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SUPPRESSION BY FLECAINIDE OF PREMATURE VENTRICULAR CONTRACTIONS REFRACTORY TO CATHETER ABLATION AND OTHER ANTIARRHYTHMIC DRUGS: A CASE REPORT

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We describe suppression of frequent premature ventricular contractions from the papillary muscle by flecainide in a patient with a history of reversible cardiomyopathy associated with arrhythmia and ineffective antiarrhythmic therapy with other IC and III class drugs, as well as refractory to repeated catheter ablation.

Key words: premature ventricular beats; flecainide; IC class of antiarrhythmics; left ventricle; papillary muscles

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Premature Ventricular Contractions (PVCs) are a common form of arrhythmia, which can also occur in the absence of structural heart disease. Besides symptoms such as irregular heartbeats, weakness, and dizziness, frequent PVCs can lead to a reduction in the systolic function of the left ventricle, resulting in reversible cardiomyopathy associated with arrhythmia (CAA).

The most common location for ectopic foci in PVCs is the outflow tract of the right and left ventricles [1]. Other possible sites include the sinus of Valsalva, the mitral or tricuspid valve rings, papillary muscles, the basal section of the antero-septal zone of the left ventricle (summit of the left ventricle), epicardial foci near the heart vessels (both venous and arterial), and some other regions [2].

Treatment of PVCs can be pharmacological, catheter ablation, or a combination of both. Catheter ablation is recommended as the first-line treatment for arrhythmia originating from the right ventricular outflow tract. In other cases, an attempt at pharmacological therapy is recommended initially. Pharmacological therapy for idiopathic PVCs is limited and consists of beta-blockers, calcium channel blockers, some IC and III class antiarrhythmic drugs, requiring individualized selection based on multiple factors [7, 8]. The efficacy of catheter ablation is up to 84% and depends on the location of the ectopic focus. For example, the basal section of the antero-septal zone of the left ventricle (summit) and papillary muscles are more challenging areas for endovascular intervention and have the lowest ablation success rates [3-6, 9]. Papillary muscles are movable structures with thick myocardium at their base, which prevents both stabilization of the ablation catheter when the arrhythmia focus is near the apex of the muscle and effective radiofrequency ablation when the focus is located at the base of the muscle.

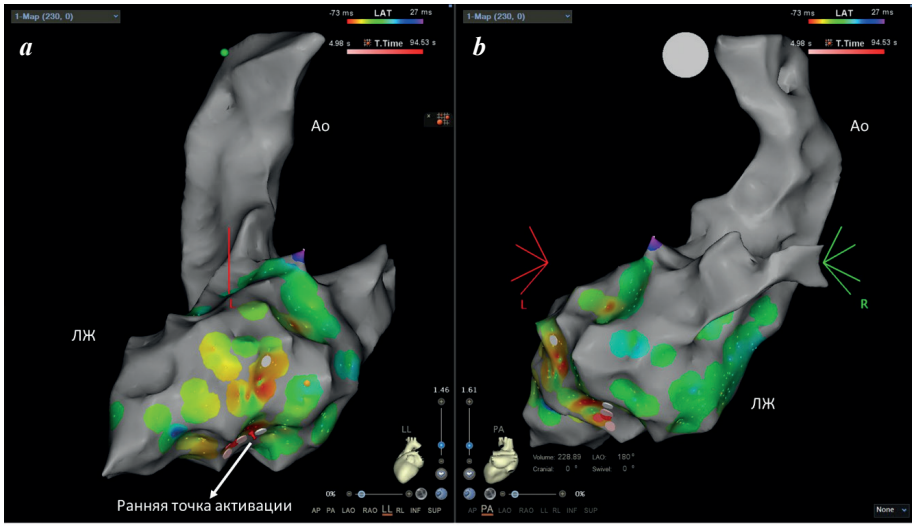

Fig. 1. Three-dimensional reconstruction and activation mapping of the left ventricle (CARTO 3 system, Biosense Webster, USA): a - left ventricle (LV) in the left lateral projection (LL), with the earliest activation point (base of the posterior-medial papillary muscle) marked by a white arrow; b - LV in the posterior-anterior projection (PA).

The aim of this case presentation is to demonstrate the effective suppression of frequent PVCs originating from the papillary muscle of the mitral valve apparatus in a patient who had previously failed antiarrhythmic therapy and multiple catheter ablations.

A 64-year-old patient with no comorbidities presented to a cardiologist in September 2022 with complaints of shortness of breath, irregular heartbeats, and decreased tolerance to routine physical activities. The examination revealed frequent monomorphic PVCs (over 20,000 per day). There was no effect from therapy with beta-blockers and sotalol. Echocardiography showed preserved left ventricular ejection fraction, no local contractility disturbances, and no valve or structural pathology. Coronary angiography showed no atherosclerotic changes in the arteries. Cardiac magnetic resonance imaging indicated an ejection fraction of 65%, normal heart chamber sizes, no local contractility disturbances, and no fibrotic changes.

The patient underwent catheter ablation of the left ventricular ectopic substrate three times using non-fluoroscopic navigation (CARTO 3 (Biosense Webster, USA) and RHYTHMIA HDx (Boston Scientific, USA)) in 2022 and 2023 (Fig. 1). The arrhythmia focus was mapped at the base of the posteromedial papillary muscle of the mitral valve apparatus. Multiple radiofrequency applications (35-40 W, irrigation at 30 ml/min) resulted in transient reduction of PVCs. Due to the inefficacy of ablation, attempts at pharmacological therapy continued with propafenone (150 mg twice daily). However, over the next four months, there was worsening exercise tolerance and increased shortness of breath. On follow-up examination, the patient experienced 35,000 PVCs per day with paroxysms of non-sustained ventricular tachycardia (Fig. 2), a reduced left ventricular ejection fraction of 44%, and left ventricular dilation. Following combined therapy with amiodarone and metoprolol succinate, the number of PVCs decreased to 1,079 per day, with clinical improvement and restored myocardial contractility. Thus, the patient experienced development of CAA with restored myocardial contractility following a reduction in PVCs.

However, after six months, the patient reported gradual progression of shortness of breath, even with minimal exertion. A subsequent ECG monitoring after 11 months showed 46,000 PVCs per day. At this time, the left ventricular systolic function remained normal.

After a medical board assessment of potential risks and benefits, therapy with flecainide (50 mg twice daily) combined with metoprolol succinate (25 mg twice daily) was initiated. The therapy was monitored via an ECG device (Fig. 3a). Upon increasing the flecainide dose to 100

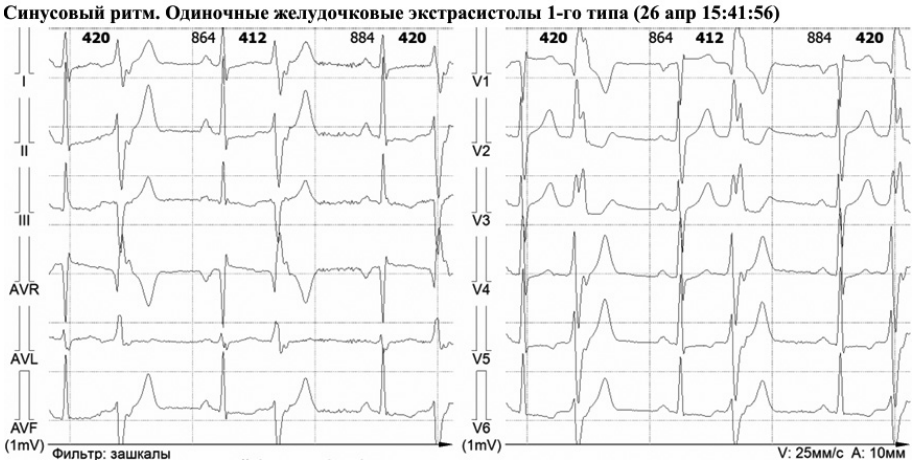

Fig. 2. Fragment of the 24-hour ECG monitoring from 26.04.2023 (analyzator "Cardiotekhnika-07-3/12", INKART, Saint Petersburg, Russia) 25 mm/s, 1 mV/cm - monomorphic ventricular premature beat (PVC) of the bigeminy type.

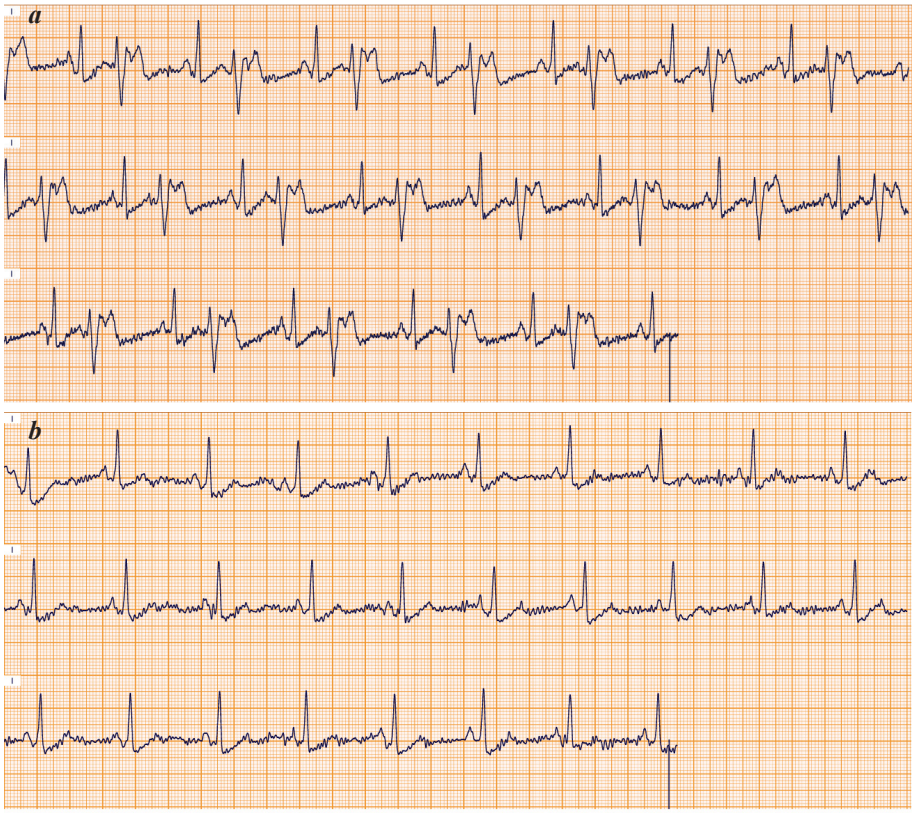

Fig. 3. Self-registration of ECG by the patient using a portable recorder (cardiorhythm indicator single-channel sound "IKRZ-1" Serdyechko, Bioss, Moscow, Russia) 25 mm/s, 20 mm/mV, lead I: a - 28.08.2024, sinus rhythm with HR 76 bpm, single ventricular premature beat of the bigeminy type; b - 29.08.2024, sinus rhythm with HR 54 bpm.

mg twice daily, there was complete suppression of PVCs, confirmed by multiple recordings from the ECG monitor (Fig. 3b) and 24-hour Holter monitoring.

Three months later, the patient independently reduced the flecainide dose to 50 mg twice daily, without adjusting the beta-blocker dose. A 24-hour Holter monitoring on November 21, 2024, showed sustained antiarrhythmic effect (Table 1). The total duration of therapy with flecainide was 5 months.

DISCUSSION

The main results of the presented clinical case are as follows: (1) effective suppression of PVCs with flecainide in a patient with arrhythmia originating from the papillary muscle, refractory to multiple catheter ablations and treatment with other antiarrhythmic drugs of classes III and IC; (2) the effectiveness of a low dose of flecainide in the long-term period, despite its initial inadequacy (the starting dose of flecainide, 50 mg twice a day, had no significant effect, while increasing the dose to 100 mg twice a day completely eliminated PVCs). Further reduction of the dose to the original level did not lead to arrhythmia recurrence.

Flecainide received registration certification in April 2024 and is not included in the Russian clinical guidelines for the treatment of ventricular arrhythmias (2020). According to the official instructions for the drug, flecainide is indicated for patients with documented life-threatening ventricular arrhythmias, such as ventricular tachycardia. At the same time, it is contraindicated for patients with asymptomatic and non-life-threatening ventricular arrhythmias. It is important to note that there is no scientific data limiting the use of flecainide for the treatment of clinically significant PVCs in patients with no structural heart pathology and preserved left ventricular function [10-14].

According to the 2022 clinical guidelines of the European Society of Cardiology for the management of patients with ventricular arrhythmias and prevention of sudden cardiac death, flecainide may be used to treat idiopathic PVCs and tachycardia. It is also recommended to consider flecainide therapy when catheter ablation of the arrhythmia substrate is impossible or carries high risks, including in cases of left ventricular fascicular arrhythmias [15].

This drug may also serve as an alternative treatment in cases where catheter ablation of complex ectopic focus locations, such as papillary muscles, is difficult.

Given the risks of side effects from flecainide, such as widening the QRS complex, prolongation of the PR interval on ECG, and bradycardia, it is advisable to use portable ECG monitors for safety and to assess the effectiveness of therapy. This allows for daily monitoring of the ECG recorded by the patient and timely adjustment of medication doses.

According to the manufacturer's guidelines, for ventricular arrhythmias, the starting dose is 200 mg per day, with a maximum allowable dose of 400 mg per day. It is also possible to reduce the dose to an acceptable low level, at which rhythm disturbances are controlled. The question remains regarding the possibility of taking a 100 mg per day dose, which proved effective in the patient in this clinical case.

Table 1.

The dynamics of the change in the number of PVCs according to the daily ECG monitoring data

Date	Therapy (mg per day)	PVC	LVEF, %
11.2022	Bisoprolol (5) / sotalol (180)	>20000	65
Ablation 1			
11.2022	Propafenone (300)	35501	44
Ablation 2			
Ablation 3			
09.2023	No AAT	25078	44
09.2023	Amiodarone (200), metoprolol (50)	1079	61
08.2024		46946	63
09.2024	Flecainide (200), Metoprolol (50)	1	65
11.2024	Flecainide (100), Metoprolol (50)	72	64

Notes: PVC - premature ventricular contraction, AAT - antiarrhythmic therapy, LVEF - left ventricular ejection fraction.

CONCLUSION

The presented clinical case demonstrates the successful use of flecainide for the suppression of PVCs originating from the papillary muscle in a patient without structural heart pathology and with no effect from multiple catheter ablations of the ectopic focus and the use of other antiarrhythmic drugs.

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