

CONFLICTS OF INTERESTS

None declared

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A clinico-pathological update in arrhythmogenic right ventricular cardiomyopathy

Actualización clínico-patológica en la miocardiopatía arritmogénica del ventrículo derecho

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To the Editor:

Arrhythmogenic cardiomyopathy (AC) is a heart muscle disease characterized clinically by life-threatening ventricular arrhythmias and pathologically by an acquired and progressive dystrophy of the ventricular myocardium with fibro-fatty replacement. With an estimated prevalence of 1:2000-1:5000, AC is listed among rare diseases. A familial background consistent with an autosomal-dominant trait of inheritance is present in most of AC patients; recessive variants have also been reported, either or not associated with palmoplantar keratoderma and woolly hair. AC-causing genes mostly encode major components of the cardiac desmosomes and up to 50% of AC probands harbor mutations in one of them. Mutations in non-desmosomal genes have been also described in a minority of AC patients, predisposing to the same or an overlapping disease

phenotype.

Compound/digenic heterozygosity was identified in up to 25% of AC-causing desmosomal gene mutation carriers, in part explaining the phenotypic variability. Abnormal trafficking of intercellular proteins to the intercalated discs of cardiomyocytes and Wnt/beta catenin and Hippo signaling pathways have been implicated in disease pathogenesis. The acquired and progressive myocyte death (either apoptosis or necrosis) typically starts in the subepicardial-midmural layers to move towards the endocardium. AC is a major cause of sudden death in the young and in athletes. The clinical picture may include a sub-clinical phase; an overt electrical disorder; and right ventricular or biventricular pump failure. Ventricular fibrillation can occur at any stage. Genotype-phenotype correlation studies led to identify biventricular and dominant left ventricular variants, thus supporting the use of the broader term

AC.

Since there is no “gold standard” to reach the diagnosis of AC, multiple categories of diagnostic information have been combined and the criteria recently updated, to improve diagnostic sensitivity while maintaining specificity. Among diagnostic tools, contrast enhanced cardiac magnetic resonance is playing a major role in detecting left dominant forms of AC, even preceding morpho-functional abnormalities.

The main differential diagnoses are idiopathic right ventricular outflow tract tachycardia, myocarditis, sarcoidosis, dilated cardiomyopathy, right ventricular infarction, congenital heart diseases with right ventricular overload and athlete heart. A positive genetic test in the affected AC proband allows early identification of asymptomatic carriers by cascade genetic screening of family members. Risk stratification remains a major clinical challenge and antiarrhythmic drugs, catheter ablation and implantable cardioverter defibrillator are the currently available therapeutic tools. Sport disqualification is life-saving, since effort is a major trigger not only of electrical instability but also of disease onset and progression.

The presentation will review the current knowledge of this rare cardiomyopathy, suggesting a flow-chart for primary care clinicians, general and forensic pathologists and geneticists.

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None declared

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Function of the Pathological Anatomy Technician in the Sudden Death Risk-Assessment Unit

Función del Técnico de Anatomía Patológica en la Unidad de Valoración del Riesgo de Muerte Súbita

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