Electrocardiography of Inherited Arrhythmias and Cardiomyopathies

From Basic Science to Clinical Practice

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Foreword

Arrhythmias associated with heritable heart diseases are important to understand, especially since they tend to strike young, and often previously asymptomatic individuals. The first test which may reveal abnormalities in these individuals is almost always the electrocardiogram. The ECG may be performed as part of screening or "case finding" in individuals with symptoms which may suggest arrhythmias. There are few comprehensive, detailed, and high-quality resources for practitioners to consult with respect to the range and nature of ECG abnormalities in inherited arrhythmia syndromes. This book fulfills an extremely important niche and brings together in a convenient and elegantly written and illustrated format the latest information regarding ECG abnormalities. Importantly, many of the syndromes discussed are only diagnosable from the ECG, which remains the essential test in clinical diagnosis.

Drs. Green, Krahn, and Alqarawi have assembled the world experts in these various conditions to produce a practical and visually appealing compendium of ECGs in these various syndromes, which can lead to serious and potentially fatal arrhythmias. The explanatory text and background in each chapter is especially informative and useful.

This book will be of great use to generalists and specialists alike, especially individuals that are called upon to evaluate individuals being screened or investigated for familial arrhythmia syndromes. If you are looking for the one definitive source of information on this topic, you have found it.

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Paul Dorian, MD, MSc, FRCPC, FHRS

Acknowledgement

The editors share a common heritage of mentors poring over an ECG, seeking to better understand those fascinating signals from the hearts of patients they care for. Founders like Hein Wellens and George Klein instilled that interest and excitement about the ECG in us, and we have turned that focus to inherited arrhythmia related conditions, our clinical passion. Remarkably, the ECG is still teaching us many things about patients and heart. This can only happen with the support of the "village" in which we live, including teachers, trainees, peers and of course, patients and their families. Fellows ask us "why challenge accepted uncertainty?" and push us to answer questions. Thank you for insisting that we better understand the ECG and its implications for patients. We have made every effort to "pay it forward", by becoming teachers and mentors to the students around us as we too continue to learn. Dr. Green taught Dr. Krahn in the 1980s, and he in turn taught Dr. Alqarawi not so long ago. Lastly, we are grateful to our partners who have shown unconditional support for our preoccupation with learning and teaching the world of ECGs. Thank you, Nancy, Susan and Arwa.

Contents

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Part I

Inherited Arrhythmias

Long QT Syndrome

1

Andrew Krahn, Wael Alqarawi, and Peter J. Schwartz

Introduction

The long QT syndrome (LQTS) is a life-threatening disease that represents a leading cause of sudden cardiac death in the young [1]. The ECG features of this disease are QTc prolongation and T-wave abnormalities at rest and failure of the QTc to shorten with exercise [2]. Approximately one in 2500 healthy live births will have an abnormally long QT interval and a genetically mediated LQTS, transmitted via an autosomal dominance inheritance pattern [3]. One of the characteristic features of LQTS is the marked heterogeneity of patients, ranging from sudden death in infancy to lifelong asymptomatic disease carriers [4]. Only one third of patients will ever be symptomatic. As many as 40% of LQTS patients will have normal or non-diagnostic QT intervals at rest [5–7].

With improved screening and therapy, the mortality rate in LQTS has dropped dramatically [1]. Lifestyle modifications such as avoidance of strenuous exercise, unsupervised swimming and QT-prolonging medications are advocated for all patients. Beta-blocker therapy is the primary treatment, offering substantial protection from fatal cardiac events [8]. Patients who have cardiac events while on

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beta-blockers, have suffered a cardiac arrest, or are deemed sufficiently high risk can be offered left cardiac sympathetic denervation or an implantable cardioverter-defibrillator (ICD) [9–11]. ICD therapy, however, has lifelong implications, and complications are common and even expected when the recipient has had the device for decades. ECG remains the cornerstone of phenotype recognition, with incremental value in provoking diagnostic QT changes with exercise testing [14, 15].

At the molecular level, there are three major LQTS genes (KCNQ1, KCNH2 and SCN5A) that account for approximately 80% of the disorder [12, 16]. Fifteen other genes have been associated with LQTS, the majority of which account for 1–2% of all cases [12, 16, 17]. Genetic testing can inform the diagnosis, prognosis and family screening of patients with suspected LQTS [12, 13, 17]. Genotype-phenotype correlations have shown distinct gene-specific triggers, response to medical therapies and ECG patterns [18]. Insufficient distinct phenotype data exist for the rare forms of LQTS, so the three major LQTS genes and Andersen-Tawil syndrome (ATS) with clear ECG patterns will be discussed in this chapter.

ECG Findings

1. Prolonged QT interval
   (a) QT measurement (Fig. 1.1a, b)
   (b) Corrected QT interval (QTc) (Fig. 1.2)
2. Specific T-wave morphologies
   (a) LQT1 (Fig. 1.3)
   (b) LQT2 (Figs. 1.4a, b; and 1.6)
   (c) LQT3 (Fig. 1.5)

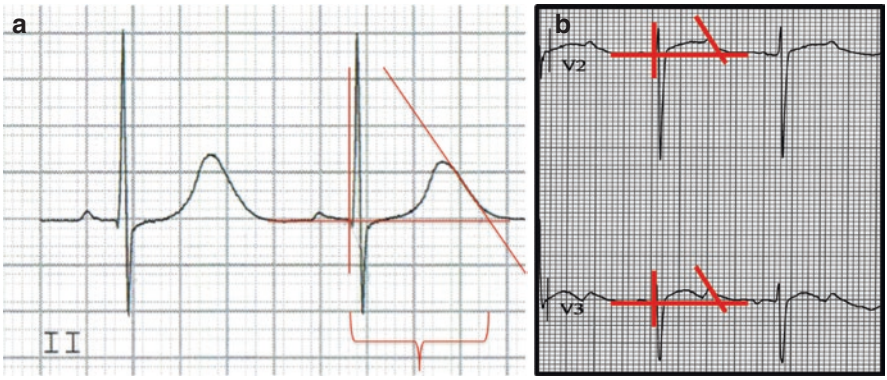

Fig. 1.1 (**a**) Tangent method: the end of the T wave is defined as the point where the tangent on the steepest point of the terminal limb of the T wave intersects with the isoelectric baseline, which is obtained by connecting the T wave of the preceding complex to the P wave. Note that the QT here is 580 ms. (**b**) Tangent method: note the notched T wave and the different slopes of the descending limb of the T wave. It is important to differentiate the notching noted here from a U wave. U waves are virtually never larger than T waves, so instances where notched T waves have a second component of the T wave that is greater in amplitude than the first (T') should include the second component of the T wave in the QT interval calculation. In this instance, it is possible that the tangent method underestimates the end of repolarization (i.e. QT duration); it is most commonly used and reproducible. The QT here is 460 ms

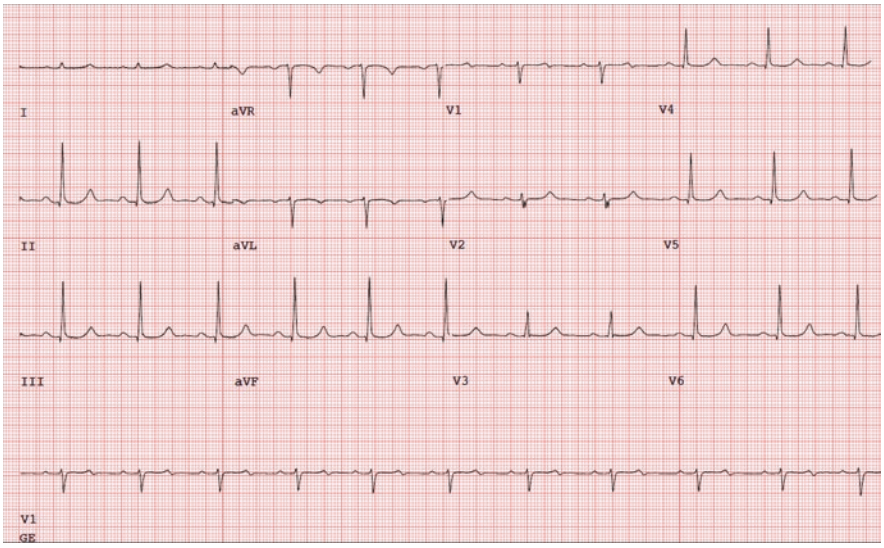

Fig. 1.2 The corrected QT interval (QTc) by Bazett's method is obtained by dividing the QT intervals in milliseconds (ms) by the square root of the preceding RR interval measured in seconds (sec) (QTms/$\sqrt{}$RRsec). The QT interval in this example is 440 ms by the tangent method. The RR interval is 0.84 sec. As such, the QTc is 471 ms. Note the long isoelectric line followed by a relatively normal morphology T wave, typical in this patient with LQT3

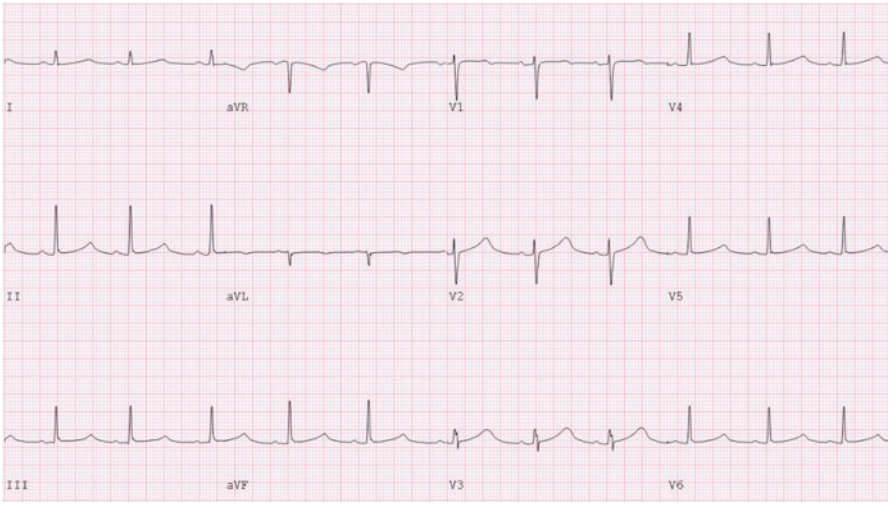

Fig. 1.3 The classic T-wave morphology in a patient with LQT1. The T wave is broad-based with normal voltages. Note the prolonged upslope of the T wave with a relatively normal terminal portion

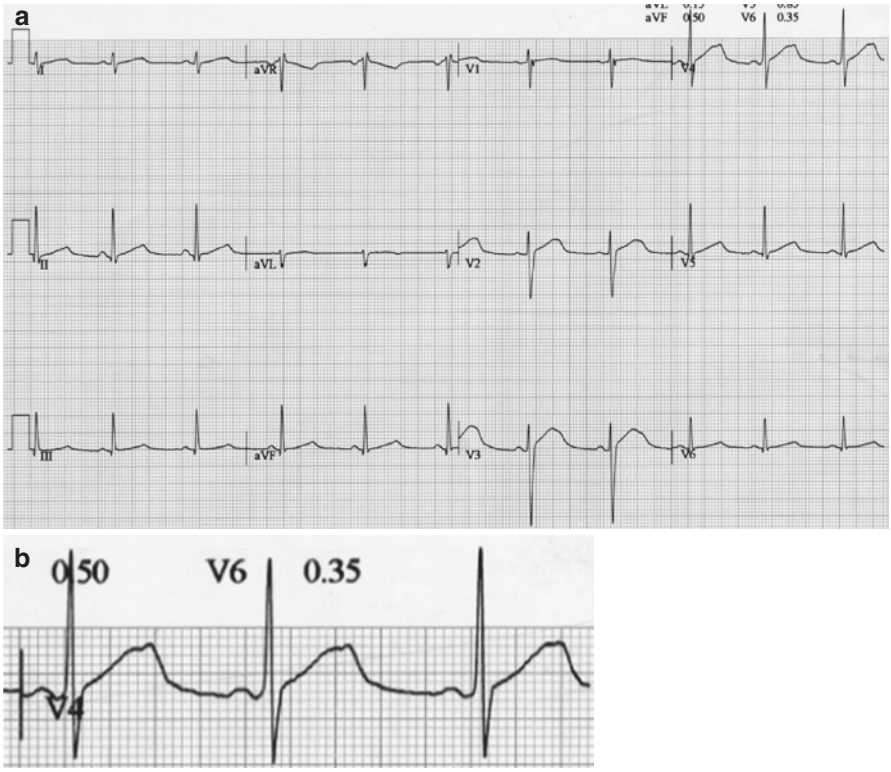

Fig. 1.4 (**a**) The classic T-wave morphology in LQT2 is notched (+/− low amplitude). Note the eccentric shape of the T wave, with notching which is most obvious in V4 (magnified in Fig. 1.5). T-wave amplitude is normal in this patient (T-wave amplitude >10% of QRS). (**b**) Magnified T-wave morphology in LQT2

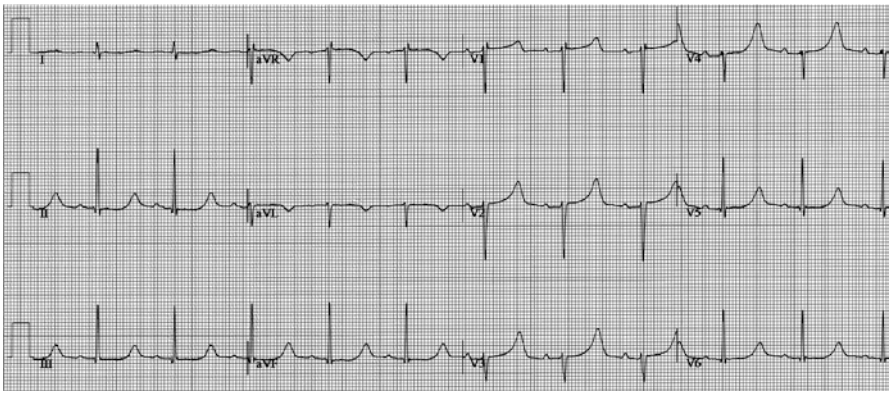

Fig. 1.5 The classic T-wave morphology in LQT3 is a long isoelectric ST segment, followed by a relatively normal T wave. The poor R-wave progression is an incidental finding that was not related to LQT3 in this patient. The patient had no other evidence of heart disease

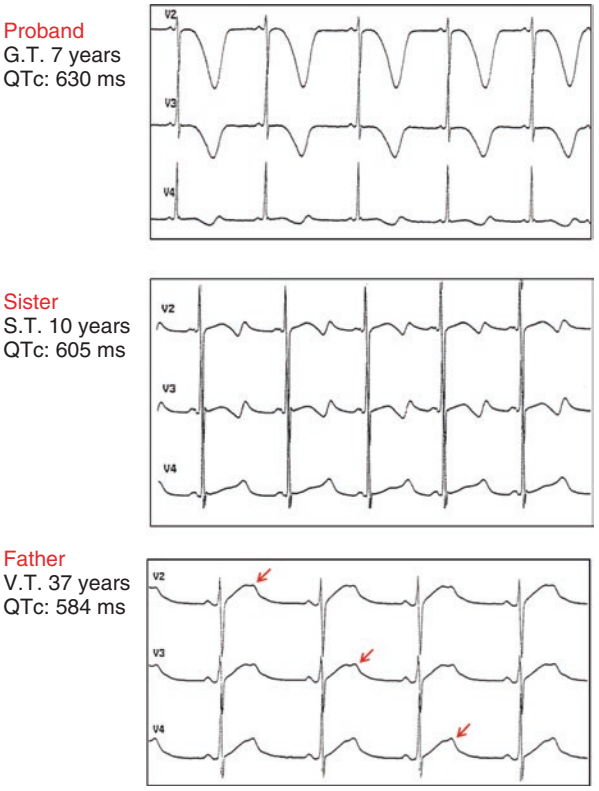

Fig. 1.6 Different T-wave morphologies in affected members of the same family. The proband, with cardiac arrest as first manifestation of LQTS, has deep negative T waves in the precordial leads and a very prolonged QTc. His asymptomatic sister has biphasic T waves. His father, with notched T waves and a QTc 584 ms, had two episodes of syncope. The arrows point to examples of notched T wave. (From: Schwartz et al. [38])

3. Andersen-Tawil syndrome (LQT7)
   (a) Prominent U wave (Fig. 1.7)
   (b) Polymorphic ventricular tachycardia (PMVT) at rest (Fig. 1.8)
   (c) Exercise treadmill test (ETT) (Figs. 1.9a, b)
4. Dynamic QT interval changes
   (a) LQT1 with ETT (Fig. 1.10a–c)
   (b) LQT2 with ETT (Fig. 1.11a–c)
   (c) LQT2 with standing test (Fig. 1.12a, b)
5. T wave alternans (Figs. 1.13, 1.14 and 1.15)
6. LQTS mimics
   (a) Hypocalcaemia (Fig. 1.16)
   (b) Structural heart disease (Fig. 1.17)
   (c) Ischaemia (Figs. 1.18 and 1.19)

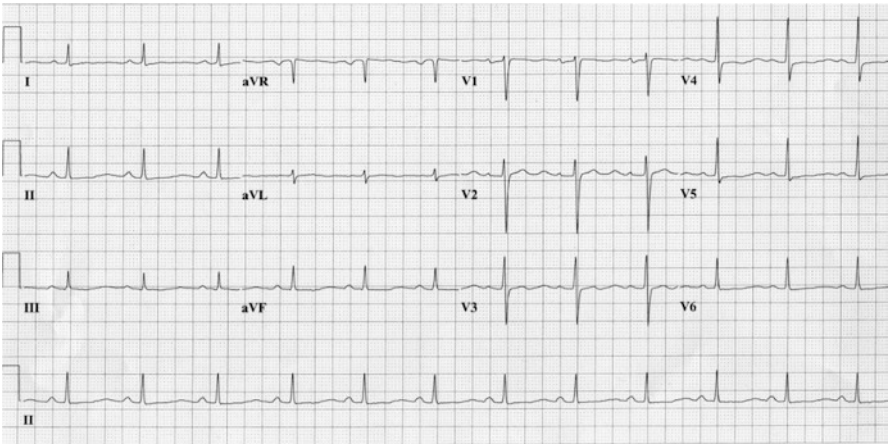

Fig. 1.7 This ECG was obtained from a patient with ATS. Note the prominent U wave in V2 and V3. It should be mentioned that the U wave should be excluded in the measurement of the QT interval, historically termed pseudo-QT prolongation in ATS. In this case, for example, the QT interval by the tangent method is 420 ms. Including the U wave would result in an extreme QT interval value ($QT = 600$ ms)

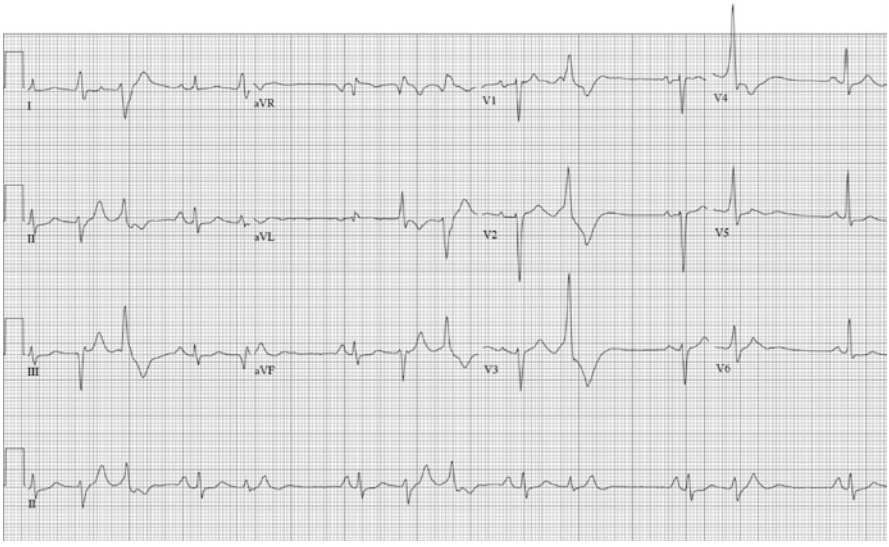

Fig. 1.8 This ECG shows frequent polymorphic (bidirectional) PVCs in a bigeminal pattern at rest in a patient with ATS

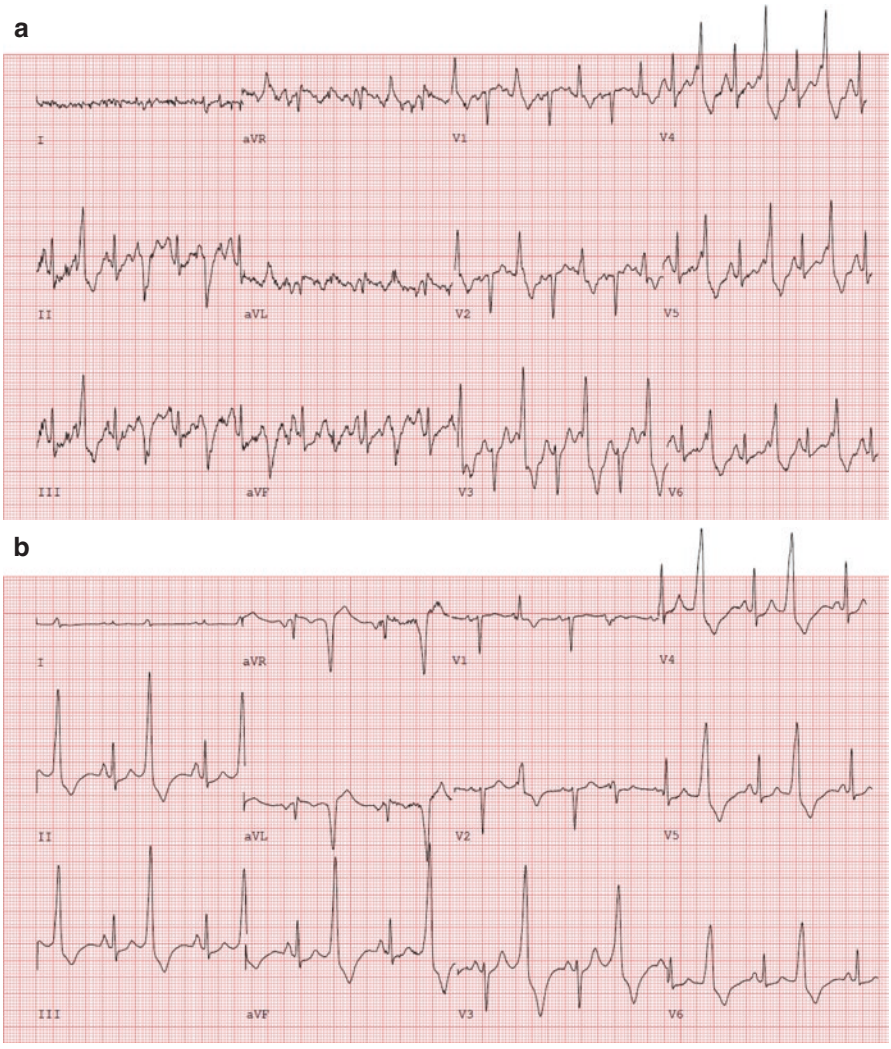

Fig. 1.9 (**a**) Exercise ECG in a patient with ATS taken at peak exercise. It shows frequent PVCs in a bigeminal pattern, with late-coupled PVCs with variable fusion with intrinsic conduction. Note two different morphologies in lead III. (**b**) This is the same patient at 11 min in recovery. The persistence of PVCs in recovery is an important feature to differentiate ATS from CPVT