

An extended family suddenly confronted with a life-threatening hereditary arrhythmia

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Objective. This exploratory study serves to illustrate the psychological impact on an extended family in the process of genetic counselling and testing for a potentially life-threatening arrhythmia, the long-QT syndrome (LQTS).

Method. All members of the third generation and their partners (n=11) were interviewed, the mutation carriers with partners twice. In addition they completed measures for anxiety and depression three times in 18 months.

Results. During the interviews these family members emphasised the damaged solidarity when the family is divided into carriers and noncarriers of a mutation in a LQTS predisposing gene. This demonstrates one way in which a family can react to the reality of being at risk of a potentially severe disease. Rewriting family history and mourning early death seem other ways to deal with this. The distress scores, especially of the women, were moderate to clinically high, not because of their own chance of having an arrhythmia but more due to their children's risk.

Conclusion. Mothers need educational even more than emotional support, because the lifestyle of

their carrier children is in need of radical change. The setting of a combined outpatient cardiogenetic clinic with a medical and psychosocial staff meets such needs efficiently. (*Neth Heart J* 2005;13: 295-9.)

Key words: long-QT syndrome, genetic testing, genetic counselling, psychological impact

The long-QT syndrome (LQTS), or Romano-Ward syndrome, is an heritable cardiac disorder characterised by prolongation of the QT interval on the electrocardiogram (ECG). The mode of inheritance is autosomal dominant, its expression is variable and its penetrance is decreased (with about 50% of carriers never getting symptoms). Carriers of a mutation in one of the six known LQTS genes are at risk of ventricular arrhythmias causing dizziness, fainting and sudden death, often (long) before the age of 40.¹⁻⁶ These arrhythmias can be triggered by certain gene-specific circumstances, especially physical exertion and emotions.⁷ In LQTS type 2, caused by mutations in the chromosome 7-linked *KCNH2* (former *HERG*) gene, arousal and loud noises may also trigger symptoms.⁸ Known mutation carriers of LQTS types 1 and 2 (85% of the LQTS population) receive prophylactic treatment with β -blockers, which decreases the risk of sudden death substantially in the majority, provided that they are taken as prescribed.^{9,10} In severe cases, the use of pacemakers or ICDs is recommended.¹¹ Prophylaxis in asymptomatic mutation carriers is started from the age at which symptoms can be expected to develop (dependent on the gene involved), usually before the age of ten years.

In the Netherlands, diagnostic DNA testing for LQTS has been possible for a decade now. If a mutation is detected in an index patient, the first-degree relatives are actively approached by means of family letters, provided by a cardiogenetics team. These letters inform relatives about the hereditary nature of the disease in their family and the possibility of clinical investigation as well as DNA testing. Such a team consists of a

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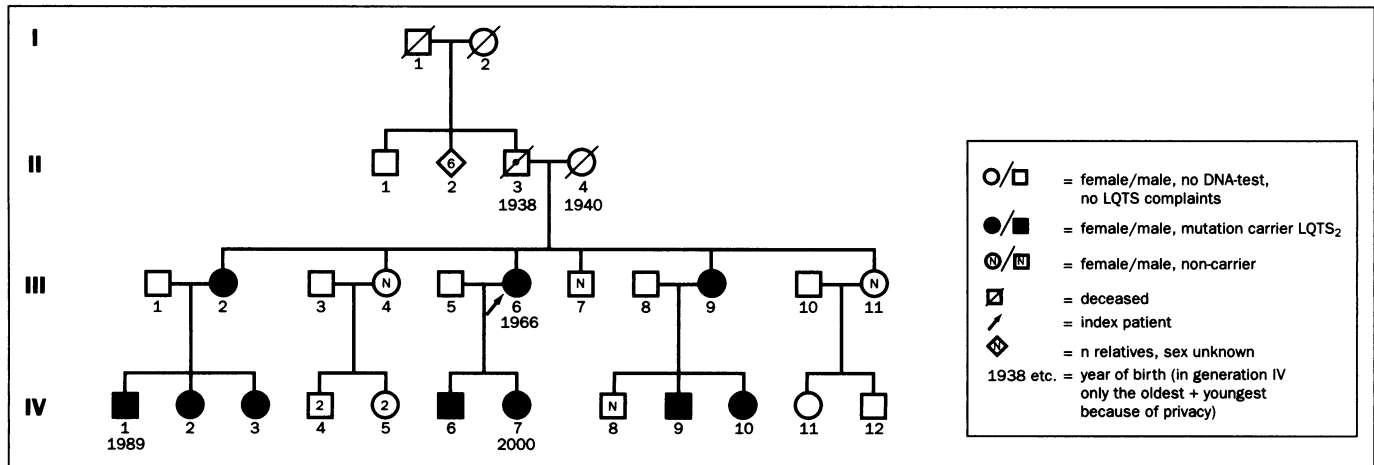


Figure 1. Four generations of a LQTS family.

cardiologist, a clinical geneticist, a genetic counsellor and a psychosocial worker. It provides genetic counselling and testing in a cardiogenetic outpatient clinic situated in an university hospital.¹² Approximately 50% of a carrier's relatives will also carry the mutation, which makes their treatment and consequent predictive DNA testing in first-degree relatives possible.

It is important to gain insight into the effects of detecting mutation in an index patient on the family. So we decided to follow one of the first Dutch families (figure 1) for whom DNA testing became available, in the form of an exploratory study. This family study is part of a series of systematic empirical studies determining what the psychological consequences are of genetic counselling and testing for LQTS.^{13,14}

The family

The family lives in a new polder in the Netherlands; the parents were pioneer farmers on the newly reclaimed land. Five girls and one boy were born; all the girls married and now have children themselves (figure 1). Together with their husbands they form a close-knit extended family, of which the ties became even stronger after the sudden death of both parents. The mother (II:4) died in 1990 at the age 49 years due to a traffic accident. The setting sun was said to have dazzled her and made her drive into the side of a truck. Seven years later the father (II:3) died of pneumonia at the age of 58 years while he also suffered from a rapidly progressive dementia.

Methods

The three carriers of the third generation and their partners were interviewed twice in three years. Those with a normal ECG and without the gene mutation were interviewed once, as were their partners. Further information came from the regular visits of this family to the cardiogenetics outpatient clinic in Amsterdam and from the social worker frequently in touch with the third generation. At three different points in time they

completed standard measurement instruments on anxiety and depression (Impact of Event Scale, Spielberger State Anxiety Inventory and Beck Depression Inventory).

Results

It was in 1997 that the family became aware of LQTS. Two weeks after her maternity leave due to the birth of a son (IV:6) and a few months after her father's death, the middle sister (III:6) collapsed on the parking lot at work. Luckily she was immediately resuscitated and she was transported to hospital in coma. There a cardiologist found that she had suffered from ventricular fibrillation in the setting of a prolonged QT interval. In the absence of potential causal external factors he diagnosed congenital LQTS and discussed the possible hereditary nature and its consequences with her husband. Both agreed that some of her blood should be taken for genetic testing. This made her the index patient of her family.

As a farmer the patient's husband was familiar with the Mendelian laws of inheritance. By asking questions, reading articles, and surfing on the internet he rapidly learned a lot more about the disease. With this information he went to his wife's sisters and brother and informed them about what was going on in their family and what would be wise to do. As a result the sisters and brother soon presented themselves to the cardiogenetic outpatient clinic in Amsterdam. Initially abnormal ECGs, suggestive of LQTS, were found in two sisters (III:2 and III:9), both free of other physical symptoms and complaints. Alarmed, both immediately took their children to this clinic where signs of LQTS were also found in the first two children (IV:1 and IV:2; then aged 9 and 7 years) of the oldest sister (III:2). At that moment (1997-8) ECGs of the other children of the third generation did not display abnormalities. The cardiological examinations neither revealed abnormalities in the other two sisters (III:4 and III:11) nor in their brother (III:7). All consented

to have a blood sample stored until a mutation was detected in the index patient.

The index patient regained consciousness ten days after the arrhythmia. She was treated with a β -blocker and an ICD was implanted. She was moved from the hospital to a rehabilitation centre because of serious impairments in speech and movement due to cerebral damage. She stayed there for months. Initially she also had amnesia; e.g. she could not remember the birth of her son and her father's death some weeks earlier. It was only little by little that these functions partially recovered. Three years after the event she dared to become pregnant again and subsequently gave birth to a daughter (IV:7). Until now the index patient has been free of symptoms.

Solidarity

Those who received normal ECG results did not feel relieved. Sister III:4 was afraid that the forthcoming DNA test results would divide the family in two separate groups: carriers and noncarriers. It seemed as if she regretted not showing LQTS features. More or less angry she said: 'The fact that the cardiogram demonstrates that I most likely don't have that gene makes me unhappier than my two sisters for whom it seems quite sure that they are carriers. I'm not so pleased with that ECG, because now I cannot have the same feelings as they have ... At home we were five girls and one boy; we have always had an intense relationship with each other, and ... I don't want anything to change that!'

At that moment she preferred to be identified as a carrier as well because of the solidarity she felt with her three probable carrier sisters. Her husband could not understand this. His reaction ('Fine! Most likely you don't have it. Then our children are also free from it!') caused her irritation. We found her brother (III:7) and the other unaffected sister (III:11) had the same feelings and thoughts, although less pronounced.

Rewriting the family history

None of the sisters with a prolonged QTc nor their children had ever had physical symptoms or complaints suggesting cardiac arrhythmias. The mother (II:4) on the other hand did have symptoms: she had fainted frequently all her life. Nobody took this seriously; fainting seemed to be part of her personality, as if psychologically induced. It was thought that having six children within eight years and the harsh life of settlers in a new polder must have been an important cause of this 'behaviour'. Initially the fatal car incident nearly ten years earlier was also explained by such a faint, since some months before she had also driven from a bridge, without any injury.

After the family had learned about the hereditary nature of this arrhythmia the mother was regarded as the person who 'brought in' the disease. This resulted in 'rewriting' the collective family history based on this new idea. Confusion arose when finally the ECGs

from father as well as mother were collected from the medical files in the archives of the regional hospital. Mother's ECG appeared to be completely normal, while father's showed an obvious prolonged QT interval. This was not completely convincing, however, because father was on QT-prolonging medication (antipsychotics) at that time.

Distress: anxiety and worries

In the first interviews, just after the ECG, nearly all stated that the awareness of having a familial predisposition for an arrhythmia would not cause them emotional burden. The scores on the measurement instruments, however, contradicted these statements, for two sisters (III:4 and III:9) scored moderately and two (III:2 and III:11) had a clinically high score on the distress questionnaires, implicating the need for psychological help. The husband of the eldest sister (III:1) was the only male with a somewhat higher score at that time, which is understandable due to the alarming ECG results of two of his children. The distress scores for both other measurements (just after DNA-test disclosure and 18 months later, respectively) were somewhat lower, but remained above the cut-off score between normal and high anxiety. The later scores of the eldest sister still showed an objective need for psychological help which she obviously had not asked for. She had only taken some sedatives for a short time.

In the interviews we noticed that the sisters' high anxiety scores were not so much due to their own health risks, but were mainly caused by the worries concerning the dangerous situation in which some of their children were in. The worries of III:2 were mainly connected with her eldest child (IV:1) who had developed into an active youngster and a talented footballer scouted for a regional youth team. Stopping him was expected to damage his self-esteem to such an extent that his parents had decided to let him play, seemingly a sensible decision generating a lot of anxiety as well. This difficult decision brought his mother to admitting that she needed professional help: 'Not so much for myself but for the problems I have with the upbringing of my children who are healthy but seriously in danger of a deadly disease'.

A social worker provided it. The mother was advised to slowly direct her children's attention to less competitive physical activities and to stimulate them in other pursuits in which they also took pleasure. The eldest daughter (IV:2) for instance enjoyed drawing and seemed talented, but despite all encouragement she and her elder brother preferred competitive sports instead of pursuing a quieter hobby. The help of the social worker facilitated emotional acceptance on the part of the parents regarding their children's own responsibilities, and eventually led to less anxiety, worry and depression on the part of their mother.

Bad news

More than two years after her serious arrhythmia a pathogenic mutation was found in the index patient,

in the so-called 'human ether a-go-go related gene' (HERG- or KCNH2-gene), responsible for LQTS type 2. After a family information meeting, the third generation decided that they wanted to be informed about their and their children's genetic status. They were not only interested in knowing who the carriers and noncarriers were, but they also wanted to be informed about each individual's risk of actually developing symptoms of the disease. The DNA testing results, more than two years after the cardiological investigations, not only confirmed the ECG results of the sisters and their children but also revealed five other carrier children. In the end all the children of the three carrier sisters except one (IV:8) turned out to be carriers.

And there was something else which they were concerned about. Based on his abnormal ECG, the clinical geneticist and the cardiologist advised the family to inform the father's relatives about the hereditary characteristics of LQTS; information leaflets were supplied to do so. At first no one wanted to be a messenger of bad news, because all were anxious about the reactions this news could provoke. The relationships within father's extended family had disintegrated in such a way that this was thought to be very possible. However, the expected anger did not follow. The distant family members were rather glad by the renewed contact as opposed to upset by the bad news.

All father's seven brothers and sisters immediately came to the cardiogenetics outpatient clinic. At first no one seemed to have a prolonged QT interval. DNA testing, however, revealed that one of these brothers (II:1) was also a carrier. From a prophylactic point of view it was very convenient that he was already being treated with a β -blocker for hypertension. In that period his eldest son, a airline captain, developed an arrhythmia during take-off and died a week before he would have come to the cardiogenetic outpatient clinic. His family decided not to have postmortal DNA testing done. The relationships between both family branches have lastingly been improved despite all the bad news. The detection of the mutation in the brother confirmed the diagnosis in the father of our index patient. Again the collective family history had to be rewritten.

Renewed mourning

III:9 was pregnant of her third child (IV:10) when her positive carrier status was disclosed. She and her brother were less worried during interview and in the questionnaires both after the ECG and the DNA test outcome than the others; she seemed neither anxious about her own risks nor was she worried about her children. She had only stopped running and playing competition volleyball because of her pregnancy. She did not know if she would practice this sports again after delivery and argued: 'I might not have time for it: three kids and this farm we recently moved into.' Seemingly she did not want to relate her behavioural

change to the reality that she had features of a serious disease; this was not a matter of denying reality, but rather an impressive decision not to let predictive medical and genetic findings of a probable nature influence her life.

It was striking that, in the same way as after receiving the normal ECG results, the noncarriers did not feel relieved with their DNA test results. Anxiety and other unpleasant feelings hardly decreased. All had the same explanation: it was not so much the hereditary disease and the future but the past that caused their worries. For a while they had considered the death of their mother from another perspective: not the dazzling by the evening sun but an arrhythmia would have caused the accident. And now with father as the probable mutation carrier they had to turn back this explanation again from arrhythmia to dazzling. Furthermore so much had been happening: their beloved father had died, followed by the painful job of emptying and selling the parental home, the index patient nearly died and had to stay in a rehabilitation centre for months, having to care for her baby she did not remember giving birth to, the mixture of joy and great worries when the index patient became pregnant again, and the move of the index patient and sister III:9 to a new farm. At the time of the DNA test disclosure all were still mourning their father's death – for which there had been no time earlier – and again that of their mother.

Discussion

Through this family's reactions – e.g. the postponed and renewed mourning for the loss of both parents and the need to 'rewrite' family history twice – we noticed differences compared with findings in studies among applicants for Huntington's disease (HD),¹⁵ multiple endocrine neoplasia (MEN)¹⁶ and hereditary breast and ovary cancer (HBOC).¹⁷ People who apply for DNA testing for these disorders have usually known for years about the hereditary disease in their family, and have also been aware of the extent of the impact. The members of this LQTS family, on the other hand, were completely surprised that a hereditary arrhythmia runs in their family.

What seems particular for this family can be found in most LQTS families.¹⁴ The solidarity and the fear of a family that they will be split up into carriers and noncarriers caused ambivalent feelings in noncarriers: on the one hand the great relief that the gene mutation was not found and that they and especially their children are no longer at risk, and on the other hand the silent wish that the DNA test nevertheless would reveal that they too are carriers of the familiar LQTS mutation. This phenomenon corresponds with what Kessler et al. labelled as survivor's guilt.^{18,19}

Nearly all LQTS families have grim experiences of family members who died totally unexpectedly: a baby with sudden infant death syndrome, a child who could swim but still drowned, a trained sportsman who died

during a race. They know of relatives who suffer from dizziness, syncopes or bed-wetting. Some have been diagnosed with epilepsy and treated with antiepileptics. When such a family learns the real cause of these miseries, a process of rewriting the collective family history takes place, which often results in renewed mourning for deceased family members.

Worry, anxiety and concern were most serious and even clinical in the carriers of this family, not so much due to their carrier status but because of the risk for their children. Due to their children's risk, parents are faced with educational dilemmas. Parents feel responsible for their children's lifestyle and especially have to urge the child to regularly take its prescribed prophylactic medication as even missing one dosage can provoke an arrhythmia.

This finding has been confirmed in another study of our group in which it was found that the carrier status of the parent seemed to have less influence on the level of distress than the carrier status of the children.¹⁴ We found that parents were more focussed on the well-being of their children than on that of their own. This finding has also been reflected in studies addressing the motivation for genetic testing for a variety of hereditary diseases. In these studies the well-being of their children was one of the main reasons for parents to apply for genetic testing.^{16,20-23}

Conclusion

The story of this family, combined with the results of the psychological measurements in LQTS families,¹⁴ underline the needs of these families as being medical as well as psychological and – because of their children – educational. Especially mothers need educational support for their children even more than psychological support for themselves; in particular they need help to change their children's lifestyle. These needs can best be answered in the setting of a combined outpatient cardiogenetic clinic, in which medical and psychosocial workers closely collaborate in testing as well as follow-up. ■

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