group myocardial and pericardial disease of the European society of cardiology and of the scientific Council on cardiomyopathies of the international society and federation of cardiology. Br Heart J. 1994;71(3):215–8.
4. Marcus FI, McKenna WJ, Sherrill D, Basso C, Bauce B, Bluemke DA, Calkins H, Corrado D, Cox MG, Daubert JP, et al. Diagnosis of arrhythmogenic right ventricular cardiomyopathy/dysplasia: proposed modification of the task force criteria. Eur Heart J. 2010;31(7):806–14.
5. Graziano F, Zorzi A, Ungaro S, Bauce B, Rigato I, Cipriani A, Perazzolo Marra M, Pilichou K, Basso C, Corrado D. The 2023 European task force criteria for diagnosis of arrhythmogenic cardiomyopathy: historical background and review of main changes. Rev Cardiovasc Med. 2024;25(9):348.
6. Corrado D, Anastasakis A, Basso C, Bauce B, Blomström-Lundqvist C, Bucciarelli-Ducci C, Cipriani A, De Asmundis C, Gandjbakhch E, Jiménez-Jáimez J, et al. Proposed diagnostic criteria for arrhythmogenic cardiomyopathy: European task force consensus report. Int J Cardiol. 2024;395:131447.
7. Nakamura M, Imamura T, Fukui T, Kataoka N, Kinugawa K. Arrhythmogenic right ventricular cardiomyopathy accompanied by chronic myocarditis. Intern Med. 2022;61(20):3063–7.
8. Olivetti NQS, Sacilotto L, Wulkan F, D'Arezzo Pessente G, Lombardi Peres de Carvalho M, Moleta D, Tessariol Hachul D, Veronese P, Hardy C, Pisani C, et al. Clinical features, genetic findings, and risk stratification in arrhythmogenic right ventricular cardiomyopathy: data from a Brazilian cohort. Circ Arrhythm Electrophysiol. 2023;16(2):e011391.
9. Yang Q, Berkman AM, Ezekian JE, Rosamilia M, Rosenfeld JA, Liu P, Landstrom AP. Determining the likelihood of disease pathogenicity among incidentally identified genetic variants in rare dilated Cardiomyopathy-Associated genes. J Am Heart Assoc. 2022;11(19):e025257.
10. Purevjav E, Arimura T, Augustin S, Huby AC, Takagi K, Nunoda S, Kearney DL, Taylor MD, Terasaki F, Bos JM, et al. Molecular basis for clinical heterogeneity in inherited cardiomyopathies due to myopalladin mutations. Hum Mol Genet. 2012;21(9):2039–53.
11. Wu G, Liu J, Liu M, Huang Q, Ruan J, Zhang C, Wang D, Sun X, Jiang W, Kang L, et al. Truncating variants in OBSCN gene associated with Disease-Onset and outcomes of hypertrophic cardiomyopathy. Circ Genom Precis Med. 2021;14(5):e003401.
12. Scheel PJ 3rd, Murray B, Tichnell C, James CA, Tandri H, Calkins H, Chelko SP, Gilotra NA. Arrhythmogenic right ventricular cardiomyopathy presenting as clinical myocarditis in women. Am J Cardiol. 2021;145:128–34.
13. Campian ME, Verberne HJ, Hardziyenka M, de Groot EA, van Moerkerken AF, van Eck-Smit BL, Tan HL. Assessment of inflammation in patients with arrhythmogenic right ventricular cardiomyopathy/dysplasia. Eur J Nucl Med Mol Imaging. 2010;37(11):2079–85.
14. Chatterjee D, Fatah M, Akdis D, Spears DA, Koopmann TT, Mittal K, Rafiq MA, Cattanach BM, Zhao Q, Healey JS, et al. An autoantibody identifies arrhythmogenic right ventricular cardiomyopathy and participates in its pathogenesis. Eur Heart J. 2018;39(44):3932–44.
15. Campuzano O, Alcalde M, Iglesias A, Barahona-Dussault C, Sarquella-Brugada G, Benito B, Arzamendi D, Flores J, Leung TK, Talajic M, et al. Arrhythmogenic right ventricular cardiomyopathy: severe structural alterations are associated with inflammation. J Clin Pathol. 2012;65(12):1077–83.

16. Corrado D, Link MS, Calkins H. Arrhythmogenic right ventricular cardiomyopathy. N Engl J Med. 2017;376(1):61–72.
17. Caforio AL, Pankuweit S, Arbustini E, Basso C, Gimeno-Blanes J, Felix SB, Fu M, Heliö T, Heymans S, Jahns R, et al. Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis: a position statement of the European society of cardiology working group on myocardial and pericardial diseases. Eur Heart J. 2013;34(33):2636–48. 2648a-2648d.

Publisher's note