

Sudden death due to Arrhythmogenic Right Ventricular Dysplasia in young men *Report of two cases*

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Abstract: Right ventricular dysplasia is a distinct cardiomyopathy characterized by progressive replacement of right ventricular myocytes by fat cells. The disease is frequently associated with ventricular arrhythmias, with a variable clinical course and a constant threat of sudden death. We report two cases of arrhythmogenic dysplasia in young men, whose death was myocardial infarction due to tachyarrhythmias. The right ventricle showed interstitial sclerolipomatosis and chronic myocarditis. Ventricular septum presented dystrophic lesions of myocardial fibers, compression of adjacent myocardial fibers, pronounced stasis and sclerolipomatosis to.

Left ventricle wall showed patchy interstitial sclerolipomatosis or fibrosis and interstitial edema. Coagulative necrosis was identified in the right ventricle wall in one case and in the left ventricle wall in the second case. As a special feature, in both cases, left ventricular involvement was observed. Since the disease is a cause of sudden death and has a vital prognosis, an early diagnosis is essential for preventing lethal arrhythmias.

Key Words: right ventricle, arrhythmia, sudden death, coagulative necrosis.

Arrhythmogenic right ventricular dysplasia has a frequency growing and is an important cause of ventricular tachycardia with left bundle block pattern, right ventricular heart failure and sudden death in young patients [1,2].

According to the medical literature, young adults sex ratio is 2.7/1 predominantly in men. The disease prevalence varies 0.02 to 0.1%. However, the true incidence is unknown because the diagnosis may be missed in some cases [3].

Case report

Case 1: A 20-year-old-patient who practiced sports, discharged after 48 hours for attempted surgical radiofrequency ablation of right ventricle wall for ventricular extrasystoles, was found in cardiopulmonary arrest by ambulance. This was called for unconscious state on March 2011. After 35 minutes of resuscitation in the emergency room patient's death was declared. Autopsy was necessary in order to elucidate the cause of death.

The young man had a previous history of asymptomatic monomorphic ventricular extrasystolic arrhythmia and was suspected of ARVD.

Autopsy findings

External examination revealed a normosthenic habitus and no signs of traumatic injury. Macroscopically, it was found dilated cardiomyopathy with left ventricular hypertrophy. The anterior side of the free wall of right ventricle showed a transmural well marked yellow area of high consistency with length of 3,5 cm (Figure 1), endocardium at this level being covered by a thin reddish hematic clot (Figure 2). Right heart wall thickness was 0,5 cm. Histopathological examination of the apex and left ventricle wall showed interstitial sclerolipomatosis and interstitial edema. Ventricular septum presented dystrophic lesions of myocardial fibers, compression of adjacent myocardial fibers, pronounced stasis and sclerolipomatosis to. Microscopic examination of the right ventricular wall revealed interstitial sclerolipomatosis (Figure 3), area of coagulation necrosis (Figure 4) and

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Figure 1: Macroscopic appearance of myocardial infarction.

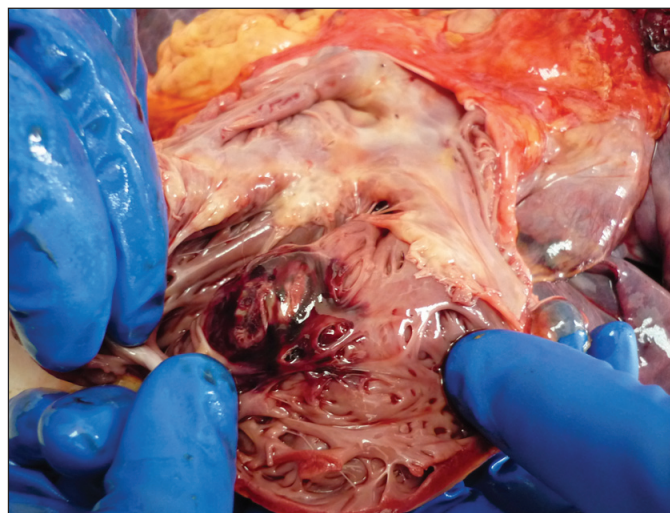


Figure 2: Right ventricle endocardium thinned and covered by a thin reddish hematic clot.

chronic myocarditis (Figure 5). The apex of the right ventricle showed myocardial atrophy. At the level of right ventricle, we found also contraction and fragmentation of myocardial fibers. Pulmonary examination revealed an area of recent infarction. No pathological changes were observed in the other organs. Postmortem toxicological analysis was negative for alcohol and drugs.

Case 2: A 21-year-old-man, with recurrent paroxysmic supraventricular tachycardia and bifascicular block (right bundle branch block and postero-inferior hemiblock) is hospitalized for heart palpitations,

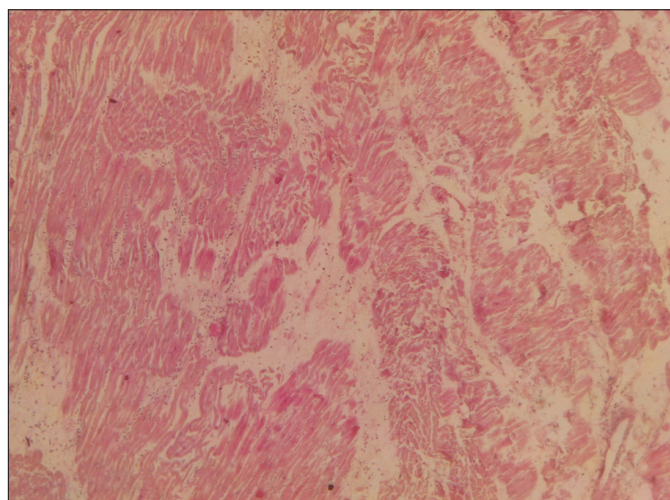


Figure 3: Interstitial sclerolipomatosis, HE, 100x.

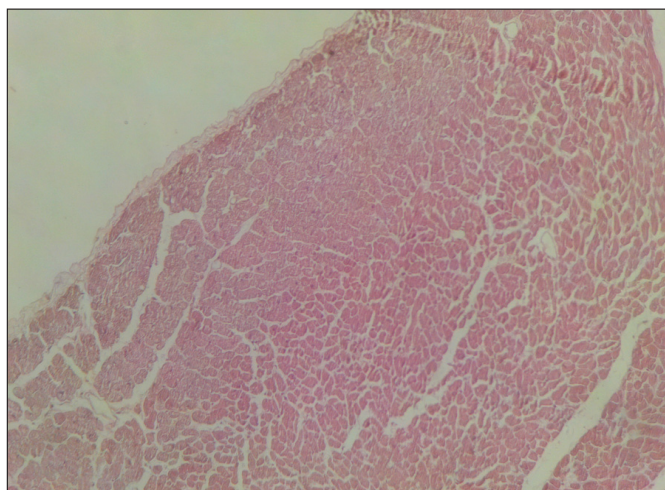


Figure 4: Coagulative necrosis area (left side), HE100x.

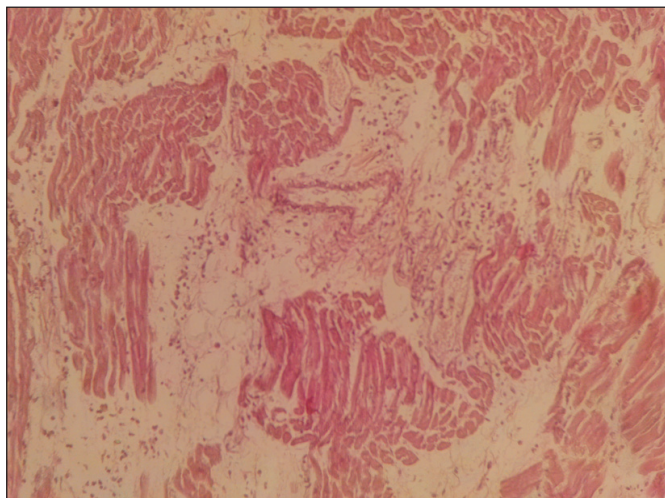


Figure 5: Interstitial chronic inflammatory infiltrate among the myocardial fibers, HE200x.

epigastric pain, nausea, vomiting. After admission he developed a paroxysmic supraventricular tachycardia alternating with sinus rhythm and short asistolas of 3-5 seconds. He was unresponsive at resuscitation.

Symptoms started two years ago, when he made his first episode of effort fainting which was repeated two times at smaller efforts. Clinical examination and echocardiography revealed no functional or organic cardiac abnormalities. In April 2011, he underwent electrophysiological study and radiofrequency ablation for TPSV slow way. After ablation, PSVT attacks were repeated intermittently. Because symptoms improved after the introduction of beta adrenergic blocker, has decided to continue medical treatment. He was also diagnosed with heart failure NYHA class 2, moderate pulmonary regurgitation and mild mitral regurgitation.

Autopsy findings

When performing autopsy, all heart cavities were dilated and right ventricular wall was infiltrated with fat. The left ventricle wall presented an elevated area, with reddish color and length of 2 cm (Figure 6).

The histopathological examination, revealed coagulation necrosis of myocardial fibers (Figure 7). The right ventricular wall displayed interstitial sclerolipomatosis (Figure 8), interstitial edema and chronic myocarditis.

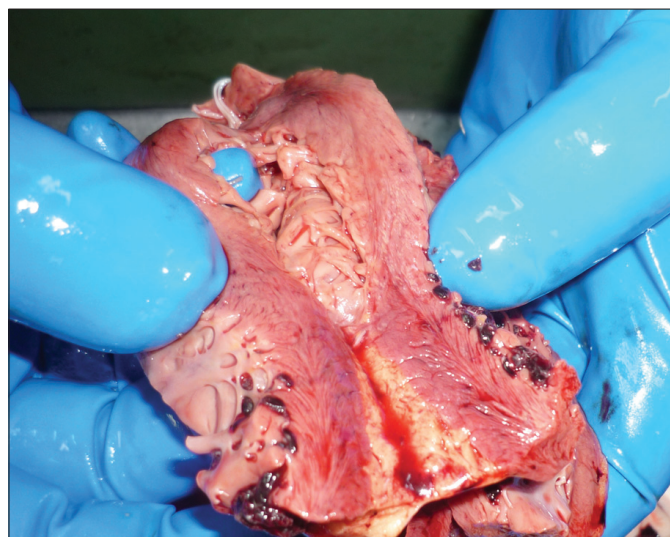


Figure 6: Myocardial infarction area – macroscopical aspect.

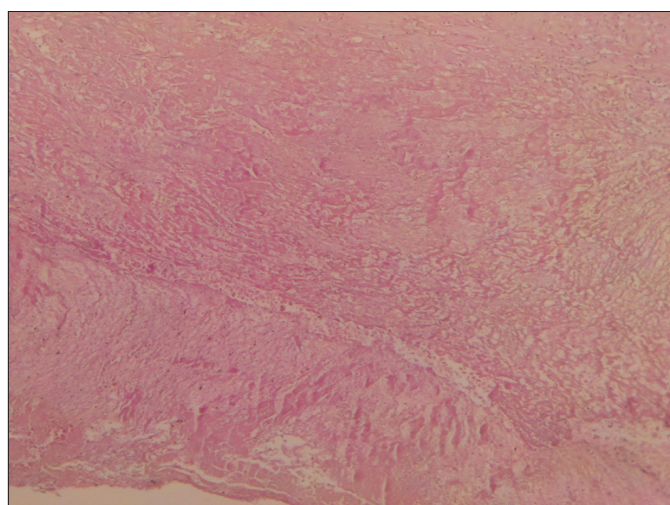


Figure 7: Left ventricle coagulative necrosis.

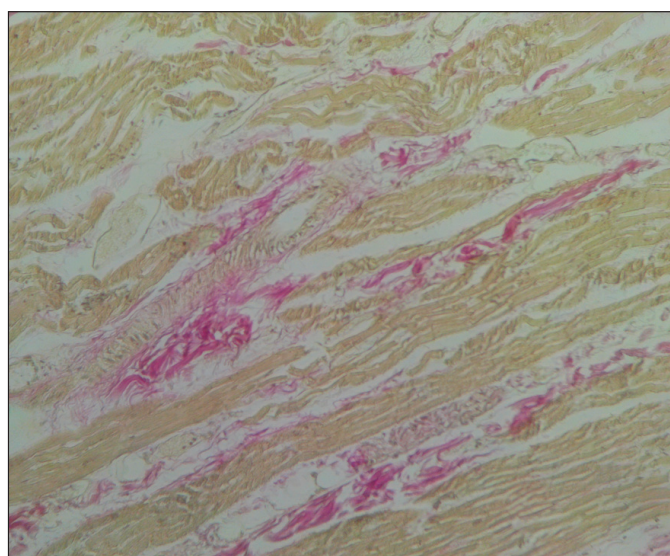


Figure 8: Interstitial fibrosis, van Gieson, 200x.

Discussion

The condition was first described by Frank and Fontaine in 1978 [4]. In 1995, the World Health Organisation and the International Society and Federation of Cardiology decided that this disease should be considered a type of cardiomyopathy [5].

The main feature of the DAVD is the tendency to ventricular arrhythmias and sudden death even in the absence of clinical ventricular dysfunction. The substrate for arrhythmias is represented by lesions known as "triangle of dysplasia". It consists of right ventricular outflow tract, infundibulum and apex of the heart. There are described right ventricle dilatation and hypokinesia [6]. The disease affects men, with a sex ratio of 2.7/1 in favor of men [7].

Thus, currently accepted definition of sudden cardiac death is natural death due to cardiac causes, announced by sudden loss of consciousness within one hour of onset the acute symptoms in a person with may have a history of heart disease, but the death is unexpected [8,9].

Accurate diagnosis is the hitopathological examination and is based on replacement of right ventricular muscle fibers with connective tissue and fat cells. These areas have a marked tendency to malignant ventricular arrhythmias [10].

Burke et al studied the correlations between ARVD and simply fat replacement of the right ventricle. In autopsy, they showed that ARVD is characterised by sclerolipomatosis of myocytes, while fatty infiltration per se is another condition that should not be considered synonymous [11].

Because of the inability to perform right ventricular biopsies, McKenna et al have established major and minor criteria for diagnosis of disease in a Task Force Report. They are based on structural parameters and histological, electrocardiographic, arrhythmic and genetic features [12].

Pathogenesis of disease is not entirely known. Replacement of myocardial tissue with fibro-fatty tissue occurs through four mechanisms: apoptosis [13], disontogenic, mechanism, myocardial inflammation and dystrophy [14,15].

Recently, it was demonstrated that several genes are involved in the etiopathogenesis: Plakoglobin and Desmoplakin. The desmosomes present in the cardiomyocytes serve to maintain cellular integrity, in apoptosis and lipid metabolism [16].

Genetic abnormalities of Desmoplakin, which controls the activity of the desmosome, lead to cell death and structural dysfunction of Tcf-Lef1 transcription factor that determines the transformation of myocytes in adipocytes [17]. Plakoglobin abnormalities disrupt intracellular connections, which facilitates the production of arrhythmias [18].

Another way to produce pathogenic disease is altered calcium homeostasis caused by mutations in the cardiac ryanodine receptor gene. Deficiency of intracellular calcium level and alteration of excitation-contraction process may predispose to arrhythmias.

In addition, intracellular calcium deficiency can lead to cell necrosis, fibrosis and myocardial tissue fat replacement [19].

Lymphocytic inflammatory infiltrate is often found in endomyocardial biopsy specimens, suggesting a focal myocarditis, which may explain in part ARVD sporadic cases.

Recently, the presence of apoptotic cells in endomyocardial biopsy specimens of patients with

ARVD associated with altered intracellular calcium was reported [20]. In advanced stage disease there is focal or diffuse reduction of ventricular wall, which functionally correspond to the areas of segmental akinesia or even dyskinesia.

Although right ventricle damage is predominant, left ventricular injury at any stage of disease progression also has been described [21,22,23].

The risk of sudden death among athletes is higher, reaching up to 20-25%. This is related to the occurrence of ventricular arrhythmias during exercise [24,25]. Exercise produces catecholamines and hyperextension discharge myocardial fibers, which can stimulate the dysplastic areas.

Thus, in a study on 160 subjects with clinical criteria of ARVD, 24 patients (18,5%) died during the study by major ventricular disorders.

Over time, several studies have investigated the impact of arrhythmias in patients with ARVD [26].

The natural evolution of disease is caused by both cardiac electrical instability and right ventricular failure. Right ventricular arrhythmias range from isolated premature ventricular beats to non-sustained tachycardia, ventricular fibrillation and sudden death [27].

Conclusion

ARVC is an important cause of sudden death and may be the first event that occurs mainly in intense exercise. As revealed in the cases presented, involving the left ventricle is possible by extension process or development of signs of congestive heart failure. Since the disease is uncommon and has a vital prognosis, is particularly important the early diagnosis and accurate treatment, to prevent fatal arrhythmias.

In conclusion, managing patients with ARVD is a challenge for all specialties involved in diagnosis and treatment of the disease.

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