G88 Arrhythmogenic Right Ventricular Dysplasia (ARVD): A Not So Rare Cause of Sudden Death in Young Adults

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The goal of this presentation is to make the forensic community aware of this entity (ARVD) as a sudden cause of death in the young adult population.

This presentation will impact the forensic science community by demonstrating how routine full autopsies may not detect the subtle pathologic changes that cause Arrhythmogenic Right Ventricular Dysplasia.

Ten (10) cases of ARVD/Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) autopsied at Danbury Hospital, CT, from June 2002 until June 2007 were reviewed. This number represents 3.75% of the total adult full autopsies performed in our institution during the same period.

Age, sex, and ethnic background were noted. Associated cardiac and non cardiac related diseases were reviewed.

Medications, social and family history (sudden death of a sibling) as well as body habitus (obesity) were tabulated.

Prior symptoms (syncopal episodes, palpitations) and pre-terminal circumstances (place of death, physical activity) were examined. Autopsy the mouth. Internal examination showed cerebral oedema; food residuals findings (both cardiovascular and systemic) were correlated.

The ten patients' ages ranged from 34 to 65. Sex ratio was 1:1. 8/10 were obese, 5/10 used alcohol frequently, 10/10 were at rest at time of pre-final event, 1/10 had family history of sibling (brother) sudden death, 10/10 had some degree of Coronary Artery Disease (CAD), 7/10 had cardiomegaly (450g to 650g), 1/10 had coexisting myocarditis, 10/10 were Caucasian (only 1 with an Italian background), 4/10 had suffered a significant traumatic injury and 3/10 used medications for depression or anxiety. In patients with ARVD, the most common findings were obesity, CAD. The authors also concluded that Caucasian ethnicity is prevalent, the pre-terminal episode happens at rest, the age group is between 4th and 7th decades, and M:F ratio is ~ 1.

This report helps to increase awareness regarding this congenital cardiac disease. It is relevant to the forensic community, because of its high incidence in children, and young adults, and it is a frequent cause of (sudden death) in the North East (New England).

Arrhythmogenic right ventricular dysplasia (ARVD, also known as arrhythmogenic right ventricular cardiomyopathy or ARVC) is a type of non-ischemic cardiomyopathy that involves primarily the right ventricle of the heart. It is characterized by hypokinetic areas involving the free wall of the right ventricle, with fibrofatty replacement of the right ventricular myocardium, with associated arrhythmias originating in the right ventricle.

ARVD is an important cause of ventricular arrhythmias in children and young adults. It is seen predominantly in males, and 30-50% of cases have a familial distribution. It is usually inherited in an autosomal dominant pattern, with variable expression. The penetrance is 20-35% in general, but significantly higher in Italy. Seven gene loci have been implicated in ARVD. The incidence of ARVD is about 1/10,000 in the general American population, although some studies have suggested that it may be as common as 1/1,000. It accounts for up to 17% of all sudden cardiac deaths in the young. In Italy, the incidence is 40/10,000, making it the most common cause of sudden cardiac death in the young.

Up to 80% of individuals with ARVD present with syncope or sudden cardiac death. The remainder frequently present with palpitations or other symptoms due to right ventricular outflow tract (RVOT) tachycardia.

Apoptosis (programmed cell death) appears to play a large role in the pathogenesis. It is unclear why the right ventricle is predominantly involved. The disease process starts in the subepicardial region and works its way towards the endocardial surface, leading to transmural involvement. The left ventricle is involved in 50-67% of individuals. If the left ventricle is involved, it is usually late in the course of disease, and confers a poor prognosis.

90% of individuals with ARVD have some EKG abnormality. The most common one seen in ARVD is T wave inversion in leads V1 to V3.

Transvenous biopsy of the right ventricle can be highly specific for ARVD, but it has low sensitivity. A biopsy sample that is consistent with ARVD is found to have > 3% fat, >40% fibrous tissue, and <45% myocytes.

A postmortem histological demonstration of full thickness substitution of the RV myocardium by fatty or fibro-fatty tissue is consistent with ARVD. There is no pathognomonic feature of ARVD. The diagnosis is based on a combination of major and minor criteria. The diagnosis is based on a combination of major and minor criteria, and requires either 2 major criteria or 1 major plus 2 minor, or 4 minor criteria.

Many of these patients have symptoms associated with ventricular tachycardia, such as palpitations, light-headedness, or syncope. Others may have symptoms and signs related to right ventricular failure, such as lower extremity edema, or liver congestion with elevated hepatic enzymes. Unfortunately, sudden death may be the first and sole manifestation of disease.

The goal of management of ARVD is to decrease the incidence of sudden cardiac death. This raises a clinical

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dilemma: How to prophylactically treat the asymptomatic patient who was diagnosed during family screening.

Sotalol, a beta blocker and also a class III antiarrhythmic agent, is the most effective antiarrhythmic agent in ARVD. Other antiarrhythmic agents used include Amiodarone and conventional beta blockers (i.e., Metoprolol). If antiarrhythmic agents are used, their efficacy should be guided by series ambulatory Holter monitoring, to show a reduction in arrhythmic events.

Individuals with decreased RV ejection fraction and dyskinetic portions of the right ventricle, may also benefit from long term anticoagulation with warfarin to prevent thrombus formation and subsequent pulmonary embolism.

Implantable cardioverter-defibrillator devices (ICD's) are the most effective prevention against sudden cardiac death.

Cardiac transplant surgery is only rarely performed in ARVD. It may be indicated if the arrhythmias associated with the disease are uncontrollable or if there is severe bi-ventricular heart failure that is not manageable with routine pharmacological therapy.

All first degree family members of the affected individual should be screened for ARVD. This is used to establish the pattern of inheritance. Screening should begin during the teenage years unless otherwise indicated. Screening tests include: Echocardiogram, EKG, holter monitoring, cardiac MRI, and exercise stress test.

ARVD, Sudden Death, Pre and Postmortem Diagnosis

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