Counselling pitfalls in Romano–Ward syndrome

We wish to comment on several issues raised by the recent paper by Reardon et al.1 on counselling pitfalls in Romano–Ward syndrome. We would strongly support their view that pedigree and phenotype analysis in this disorder can prove difficult. The fact that affected subjects may have a normal corrected QT interval (QTc) has been well documented.2

Romano–Ward syndrome is a disorder of ventricular repolarisation, and in the assessment of a patient’s status, T and U wave morphology may be helpful,3 as abnormalities are common. Biphasic, bifid, and notched T waves are described,4 as are T U wave alternans.5 It would be useful to know whether such abnormalities were seen in the family reported by Reardon et al.,6 as this might help determine whether a person such as II-1 should be considered affected, despite his normal QTc. The finding that QTc tends to decrease in affected males after the age of 40 may be relevant.

Another aspect of the assessment of penetrance of the gene for counselling purposes is illustrated by the authors’ use of Vincent’s data from one family suggesting that only 24% of those who have inherited Romano–Ward had a prolonged QTc. This is not true of every family, however. In our own study of two families 18/36 and 4/7 persons at 50% risk of each family respectively had prolonged QTc or recognisable T or U wave abnormalities or both. A Japanese study similarly reported near 100% penetrance.7

The variability in ECG findings and in the clinical history of families does suggest underlying genetic heterogeneity, which may be increasing as further Romano–Ward-like disorders are lumped under this heading (for example, recurrent polymorphic VT with normal QTc8 and bradycardia dependent long QT syndrome).9 The finding of genetic linkage to two different chromosomal regions in different families,10 11 and to neither in others12 13 also suggests underlying heterogeneity.

With regard to treatment, it is certain that a beta-blocker reduces the frequency of arrhythmias,14 it is not true to state that cardiac arrhythmias (as defined) never occur in medically treated affected subjects. At least one case of death while on a beta-blocker has been published,15 and the prospective international study of 328 families reported by Moss et al.16 found that 9/147 patients who died under the age of 50 (from presumed cardiac arrhythmias) were on antiarrhythmic therapy (beta-blockers or left cerebral sympathetic ganglionectomies or both). Moss et al.16 also have reported on the efficacy of permanent pacemakers in those patients with long QT syndrome whose symptoms and arrhythmias are not abolished by antiarrhythmic therapy. This accords with our experience, where two members of one family have required the addition of permanent pacemaker therapy to abolish their episodic ventricular tachycardias,17 and this is now a well accepted form of treatment.18

In summary, we agree with the conclusion of Reardon et al.1 that counselling in the long QT syndromes is not straightforward. It is complicated by the presence of severity, penetrance, and ECG findings, and also by genetic heterogeneity. We agree that assignment of a subject’s status should not be by QTc alone, but suggest that it should include an assessment of the T U wave morphology in the light of the family ECG pattern, in addition to clinical assessment of symptoms. There may be some guide to prognosis from the family history, and from a subject’s past history and sex (previous symptoms and female sex are strong risk factors for future cardiac events9). The benefits of modern therapy for affected patients, at risk for arrhythmias and sudden death, are such that careful family investigation, where possible, and treatment where appropriate, are strongly advised, despite the difficulties outlined above.

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4 Moss AJ, Schwartz PJ. Delayed repolarisation (or QTU prolongation) and malignant ventricular arrhythmias. Modern Concepts Cardiol 1982;51:85-90.