HISTOLOGICAL EVIDENCE OF LEFT VENTRICULAR INVOLVEMENT IN ARRYTHMOGENIC RIGHT VENTRICULAR DYSPLASIA

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A 40-year-old female with arrhythmogenic right ventricular dysplasia (ARVD) demonstrated a reduced motion of the left ventricular (LV) apex. Specimens of LV free wall, obtained by endomyocardial biopsy, histologically revealed prominent interstitial fibrosis with sparse distribution of myocytes. The myocytes were hypertrophic and disrupted with loss of myofibrils. This is a case of ARVD, where LV involvement was histologically verified.

ARRHYTHMOGENIC right ventricular dysplasia (ARVD) has been characterized by enlargement and wall motion abnormality of the right ventricle (RV), replacement of myocardium with fatty and fibrous tissue, and ventricular tachycardia (VT) originating in the RV.2 ARVD was also recognized as an isolated cardiomyopathy that primarily affected the RV. Several reports3–7 have recently suggested left ventricular (LV) involvement in ARVD by demonstrating LV dysfunction. However, histological identification of LV involvement in ARVD has rarely been made. This report describes a patient with ARVD, in whom apical reduced motion and a replacement of myocytes with pronounced fibrosis were identified in the LV.

CASE REPORT
A 40-year-old woman who had no noticeable past history was hospitalized with palpitation. On electrocardiography (ECG), LV was diagnosed, being abolished by intravenous administration of lidocaine. Physical examination revealed an irregular pulse of around 90 beats/min and a blood pressure of 90/64 mmHg. Heart sounds were normal and no murmurs were heard.

A chest X-ray film was normal and an ECG (Fig. 1-a) during palpitation showed VT with a left bundle-branch-block pattern. Multiform ventricular premature beats were noticed after the abolition of VT. An ECG (Fig. 1-a) then showed T-wave inversions in leads II, III, aVF and V1-6, and a ventricular premature beat with a left bundle-branch-block pattern. Delayed potentials were not discernible on the ECG. Two-dimensional echocardiography (Fig. 2) disclosed a pronouncedly enlarged RV, a normally located tricuspid valve and a normally sized LV without thinning of its wall. The motion and thickness of the ventricular septum and LV posterior wall were normal on an M-mode echocardiogram. Moderate tricuspid regurgitation was noted on a color-Doppler echocardiogram.

Right ventricular endocardial mapping (Fig. 1-b) revealed delayed potentials at the ventricular septum of the RV outflow tract and at the RV inferior wall just beneath the tricuspid valve. The results of cardiac catheterization showed normal pressures in the right heart, pulmonary artery and left ventricle. Both cardiac and stroke indices were within normal limits. Right ven-

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Fig. 1. (a), On the left, ECG shows ventricular tachycardia with a left bundle-branch-block pattern. On the right, ECG shows inverted T-waves in leads II, III, aVF and V1-4, ST-segment depressions in leads V4-6, and a ventricular premature beat with a left bundle-branch-block pattern. (b), Right ventricular endocardial mapping disclosed delayed potentials (DP) at the RV outflow tract (RVOT) and at the inferior wall of the RV inflow tract (RVIT). HBE: His bundle electrogram. HRA: high right atrium.

Echocardiograms (Figs. 3-a, 3-b) showed the enlarged RV with moderate tricuspid regurgitation, and akinetic wall motions of the apex and infero-posterior wall. Left ventriculograms (Figs. 3-c, 3-d) revealed a marked hypokinesia of the apex with a total ejection fraction of 0.68. The coronary arteries were intact on coronary angiograms.

Endomyocardial biopsy was performed on the RV, LV, and right atrium (RA). Two of 3 specimens of RV infero-apical wall showed replacement of myocytes with massive adipose tissue and interstitial fibrosis (Fig. 4-a). The other specimen showed bizarre arrangements and hypertrophy of myocytes with deformed and variably sized nuclei and loss of myofibrils. Both specimens of the LV postero-lateral wall revealed a loss of myocytes and prominent interstitial fibrosis (Fig. 4-b). The sparsely remaining myocytes with loss of myofibrils were hypertrophic and disrupted (Fig. 4-c). Infiltration of adipose tissue as shown in the RV wall was not distinct in the LV wall. The specimen of the RA posterior wall disclosed vacuolation and disruption of myocytes and remarkable interstitial fibrosis (Fig. 4-d).

DISCUSSION

Our patient was diagnosed as having ARVD from the findings of ventricular tachycardia with a left bundle-branch-block pattern, delayed potentials by RV endocardial mapping, the enlarged RV with focal wall motion abnormalities
Fig.2. M-mode echocardiography showed an enlarged RV and a normally sized LV. The thickness and motion of the ventricular septum and LV posterior wall were normal (a). Apical four-chamber view exhibited an enlarged RV and a normally positioned tricuspid valve (b). Short-axis view of the LV and RV at end-diastole (c) and end-systole (d) showed a normokinetic motion of the RV and LV and a markedly enlarged RV.

and a replacement of myocytes in RV wall with fat and fibrous tissue.

It was hitherto believed that myopathy in ARVD was exclusively confined to the RV. However, recent reports using echocardiography and radionuclide ventriculography\textsuperscript{3–7} have suggested LV involvement in ARVD. Manyari et al\textsuperscript{4} uncovered a latent LV dysfunction in ARVD. Higuchi et al\textsuperscript{5} reported a case of ARVD, which developed LV dysfunction and VT with a right bundle-branch-block morphology. Webb et al\textsuperscript{6} also demonstrated LV dysfunction, and enlargement or wall motion abnormality of the LV.

In our case, LV wall motion was markedly reduced in the apex, while the motion remained normal in other sites on the LV wall. Therefore, extensive myocardial fibrosis located in the LV apex and patchy distribution of the fibrosis in the LV wall except the apex were highly suspected. Interestingly, a localized dyskinetic bulge in the inferior or antero-septal wall of the LV was previously mentioned in ARVD by Webb et al\textsuperscript{5}. It remains unknown why wall motion abnormality, i.e., presumed severe myocardial involvement was localized in a portion of LV wall rather than equivalently distributed. Since the location of severe myocardial dysplasia in ARVD is generally known as a triangle of dysplasia in the LV,\textsuperscript{3} severity of myocardial involvement in the LV may also be unevenly distributed.

Our patient presented with neither chest pain nor any findings of myocardial infarction on ECGs. Additionally, the coronary artery was found to be intact on coronary arteriograms and no perfusion defect in the LV apex was found on \textsuperscript{201}Tl-hallium myocardial scintigraphy. Thus, as a pathogenesis of the marked reduced motion of the LV apex, myocardial infarction ascribed to
coronary vasospasm was unlikely and myocardial involvement associated with ARVD was considered most probable.

Discrimination of our case from Uhl’s anomaly, where a loss of myocytes and their replacement by fat and fibrous tissue are striking, was made as follows. In Uhl’s anomaly, characteristic parchment-like thinning of ventricular walls, fibroelastic thickening of RV endocardium, paradoxical motion of the ventricular septum, and elevated RA and RV end-diastolic pressure with reduced cardiac index were previously mentioned. However, none of these findings were recognized in our patient and ventricular tachyarrhythmia was rarely documented in Uhl’s anomaly. Thus, this anomaly was ruled out in our case.

In conclusion, our report histologically verified LV involvement in ARVD, which chiefly comprised a replacement of myocytes with remarkable fibrosis. Infiltration of adipose tissue in the LV wall was much less conspicuous than in the RV wall. Vacuolation and disruption of myocytes as well as interstitial fibrosis were shown in the RA wall. Therefore, it was most likely that ARVD is not a localized cardiomyopathy confined to the RV but a generalized one affecting the RV, LV and RA.

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Fig.4. Histology of the myocardium (Hematoxylin-Eosine staining). Myocytes in the RV infero-apical wall are replaced by adipose tissue and interstitial fibrosis (a, x 50). In the postero-lateral wall of the LV, the sparsely remaining myocytes are surrounded by marked fibrosis (b, x 50), the hypertrophic myocytes with depletion of myofibrils (c, x 100) being disrupted. In the RA posterior wall, interstitial fibrosis and disruption and vacuolation of myocytes with deposits of glycogen are shown (d, x 100).

REFERENCES