The Brugada syndrome: do we need more than the 12-lead ECG?

See page 321 for the article to which this Editorial refers

Sir Thomas Lewis ceased his investigations on clinical electrocardiography and electrophysiology by 1926. Although the reasons for this abandonment remain unknown, Lewis apparently had declared that the ‘cream of electrocardiography was off’ and that he did not foresee new things to be discovered with this tool[1]. I personally doubt that Lewis seriously believed that his forecast was going to be true. In spite of Lewis’ pessimistic declaration, the 12-lead ECG has continued to serve as a valid instrument for clinical investigation. The Wolff–Parkinson–White syndrome, the long QT syndrome, hemiblocks, arrhythmogenic right ventricular dysplasia, the Brugada syndrome, not to mention the role of the ECG in defining the site of origin and the pathway of tachycardia, are examples of questions not addressed by Lewis’ investigations.

Although the ECG plays a crucial role in the diagnosis of the Brugada syndrome, several uncertainties must be sorted out in the new millennium. It is obvious that the ECG will not be enough to answer all the obscure points of this new syndrome. Some of the gaps in our knowledge are commented on this Editorial, since they are not unravelled by the paper in this issue on sudden death in members of families with this syndrome by Pedro, Ramón and Josep Brugada[2]. The major contribution of this study is to indicate that not all sudden deaths in members of families with this syndrome by Pedro, Ramón and Josep Brugada[2]. The major contribution of this study is to indicate that not all sudden deaths in members of affected families are related to the syndrome. If that is the case for members of families known to suffer from the disease, in asymptomatic patients with an ECG ‘typical’ of the Brugada syndrome, it should not be taken for granted that a non-documented sudden death in a family member is related to the syndrome.

**Does a normal ECG rule out the ionic channel disorder and the potential risk?**

In family members of affected subjects it is usually considered that a normal ECG, both in the basal state and after sodium channel blockers, rules out the disease. The paper by the Brugada brothers states that there is a 100% correlation between phenotype (the typical ECG, persistent, intermittent or unmasked by drugs with class I effect) and genotype[2]. They base this assertion on an abstract that actually contradicts this matter since the ECG became positive in only six of 10 members of a family with one of the reported mutations in the sodium channel[3]. More recently it has been shown that the flecainide test can be negative in as many as 80% of asymptomatic gene carriers who also had a normal resting ECG[4]. What remains unknown is the risk of phenotypically negative, asymptomatic gene carriers.

**Does an abnormal ECG always indicate a mutation in the sodium channel?**

Conditions electrocardiographically mimicking the Brugada syndrome have been reported such as a mediastinal tumour compressing the right ventricular outflow tract, that most likely had nothing to do with a generalized mutation in the sodium channel[5]. In addition, there are patients with the electrocardiographic phenotype and a history of resuscitated cardiac arrest in whom no mutations in the sodium channel can be found thus suggesting that other genes can also be responsible for this syndrome[6]. In fact it is possible that the sodium channel mutation is present in only a minority of patients with the Brugada syndrome.

**Does an abnormal ECG always indicate risk for arrhythmic events?**

The approach in the asymptomatic individual with the electrocardiographic markers of the Brugada syndrome is difficult. There are three types of patients under this umbrella: (1) asymptomatic patients with a positive ECG (either basal or after a class I drug) that belong to families with clearly affected members (ECG plus syncope or resuscitated cardiac arrest), (2) similar asymptomatic patients with a family history of undocumented sudden, instantaneous, death, (3) asymptomatic patients with no personal or family history of syncope or sudden death.

We know that there are completely asymptomatic patients with the ECG abnormality, and asymptomatic relatives with the typical electrocardiographic changes, either spontaneously or after the administration of a sodium channel blocker. In some of
these patients, but not in all, ventricular fibrillation has been induced with a single ventricular extrastimulus, a finding that is particularly worrying[7]. In addition, there are patients whose ECG showed the typical phenotype of the Brugada syndrome after receiving flecaïnide for supraventricular arrhythmias, usually atrial fibrillation[8]. In none of the latter two situations did the patients or their relatives, have a history of syncope or instantaneous death.

Counselling in asymptomatic patients is difficult and based more on wishful thinking than evidence. In a previous report by the Brugada brothers, they observed that 27% of their asymptomatic phenotypically positive patients, developed arrhythmic events during follow-up[9]. However, they did not differentiate asymptomatic subjects presenting arrhythmic events at follow-up as belonging or not to families with a positive history of sudden arrhythmic death. To gather this information seems to be of great importance to guide our counselling. In a recent paper on prophylactic defibrillators, Brugada et al. state that an implantable defibrillator should be recommended in asymptomatic patients with the typical ECG if there is a history of syncope or familial sudden death or if multiform ventricular tachyarrhythmias are induced by programmed ventricular stimulation[10]. They did not recommend implanting a prophylactic defibrillator in asymptomatic patients without a positive family history not inducible with programmed ventricular stimulation. Although it might seem logical to prescribe an implantable defibrillator in asymptomatic inducible patients without a positive family history, there are no hard data supporting this practice.

How specific is the typical ECG?

We must remember that the Brugada syndrome is a clinical-electrocardiographic association in which the typical ECG (right bundle branch block and ST-segment elevation from V1 to V3) is combined with the development of ventricular tachyarrhythmias in patients with an otherwise structurally normal heart. How specific is the ‘typical’ ECG pattern? I got the impression that the ‘typical’ ECG is being identified more frequently every day, most of the time in patients that are asymptomatic or in subjects that have syncope of probable vaso-vagal origin. This poses a difficult problem, particularly when the patient does not recall a history of sudden death in the family. Should we perform programmed stimulation in all these patients? Should we study their relatives? Should we subject them to genetic scrutiny? These and all the other questions in this editorial will have to be faced in the new millennium with research tools other than the ECG.

J. FARRÉ
Fundación Jiménez Díaz,
Madrid, Spain

References