Not just any ICD device in patients with long-QT syndrome

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Patients with LQT syndrome are prone to life-threatening arrhythmias. After surviving such an event, implantation of an ICD is indicated. There are, however, special subtle demands in the treatment of these patients. In this case report we describe our findings in a patient with LQT1 syndrome, and the pitfalls that can and must be avoided. (*Neth Heart J* 2007;15:418-21.)

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A 50-year-old female patient was brought in by paramedics after an out-of-hospital cardiac arrest. She had been successfully resuscitated by her husband and son. When the paramedics arrived the electrocardiogram showed ventricular fibrillation. After two defibrillation shocks and infusion of amiodarone, sinus rhythm was restored.

In the emergency room, the patient was hypotensive and had respiratory insufficiency. The electrocardiogram showed sinus rhythm with a prolonged QT interval of 600 ms and no signs of myocardial ischaemia (figure 1). Laboratory testing revealed hypokalaemia (potassium 3.0 mmol/l). The patient was on the diuretic indapamide for pre-existing hypertension.

Because of the respiratory insufficiency and cardiac failure caused by left ventricle systolic dysfunction, she was admitted to our intensive care unit. She was treated

with mechanical ventilation and diuretics for heart failure, electrolytes were substituted and the use of the provoking medication (indapamide) was discontinued. With this treatment she quickly recovered. Because of a slight elevation in troponin level, a diagnostic coronary angiography was performed, which showed no significant stenoses. Echocardiogram showed an overall diminished systolic cardiac function. The QT interval on the electrocardiogram remained prolonged and initially even increased. The diagnosis of primary ventricular fibrillation in a patient with long-QT syndrome was established. A profound and persisting bradycardia was present, so treatment with β -blocking agents was not initiated. Because of the preceding ventricular fibrillation she was subsequently referred to a specialised centre for implantation of an internal cardioverter defibrillator (ICD). Three weeks after the primary event an ICD was implanted with one single shock lead in the right ventricle only.

After this acute episode, further evaluation of the patient was carried out in our outpatient clinic. ECG showed a sinus bradycardia with prolonged QT interval. Exercise ECG testing was performed and showed an inadequate shortening of the QT interval with an increase in the heart rate. The echocardiogram was repeated and showed near normalisation of the systolic function and no other structural cardiac deformities. Subsequent molecular genetic testing revealed a mutation (c.1066c>t) in the KCNQ1 gene on chromosome 11p15.5, which leads to an amino-acid substitution (Gln356X). This confirmed the diagnosis of congenital LQT1 syndrome. In collaboration with a geneticist the patient's first-degree relatives were screened (presymptomatic investigation). There was no family history of sudden cardiac death. Genetic testing revealed the same mutation in the patient's son; other family members were not affected. Because the son had no history of collapse, there was no indication for ICD implantation and consequently he was (successfully) treated with β -blocking agents.¹

In April 2006, five months after the first event, this patient was readmitted in our clinic. She had had an

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Figure 1. Electrocardiogram after first admission, showing sinus rhythm 59 beats/min, intermediate axis, PQ 0.16 s, QRS 0.90 s, and prolonged QT interval (QTc 600 ms).

episode of recurrent (near) collapse with appropriate ICD shocks (figure 2). Once more, she was hypokalaemic (potassium 3.0 mmol/l), this time due to the use of a loop diuretic (furosemide 40 mg). In addition she was taking an ACE inhibitor because of mild left ventricular systolic dysfunction. After stabilisation, we referred the patient to the cardiology department of the University Hospital Amsterdam (AMC Amsterdam) for upgrading of her ICD to a dual chamber system with pacing capacities. However, this was not followed through because of alleged thrombosis of the brachiocephalic vein as a complication of the first procedure.

In May 2006 the patient was admitted again because of an episode of torsades de pointes (TdP). At that admission no electrolyte disturbances were found. The patient was again referred to AMC.

Amsterdam and a dual chamber ICD with pacing capacities was successfully implanted (figure 3). In addition, she was treated with a β -blocking agent.

Congenital long-QT syndrome type 1 (LQTS1)

Congenital long-QT syndrome (LQTS) is a family of clinically heterogeneous entities characterised by prolonged QT intervals on the ECG and often abnormally appearing STT segments. It predisposes patients to malignant polymorphic ventricular arrhythmias (torsades de pointes) which can lead to syncope, cardiac arrest or sudden cardiac death. The syndrome, without concomitant deafness, was first described by Romano and Ward in 1963.^{2,3} The molecular background of this disorder became apparent in 1995 due to exciting developments in molecular genetics. Since then ten

Figure 2. Electrocardiogram registration of the ICD showing ICD storm: polymorphic VT deteriorating to VF followed by ICD shock and recurrent VF after a relatively long RR interval.

Figure 3. Electrocardiogram after upgrading of the ICD device with an atrial pacing lead. Notice the prolonged QT interval (520 ms) with the typical ST-T morphology for LQTI.

different types have been described. Hence, the congenital LQTS appears to be a genetically heterogeneous primary electrical heart disease with a monogenetic origin. There is an autosomal dominant mode of inheritance with variable penetrance and expression.

The long-QT syndrome type 1 accounts for approximately 50% of all cases and its prevalence is estimated at one in 10,000 persons.⁴ It is caused by a mutation in the *KCNQ1* gene on chromosome 11 which leads to a loss of function of the slowly activating delayed rectifier potassium channel (I_{Ks} ion channel) of the cardiac myocyte. As a result there is a net reduction in repolarising current and an increase in action potential duration.⁵ The latter can be seen on the ECG as a prolongation of the QT interval, which, however is not present in all patients.⁶

The trigger for ventricular arrhythmias and life-threatening symptoms in the LQTS type 1 is related to stimulation of the adrenergic nervous system and includes intense physical and emotional stress. A very specific trigger in LQTI is swimming and diving.^{7,8} Exposure to QT-prolonging medication, including I_{Kr} blockers is, of course, another very dangerous trigger.⁶ The overall mortality in untreated, symptomatic LQT patients is high and approached 50% over ten years in early series.⁴ There is a 20% mortality in the first year after the initial syncope.

Treatment with a β -blocker significantly reduces morbidity and mortality in symptomatic and asymptomatic patients.⁶ Patients who experience syncope despite the use of β -blockers and patients with an aborted cardiac arrest are eligible for ICD implantation.¹

In special cases there can be an indication for left cardiac sympathetic denervation.⁶ All patients should refrain from any medication that possibly prolongs the QT interval and risk factors for drug-induced TdP (for example hypokalaemia or hypomagnesaemia) should be avoided and corrected.⁹

Considerations

In our patient the first episode of ventricular arrhythmia (i.e. ventricular fibrillation) on presentation in 2005 was evoked by the use of the diuretic indapamide. This drug functions as an I_{Ks} blocker. Especially the combination of an I_{Ks} blocker and hypokalaemia makes the patient prone for malignant ventricular tachyarrhythmias including torsades de pointes.⁹ Because of the aborted cardiac arrest our patient had an indication for ICD implantation.¹ This was implanted three weeks after the primary event.

The recorded electrocardiograms in the intensive care unit showed persistent QT prolongation on which the diagnosis congenital LQT syndrome was made. The treatment of choice for LQT syndrome is β -blocking agents at a maximum dose.^{4,6} The benefit in terms of risk reduction is dependant on the specific genotype, with most benefit for LQTI.¹⁰

Treatment with a β -blocker does not shorten the QT interval,⁴ but it does reduce events and mortality in symptomatic and nonsymptomatic patients,⁶ by reducing the number of cardiac arrhythmias.⁷ On average, cardiac events in a patient with LQTI can be reduced from 57 to 19% with five years of β -blocker therapy.¹¹

Because of the pre-existent and profound sinus bradycardia, our patient did not receive treatment with

β -blocking agents. Sinus node dysfunction is a trait often seen in patients with LQT1 syndrome. This is manifested by a lower (maximal) heart rate on exercise and with sinus bradycardia or sinus pauses.¹² Because the bradycardia is often not worsened by the β -blocker, in our patient withholding this treatment was in retrospect not necessary.

After the first recurrence of malignant tachyarrhythmia the patient was referred for upgrading of her ICD to a dual chamber system with pacing capacities in order to open the way for treatment with β -blockers. Unfortunately, this was not followed through because of alleged thrombosis of the brachiocephalic vein as a complication of the first procedure.

After her second presentation with ICD shocks, the single chamber ICD was finally upgraded to a dual chamber system. Because of the possibility for atrial pacing it was finally possible to start negative chronotropic β -blockage.

After an ICD shock the patient will be stressed and the cardiac rhythm might be irregular. Both factors may contribute to an increased propensity for a new arrhythmic event.¹³ This phenomena is known as an ICD storm and occurs in about 5% of patients.¹⁴ To interrupt this negative cycle the newly implanted ICD should ideally have an after-shock overdrive-pacing mode.¹⁵ After an ICD shock the pacemaker starts an overpacing programme keeping the heart rate up, and thereby shortening the QT time. Previously, overdrive-pacing was shown to be effective in 23 out of 26 patients with recurrent VF/VT and not treated with antiarrhythmic drugs.¹⁶ Devices with this feature are currently being tested.

Conclusion

All symptomatic and most of the asymptomatic patients with LQT1 syndrome should be treated with a β -blocker. Withholding this treatment in symptomatic patients because of pre-existing bradycardia is an error. Such patients could always receive an atrial pacing device (AAI or DDD/ICD) when sinus bradycardia becomes symptomatic. Secondly, just treating the risk of sudden cardiac death due to VF with a single shock lead ICD is probably a suboptimal treatment. Patients with LQT will most likely benefit from an after-shock overdrive pacing feature to help prevent recurrent TdP resulting from the adrenergic stimulation following an ICD shock. Devices with this feature are currently being tested.

Furthermore, because of these subtle but extremely important aspects in the optimal care of these rare patients, this case illustrates the importance of clustering care in a highly specialised centre. ■

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