DOI: 10.5350/SEMB.20160710113812

A Rare Cause of Neonatal Death: Long QT Syndrome

Duygu Besnili Acar[1], Sinan Uslu[1], Taliha Oner[2], Umut Zubarioglu[1], Ali Bulbul[1], Evrim Kiray Bas[1], Ebru Turkoglu Unal[1]

ABSTRACT:

A rare cause of neonatal death: Long QT syndrome

Objective: Long QT syndrome is a rare syndrome with a high mortality rate in neonatal period. We report a newborn who was admitted to the outpatient clinic with complaints of cyanosis and breastfeeding difficulties, diagnosed as ventricular tachycardia due to long QT syndrome with no response to the treatment, and evaluate the diagnostic and therapeutic approaches in the context of current literature.

Case: A newborn delivered at 41th week of pregnancy by cesarean delivery with a birth weight of 3460 grams was admitted to the emeregency outpatient clinic at postnatal seventh day with complaints of breastfeeding difficulty and cyanosis. Newborn was in a poor general condition with impaired peripherical circulation, with respiratory rate 80/min, heart rate 280/min, and oxygen saturation 60%. The newborn was intubated and admitted to the neonatal intensive care unit (NICU). Electrical cardioversion at 1 joule/kg was performed due to ventricular tachycardia (VT) detected at electrocardiography (ECG). After restoration of sinus rhythm, corrected QT (QTc) interval was measured as 0.53 sec. Echocardiography was performed and no structural cardiac anomaly was detected but severe mitral and tricuspid valve regurgitations were present and the ejection fraction (EF) was 30%. Because of recurrence of ventricular tachycardia (VT), synchronized cardioversion at 1 joule/kg and 2 joule/kg were performed, followed by lidocaine therapy when no response was obtained. Due to the resistant VT, amiodarone, flecainide and esmolol were administered subsequently. Patient failed to respond to any antiarrhythmic treatment and was lost on day 3 of follow-up, after emerging ventricular fibrillation.

Conclusion: Long QT syndrome is a rare disease with high mortality in the newborn. Early diagnosis may help in terms of treatment but the main prognostic factors are the length of QT interval and the associated structural anomalies. Screening of newborns with risk factors by electrocardiography is controversial, but it may be considered in cases with determined risk factors. Also interventional procedures may be considered in severe cases resistant to medical treatments.

Keywords: Long QT, mortality, newborn

ÖZET:

Yenidoğan mortalitesinin nadir bir nedeni: Uzun QT sendromu

Amaç: Uzun QT sendromu yenidoğan döneminde nadir görülen mortalitesi yüksek bir sendromdur. Olgumuz yenidoğan polikliniğine morarma ve emmede azalma şikayeti ile getirilen, uzun QT'ye bağlı venriküler taşikardisi gelişen ve tedaviye yanıt alınamayan hastada gerçekleştirilen tanısal ve tedavisel yaklaşımların güncel literatür eşliğinde tartışılması amacıyla sunuldu.

Olgu: 41 gestasyonel haftasında sezaryen ile 3460 gr doğan bebek, postnatal 7. gününde emmede azalma ve morarma nedeniyle acil polikliniğimize getirildi. Genel durumu kötü, periferik dolaşımı bozuk, solunum sayısı 80/dk, kalp tepe atımı ise 280/dk, oksijen saturasyonu %60 olan hasta entübe edilerek yenidoğan yoğun bakım ünitemize alındı. Elektrokardiyogramında ventriküler taşikardisi saptanan (VT) hastaya 1j/kg kardiyoversiyon uygulandı. Sinüs ritmine döndükten sonra çekilen EKG'sinde düzeltilmiş QT süresi 53 sn saptandı. Ekokardiyografisinde; yapısal anomali izlenmemekle beraber ejeksiyon fraksiyonu %30, önemli mitral ve triküspit yetmezliği saptandı. VT'si devam eden hastaya 1 joule/kg ve 2 joule/kg'dan senkronize kardiyoversiyon yapıldı ve cevap alınamayınca lidokain tedavisi başalndı. Ventriküler taşikardisi dirençli seyreden hastaya amiadoron, flekainid ve esmolol tedavileri sırasıyla uygulandı. Antiaritmik tedavilere yanıt vermeyen hasta takibinin 3. gününde ventriküler fibrilasyona girerek kaybedildi.

Sonuç: Uzun QT sendromu yenidoğanda nadir görülen mortalitesi yüksek hastalıktır. Erken tanı tedavi açısından yardımcı olabilmekle beraber QT süresinin uzunluğu ve eşlik eden yapısal anomaliler prognozu belirlemektedir. Risk faktörü olan yenidoğanların EKG ile taranması tartışmalıdır. Hastalığın risk faktörleri belirlenmiş vakalarda erken tanımlanması için EKG çekilerek taranması ve medikal tedaviye dirençli ağır olgularda girişimsel metodolojinin uygulanması düşünülebilir.

Anahtar kelimeler: Uzun QT, mortalite, yenidoğan

Ş.E.E.A.H. Tıp Bülteni 2017;51(4):329-33

[1]Sisli Hamidiye Etfal Training and Research Hospital, Department of Neonatology, Istanbul - Turkey
[2]Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital, Department of Children's Cardiology, Istanbul - Turkey

Address reprint requests to / Yazışma Adresi:
Duygu Besnili Acar,
Sisli Hamidiye Etfal Training and Research Hospital, Department of Neonatology, Istanbul - Turkey

E-posta / E-mail:
dbesnili@hotmail.com

Date of receipt / Geliş tarihi:
April 12, 2016 / 12 Nisan 2016

Date of acceptance / Kabul tarihi:
July 10, 2016 / 10 Temmuz 2016

INTRODUCTION

Long QT syndrome is a rare disease that does not accompany structural cardiac anomalies, characterized by myocardial repolarization disorder, with increased the risk of sudden infant death. The frequency of congenital long QT syndrome is estimated to be 1/2500-7000 (1). This syndrome, which may be congenital and acquired, is named in two distinct phenotypes according to accompanying findings and its inheritance pattern. Acquired type is usually caused by drugs and electrolyte disorders, while congenital type is caused by mutations in various genes that encode ion channels in the heart cell membrane (2-6). The congenital long QT syndromes are the pathologies consisting the autosomal recessive Jervell and Lange-Nielsen syndrome with accompanying sensorineural deafness the most, and the autosomal dominant Romano-Ward syndrome with no deafness accompanying, and the number is increasing with other newly identified syndromes (7,8). Patients with long QT syndrome diagnosis in the neonatal and prenatal period have been reported in the literature (9). This case was presented with an aim to discuss the diagnostic and therapeutic approaches in the context of the literature, in a patient with long QT-associated ventricular tachycardia with no response to treatment.

CASE PRESENTATION

A female baby, who was born with cesarean section due to prolonged labor at 41th week of gestation, with measurements of 3460 gr (50-75 p) birth weight, 50 cm height and 35 cm head circumference, in a second level private hospital with no complications and discharged as a healthy mother-infant couple on postnatal day 2, was brought to our emergency outpatient clinic on the postnatal 7th day with complaints of breastfeeding difficulty and cyanosis for the last 2 days. In the family history; the infant had 23 and 25 year old parents, who was found to have a second degree of consanguinity between the mother and father, and the 3rd children of this couple. Before, he had a brother who was born full-term, and developed breastfeeding difficulty and cyanosis on the 3rd postnatal day, and lost for unspecified reason. In the physical examination of the patient who did not have any pathologic features in the antenatal follow-up period, the patient revealed poor general condition, cyanosis, impaired peripheral circulation, weak femoral pulses, peak heart rate: 280/min, tachypnea (respiratory rate: 80/min) and liver in midclavicular line and 4 cm in size, palpable. The patient with a partial oxygen saturation level of 60% was admitted to the assisted respiratory support unit with the findings of respiratory failure. Chest X-ray, hemogram and biochemical examination revealed no pathology. Cardioversion was applied at 1j/kg upon detection of ventricular tachycardia on the electrocardiogram (ECG) of the patient (Figure-1). The QTc interval on the next ECG after conversion to sinus rhythm was calculated as 53 seconds. In the patient with no structural cardiac anomaly on ECG, the ejection

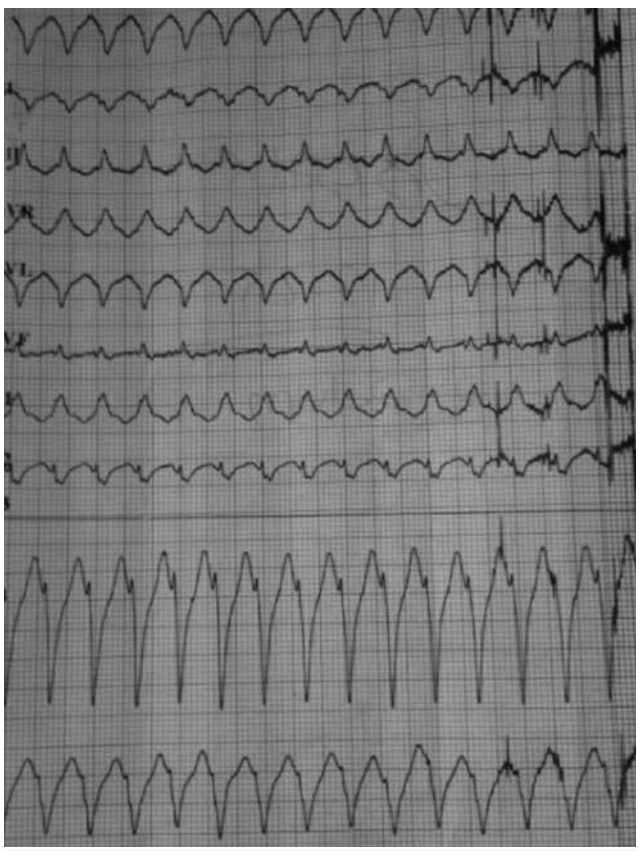

Figure-1: Ventricular tachycardia

fraction (EF) was 30%, and there was significant mitral and tricuspid insufficiency. The patient had low blood pressure and 10 mcg/kg/min dopamine and 10 mcg/kg/min dobutamine infusions were started. Synchronized cardioversion was performed with 1 joule/kg and 2 joule/kg to the patient who had ongoing ventricular tachycardia at follow-up. When no response was obtained, iv infusion of lidocaine 1 mg/kg bolus was given and continued with 50 mcg/kg/dk infusion. In the patient with resistant ventricular tachycardia, amiodarone treatment was terminated due to the development of torsades de pointes following iv bonus of 5 mg/kg amiadorone. Milrinone 0.5 mcg/kg/min was added to the treatment of the patient with ongoing hypotension and low ejection fraction. At the 30th hour of follow-up, furosemide infusion was initiated in the patient with impaired renal function and anuric renal failure. Cardioversion was performed again in the patient with undergoing ventricular tachyarrhythmia, but ventricular tachycardia continued. The lidocaine therapy was discontinued due to unresponsiveness, and flecainide 100 mg/m^2/day in 3 doses and esmolol 500 mcg/kg IV bolus, followed by 100 mcg/kg/min IV infusion was initiated. The patient who still had ventricular tachycardia underwent cardioversion again for 2 times. The dose of esmolol of the patient was reduced, who subsequently conversed to the sinus rhythm and had bradycardia (72 beats/min). However, ventricular tachycardia recurred after a short period of time. The patient was evaluated for long QT syndromes; QT durations and echocardiography evaluations of the mother, the father and the living siblings were found at normal limits. It was found that the patient could not pass the hearing screening (otoacoustic emission test) on the postnatal day 1 in the hospital where she was born. Hematological and biochemical examinations of the patient who had no history of drug use were normal and no pathological data was detected in the cranial and abdominal ultrasonography. Patient whose ventricular tachycardia persisted and was treated with various antiarrhythmic therapies but was unresponsive, was lost due to ventricular fibrillation on day 3 of follow-up.

DISCUSSION

The criteria published by Schwartz et al. (9) in 1993 for long QT syndrome have been indicative. The major criteria were; QTc value to be >0.44 sec, typical symptoms and positive family history, and the minor criteria were; bradycardia, hearing loss, typical T-wave morphology, and T-wave alternans. The diagnosis can be made with two major criteria or one major and two minor criteria. In addition, patients with the QTc time measured over 50 sec and no secondary reason found to cause this situation can be diagnosed. Long QT syndrome was diagnosed because the duration of QTc was 53 sec and there was no reason for a secondary cause found. Garson et al. (10) diagnosed 17 (6%) of their 287 patients with long QT syndrome, although QTc was <0.44 sec, but with positive family history and the presence of long QTc during exercise.

Villain et al. (5) followed 15 newborns with persistent QT prolongation in their study and suggested that this could be transient in the newborns or could be an early form of long QT syndrome. In the same study, they reported that serious arrhythmias were seen and 50% of neonates were lost whose QT was >0.50 sec. Wu et al. (11) reported ventricular tachycardia and atrioventricular block in two newborns with ventricular septal defect and positive family history of long QT syndrome, and reported that these patients were lost due to ventricular tachycardia unresponsive to treatment. The presence of 53 sec of QTc in our case suggested that the prognosis was poor and she was lost due to ventricular tachycardia with no response to treatment.

Congenital long QT syndrome is characterized by ventricular arrhythmias, due to mutations in the sodium and potassium ion channels of the anatomically normal heart. The most common hereditary form is the autosomal dominant Romano-Ward syndrome (8). Jervell and Lange-Nielsen syndrome is seen less, and is associated with and deafness (7). Mutations in the LQT1, LQT2 and LQT3 genes were observed in a large majority of patients, although more than a dozen of genotypes have been detected (12,13). When our patient was

evaluated for congenital long QT syndrome, it is thought that it may be Jervell and Lange-Nielsen syndrome, which is associated with AR inheritance and accompanied by hearing loss, with it's characteristics such that the patient couldn't pass the hearing screening test on postnatal day 1, she had parents with normal QT intervals on their ECGs, however, a sibling of the patient to be lost as the neonatal period due to similar symptoms with unspecified cause. Jervell and Lange-Nielsen syndrome diagnosis could not be confirmed because genetic analysis could not be obtained from the patient and her family, because of loss of the patient in short-term despite all treatment approaches.

It was determined that cisapride, used as a prokinetic agent sometime in the treatment of gastroesophageal reflux of neonatal period caused long QT syndrome and that QTc returned to normal after drug discontinuation. For this reason, the use of cisapride in newborns has been officially banned by the FDA (Federal Drug Administration) in the United States since June 2000. No history of drug use or organic cardiac lesions were found in our patient that could lead to long QT syndrome.

In congenital long QT syndrome, the vast majority of arrhythmias are ventricular tachyarrhythmias, and bradycardia, atrioventricular block, and atrial arrhythmias can also be seen in a small proportion. Of the 287 patients who were followed up by the pediatric electrophysiology society for long QT syndrome, 61% were symptomatic at the time of admission, 16% of these patients had ventricular arrhythmia, 9% ventricular premature contraction, 1% monomorphic ventricular tachycardia, 20% bradycardia, and 5% had atrioventricular block (14). Ventricular tachycardia was present when our patient applied to the clinic and during the follow up.

The disease usually manifests itself with episodes of syncope or sudden death in childhood. Many patients have been reported to be misdiagnosed as epilepsy and have been using antiepileptic treatment for many years. Schwartz et al. (14) showed in their study that there was QT prolongation in half of the patients who were lost due to sudden infant death syndrome and suggested that sudden infant death syndrome might be a variant of long QT syndrome. The fact that the sibling of our patient has been lost on the third postnatal day due to an unspecified reason makes us think that he also had a possible long QT syndrome.

The objective of the treatment is the prevention of ventricular tachycardia and sudden death. Cardioversion, lidocaine infusion, and magnesium are recommended when ventricular tachycardia is detected. Mainly beta blockers, left stellate ganglion block in the newborn and implantable cardioverter-defibrillators are being used in gradually to prevent attacks in the long term. Gene-specific therapies have been studied in the recent years as the genetic structure of the disease has been emerging. No response to any antiarrhythmic therapies in our patient could be obtained.

Long QT syndrome is a rare disease with a high mortality rate in the neonatal period. Early diagnosis may help in terms of treatment, and the length of the QT interval and the associated structural anomalies specify the prognosis. Electrocardiogram screening of newborns with present risk factors is controversial. In addition to defining the disease by ECG screening for early diagnosis in patients with defined risk factors, the interventional methodology may be considered to be applied for severe cases who are resistant to medical therapy.

REFERENCES

1. *Schwartz PJ, Stramba-Badiale M, Crotti L, Pedrazzini M, Besana A, Bosi G, et al. Prevalence of the congenital long-QT syndrome. Circulation 2009; 120: 1761-7.* **[CrossRef]**
2. *Vincent GM. Long QT syndrome. Cardiology Clinics 2000; 18: 309-25.* **[CrossRef]**
3. *Viskin S. Long QT syndrome and torsade de pointes. Lancet 1999; 354: 1625-33.* **[CrossRef]**
4. *El-Sherif N, Turitto G. The long-QT syndrome and torsade de pointes. Pacing Clin Electrophysiol 1999; 22: 91-110.* **[CrossRef]**
5. *Splawski I, Shen J, Timothy KW, Lehmann MH, Priori S, Robinson JL et al. Spectrum of mutations in long-QT syndrome genes. KVLQT1, HERG, SCN5A, KCNE1, and KCNE2. Circulation. 2000;102:1178-85.* **[CrossRef]**

6. *Camm AJ, Janse MJ, Roden DM, Rosen MR Cinca J, Cobbe SM. Congenital and acquired long QT syndrome. Eur Heart J 2000; 21: 1232-7.* **[CrossRef]**
7. *Jervell A, Lange-Nielsen F. Congenital deaf-mutism, functional heart disease with prolongation of the QT interval, and sudden death. Am Heart J 1957; 54: 59-68.* **[CrossRef]**
8. *Vincent GM, Jaiswal D, Timothy KW. Effects of exercise on heart rate, QT, QTc, and QT/QS2 in the Romano Ward inherited long QT syndrome. Am J Cardiol 1991; 68: 498-503.* **[CrossRef]**
9. *Villain E, Levy M, Kachaner J, Garson A Jr. Prolonged QT interval in neonates: benign, transient, or prolonged risk of sudden death. Am Heart J 1992; 124: 194-7.* **[CrossRef]**
10. *Schwartz PJ, Priori SG, Spazzolini C, Moss AJ, Vincent GM, Napolitano C, et al. Genotype-phenotype correlation in the long-QT syndrome: gene-specific triggers for life-threatening arrhythmias. Circulation 2001; 103: 89-95.* **[CrossRef]**
11. *Wu MH, Hsieh FC, Wang JK. A variant of long QT syndrome manifested as fetal tachycardia and associated with ventricular septal defect. Heart 1999; 82: 386-8.* **[CrossRef]**
12. *Schwartz PJ, Stramba-Badiale M, Segantini A, Austoni P, Bosi G, Giorgetti R, et al. Prolongation of the QT interval and the sudden infant death syndrome. N Engl J Med 1998; 338: 1709-14.* **[CrossRef]**
13. *Garson A Jr, Dick M 2nd, Fournier A, Gillette PC, Hamilton R, Kugler JD, et al. The long QT syndrome in children. An international study of 287 patients. Circulation 1993; 87: 1866-72.* **[CrossRef]**
14. *Schwartz PJ, Moss AJ, Vincent GM, Crampton RS. Diagnostic criteria for the long QT syndrome: An update. Circulation 1993; 88: 782-4.* **[CrossRef]**