Evening Seminer

Brugada syndrome and idiopathic ventricular fibrillation, new developments

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Brugada syndrome (BrS), now clearly recognized as characteristic subset of idiopathic ventricular fibrillation (IVF, i.e. ventricular fibrillation in the absence of structural heart disease or a clear QT-interval related disorder), is a disease entity associated with sudden cardiac death in, most often, relatively young individuals. The signature ECG is represented by right precordial ST-segment elevation and discrete prolongation of diverse conduction parameters. Type 1, i.e. the 'coved type' ST-segment and one of the 3 ECG types, is mandatory for the diagnosis, although this might not be too strict in all ethnic populations. BrS is diagnosed when it is associated with documented (or inducible) ventricular arrhythmias or premature sudden cardiac death or similar ECGs in family members or nocturnal agonal respiration[1]. When the ECG is absent at baseline, drug challenge (i.v. flecainide, ajmaline or other sodium channel blockers) almost always unmasks the required ECG features. A genetic diagnosis is not critical for the clinical diagnosis. SCN5a mutations are found in up to 30% of patients. Five other genes have been identified to date to be causal to BrS, most likely, however, responsible for a significant smaller subset of patients.

In BrS a number of issues are highly controversial, among which the pathogenesis of the ECG characteristics. The theory of repolarization inhomogeneity over the right ventricular wall competes with the depolarization theory focussing on significant delayed activation of the right ventricular outflow track[2]. Another highly controversial issue relates to risk stratification. Indeed, the risk for malignant ventricular arrhythmias of patients with a spontaneous or drug-induced coved-type ECG is ill-defined. On the (Japanese) population level it has been shown that a Brugada ECG discloses a significantly increased life-time risk for unexpected sudden death. What this means in terms of treatment neccesity of asymptomatic ptients is completely unknown. At the other hand, it is clear that patients that have been successfully resuscitated or otherwise symptomatic patients (with a type 1 ECG) should be treated with an ICD. Both risk in absolute terms as well as risk predictors are disputed. As to the latter in particular the role of programmed electrical stimulation is controversial. Reasons for the different obeservations in different cohorts are unknown but potentially relate to patient characteristics. There seems a potential bias towards more severe cases in the Brugada registry[3], but this is no more than speculation at the moment. Non-invasive markers are hardly available although some small studies indicate a potential role for daily fluctuations in the magnitude of the right precordial ST-segment elevation and in the appearance of late potentials[4)~6)].

IVF other than BrS is even less well studied. It is recognized as an inherited disease but potentially causal genes other than SCN5a are not known. We recently described a founder haplotype on chr 7 associated with IVF with a very malignant course[7]. At age 50 almost 50% of affected individuals has experienced OHCA or SCD. In a large number of patients we have sofar not been able to identify any structural (i.e. imaging) or electrophysiological marker that could be useful in riskstratification. The identity of the causal genetic variant is as yet unknown. Further studies are ongoing.

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