PERINATAL JOURNAL

Case(s) Report
Perinatal Journal 2023;31(2):101-104

Management of catecholaminergic polymorphic ventricular tachycardia in pregnancy: a case report

Jennifer McCormick[1], Maggie Kuhlmann[1]

[1]Creighton University Medical Center, Department of Maternal-Fetal Medicine, OMAHA, United States

Abstract

Objective: To report the case of a successful pregnancy in a patient with catecholaminergic polymorphic ventricular tachycardia with a history of cardiac arrest and placement of an implantable cardioverter defibrillator (ICD).

Case(s): A 29-year-old Caucasian G1P0 presented to the maternal fetal medicine service at seven weeks gestation with known CPVT. She was medically managed with nadolol and experienced no arrhythmias or ICD shocks during her pregnancy. Her pregnancy was complicated by severe fetal growth restriction. She ultimately delivered by urgent cesarean section due to fetal intolerance of labor.

Conclusion: Episodes of catecholaminergic polymorphic ventricular tachycardia during pregnancy can be life-threatening for both mother and baby, though successful management is possible with care from a multidisciplinary team.

Keywords: arrhythmia, catecholaminergic polymorphic ventricular tachycardia (CPVT), pregnancy

Introduction

Catecholaminergic polymorphic ventricular tachycardia (CPVT) is an inherited arrhythmia syndrome in which potentially-fatal ventricular tachyarrhythmias are triggered by the release of catecholamines with physical and/or emotional stress. Patients usually present in the first or second decade of life with syncope or sudden cardiac arrest, though presentation may occur in adulthood. [1] Workup demonstrates a structurally-normal heart and a normal resting electrocardiogram (though the QT interval may be abnormal).[2] First-line treatment is with a non-selective beta blocker, and patients with a history of cardiac arrest require placement of an implantable cardioverter defibrillator (ICD). In refractory cases, additional treatment options include the addition of Flecainide, Verapamil, or left cardiac sympathetic denervation. [3]

CPVT can be inherited or occur as a de novo mutation. There are multiple identified mutations, the most common of which include those of the cardiac ryanodine receptor (RyR2) and the sarcoplasmic reticulum protein calsequestrin 2 gene (CASQ2). RyR2 mutations demonstrate an autosomal-dominant pattern of inheritance and lead to impaired handling of calcium within myocytes. CASQ2 mutations follow an autosomal-recessive pattern and are much rarer than RyR2 mutations, though considered to be more malignant. [1,2]

Pregnancy is associated with a more frequent occurrence of arrhythmias. The physiologic cardiovascular changes that occur during pregnancy (increased heart rate, cardiac output, and blood volume) facilitate the generation of arrhythmias such as sinus tachycardia and premature atrial and/or ventricular complexes. Atrial arrhythmias are far more common, and their management is better understood than that of ventricular arrhythmias during pregnancy. [4] In patients with CPVT, the risk of arrhythmia may be further increased owing to maternal stress and resultant catecholamine release. Hormonal changes during pregnancy may also play a role via increased sensitivity of adrenergic receptors. [5,6] With the potential for developing a fatal arrhythmia, it is crucial to

Correspondence: Jennifer McCormick, Creighton University, Medical Center Department of Maternal-Fetal Medicine, OMAHA, United States, **e-mail:** jennifermccormick1@creighton.edu, **Received:** March 01, 2023, **Accepted:** April 07, 2023

How to cite this article: McCormick J, Kuhlmann M. Management of catecholaminergic polymorphic ventricular tachycardia in pregnancy: a case report. Perinatal Journal 2023;31(2):101-104 DOI: 10.59215/prn.23.0312003

ORCID ID: J. McCormick 0009-0006-6016-7373; M. Kuhlmann 0000-0002-7632-121X.

CETUS Publishing

understand whether these patients are at an increased risk for an episode during pregnancy. In addition to the risk of fatal arrhythmia, CPVT imposes a risk of reduced uteroplacental blood flow during maternal arrhythmias and/or as a result of beta blocker therapy, which directly affects growth and survival of the fetus.

Despite the possible implications, little remains known on the overall risk of arrhythmic events during pregnancy in patients with CPVT. It therefore also remains a question on how to best manage these patients in the antepartum, intrapartum, and postpartum periods. Here we present the case of a successful pregnancy and delivery of a term infant to a mother with CPVT.

Case(s)

A 29-year-old, G1 Caucasian female presented to the maternal fetal medicine clinic at 7 weeks gestation for consultation with CPVT. Pregnancy was further complicated by hypothyroidism, arcuate uterus, and BMI of 42.

At age 12, the patient suffered a cardiac arrest when her mother's car hit a curb. Arriving at the correct diagnosis took several years, eventually reaching the diagnosis of CPVT with a pathogenic mutation of RyR2. The patient underwent placement of a Medtronic single chamber dual coil ICD in 2004, which was replaced in 2014. Interrogation of her ICD is done on a yearly basis, and her visit at gestational age 24 weeks revealed no arrhythmia events within the past year. Medical management consisted of nadolol 80 mg PO BID, which she was advised to continue throughout pregnancy and the postpartum period. Our team planned for a vaginal delivery with induction of labor no later than 39 weeks, with cesarean section reserved for standard obstetric indications. Her pregnancy was eventually further complicated by suspected fetal growth restriction, and due to severity, recommendation for delivery was modified to 37 weeks.

She presented to labor and delivery at 37 weeks for scheduled induction of labor. Vital signs were within normal limits and physical exam unremarkable. Laboratory workup was significant for hemoglobin of 11.9 g/dL, potassium of 3.6 mmol/L, and TSH elevated at 4.49 UIU/mL though free T4 reassuring at 0.9 ng/dL. Baseline EKG was within normal limits and she was placed on continuous telemetry.

Cervical ripening was performed without issue. Early epidural placement without bolus was performed to minimize the stress response to pains of labor. Bolus was withheld due to concerns of resultant hypotension and reflex tachycardia precipitating a ventricular arrhythmia. Pitocin was initiated following epidural placement. Baby was eventually delivered by urgent cesarean section due to fetal intolerance of labor.

Our patient delivered a live female newborn with APGARs of 8 at one minute and 9 at five minutes. Baby had a birthweight of 4lb 14.3oz (2220 g). Umbilical artery pH was 7.17. The infant experienced an episode of hypoglycemia on her first day of life and was brought to the neonatal intensive care unit (NICU) for monitoring. Genetic testing for RyR2 mutation was sent for the infant. She was started on Propranolol 4mg/kg/day divided TID, though discontinued after two doses secondary to low resting heart rate. She received prolonged care in the NICU for 12 days. The infant's gene testing ultimately returned positive for the pathogenic variant of RyR2.

Mother's postpartum course was complicated by postpartum depression but otherwise uneventful.

Discussion

Our case demonstrates the successful management of pregnancy in a patient with CPVT. Our patient had a relatively stable disease state prior to pregnancy, which was maintained throughout with no recorded arrhythmic events. Despite concern for the more frequent occurrence of arrhythmia in these patients, the limited data available has not shown an increased risk for cardiac events during pregnancy compared to non-pregnant women with CPVT. [9] Of note, Cheung et al 9 recorded 6 arrhythmic events out of 228 total pregnancies. Each of these events occurred in those not on beta blocker therapy at the time. This demonstrates the importance of compliance with medical management throughout pregnancy.

Conflicting data exists regarding the influence that method of delivery has on maternal catecholamine levels. While some studies have found fetal and maternal plasma catecholamine levels to be higher with vaginal delivery versus scheduled cesarean section, [10,11] others have demonstrated no significant difference in cord plasma levels of infants delivered via either method. [12] While scheduled cesarean section remains an option for these patients, [13] there are reports of successful vaginal delivery with CPVT. [14,15] Given our patient's well-controlled disease and excellent compliance with her beta blocker, we felt it was safe to anticipate a normal vaginal delivery, with cesarean section reserved for standard obstetric indications. Similar to the case reported by Romagano et al, [16] our patient's need for emergent cesarean section was not a direct consequence of CPVT, which remained well-controlled during her labor

and delivery with no recorded ventricular arrhythmias and no ICD discharges.

Medical management with beta blockers is relatively safe in pregnancy; there is, however, risk of reduced uteroplacental blood flow with potential complications of intrauterine growth restriction (IUGR) and preterm delivery. [17,18] While several different beta-blockers have been investigated in relation to IUGR, little data exists regarding nadolol specifically. This is of importance as studies have found that certain beta-blockers pose increased risk of IUGR compared to others: namely, atenolol and labetalol bearing the highest risk for IUGR. [19] Recently, a study by Hammond et. al investigated the relationship between nadolol exposure during pregnancy and IUGR; the authors did not find evidence of increased risk of IUGR in nadolol-exposed fetuses. [20] Though this study was limited by small sample size and varying dosages of nadolol, it does prompt the need for further investigation. Regardless, the benefit of beta blocker therapy on suppression of arrhythmic events outweighs this potential fetotoxicity in patients with CPVT. Close surveillance for signs of fetal growth restriction is therefore needed in these cases, with standard management of suspected FGR if observed.

Infants born to mothers with the pathogenic RyR2 mutation have a 50% chance of inheriting the mutation themselves. Prolonged monitoring for minimum 2-3 days in the NICU and an EKG within the first 24 hours can provide an assessment of the infant's cardiac status while awaiting genetic testing. Our infant's initial EKG was abnormal for a QT interval of 348ms with a QTc of 497ms. However, repeat EKG and 24-hour Holter monitoring did not demonstrate QT interval prolongation. This suggests the prolonged QT interval was not a manifestation of cardiac disease, but rather due to transient electrolyte abnormalities, which is a common occurrence in the neonatal period. [7,8]

As it can take several weeks to receive the genetic testing results, it is worth considering initiation of beta blocker therapy in the interim. It has been proposed that CPVT in infancy may present as sudden infant death syndrome (SIDS), based on postmortem genetic testing revealing the pathologic RyR2 mutation; [21,22] however, more recent studies indicate the SIDS-associated RyR2 variant may lack pathogenicity. [23] 2While association of CPVT and SIDS remains unclear, the potential for arrhythmias during infancy persists. These infants can be started on beta blocker therapy with close monitoring for bradycardia and hypoglycemia.

As demonstrated by our case, a multidisciplinary team is crucial when managing these complicated pregnancies. Our team consisted of maternal-fetal medicine, obstetrics and gynecology, pediatric cardiology, anesthesiology, and neonatology. Such a team is necessary to address the multitude of factors influencing the ability of these patients to carry a successful pregnancy to term. Care should include, but is not limited to, preconception counseling (when possible), management of anti-arrhythmic medications, achieving optimal programming of ICDs, managing any comorbidities while ensuring teratogenic medications are discontinued when feasible, and planning for the hyperadrenergic state of labor and delivery to minimize maternal stress during this period. [24]

Conclusion

Pregnancy is believed to put women at a higher risk for arrhythmic events, though little information is known regarding ventricular arrhythmias due to scarcity of cases. Managing CPVT in pregnancy is possible with care from a multidisciplinary team. Beta blockers remain the mainstay of treatment, with ICDs, additional antiarrhythmics, and/or left cardiac sympathetic denervation reserved for select cases. With the implications that episodes of CPVT have on both mother and baby, it is important to bring attention to the management of this syndrome during pregnancy and the postpartum period.

Conflicts of Interest: No conflicts declared.

References

1. Mazzanti A, Priori SG. Inherited arrhythmias: LQTS/SQTS/CPVT. In: Cardiovascular genetics and genomics. Cham: Springer International Publishing; 2018:413-435. http://link.springer.com/10.1007/978-3-319-66114-8_13. 10.1007/978-3-319-66114-8_13. [CrossRef]

2. Leenhardt A, Denjoy I, Guicheney P. Catecholaminergic polymorphic ventricular tachycardia. Circulation. Arrhythmia and electrophysiology. 2012;5(5):1044-1052. [PubMed] [CrossRef]

3. de Ferrari GM, Dusi V, Spazzolini C, et al. Clinical management of catecholaminergic polymorphic ventricular tachycardia the role of left cardiac sympathetic denervation. Circulation (New York, N.Y.). 2015;131(25):2185-2193. https://www.narcis.nl/publication/RecordID/oai:pure.amc.nl:publications%2F5c32c131-c75f-48a9-b812-660f46f9ec61. [PubMed] [CrossRef]

4. Moore J, Teefey P, Rao K, Berlowitz M, Chae S, Yankowitz J. Maternal arrhythmia: A case report and review of the literature. Obstetrical & gynecological survey. 2012;67(5):298-312. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&NEWS=n&CSC=Y&PAGE=fulltext&D=ovft&AN=00006254-201205000-00017. [PubMed] [CrossRef]

5. Page RL. Treatment of arrhythmias during pregnancy. The American heart journal. 1995;130(4):871-876. [PubMed] [CrossRef]

6. Sanghavi M, Rutherford J. Cardiovascular physiology of pregnancy. Circulation (New York, N.Y.). 2014;130(12):1003-1008. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&NEWS=n&CSC=Y&PAGE=fulltext&D=ovft&AN=00003017-201409160-00012. [PubMed] [CrossRef]

7. SCHWARTZ PJ, GARSON AJ, PAUL T, et al. Guidelines for the interpretation of the neonatal electrocardiogram: A task force of the european society of cardiology. European heart journal. 2002;23(17):1329-1344. h[PubMed] [CrossRef]

8. Delogu AB, Iannotta R, Saracino A, Barone G, Romagnoli C. Long QT interval in the newborn. Early human development. 2013;89:S39-S40. https://www.clinicalkey.es/playcontent/1-s2.0-S0378378213700926. [CrossRef]

9. Cheung CC, Lieve KV, Roston TM, et al. Pregnancy in catecholaminergic polymorphic ventricular tachycardia. JACC. Clinical electrophysiology. 2019;5(3):387-394. [PubMed] [CrossRef]

10. Li W, Weiyuan Z, Yanhui Z. The study of maternal and fetal plasma catecholamines levels during pregnancy and delivery. Journal of perinatal medicine. 1999;27(3):195-198. https://api.istex.fr/ark:/67375/QT4-LZX0BSGF-T/fulltext.pdf. [PubMed] [CrossRef]

11. Irestedt L, Lagercrantz H, Hjemdahl P, Hagnevik K, Belfrage P. Fetal and maternal plasma catecholamine levels at elective cesarean section under general or epidural anesthesia versus vaginal delivery. American journal of obstetrics and gynecology. 1982;142(8):1004-1010. [PubMed] [CrossRef]

12. POHJAVUORI M, ROVAMO L, LAATIKAINEN T, KARINIEMI V, PETTERSSON J. Stress of delivery and plasma endorphins and catecholamines in the newborn infant. Biological research in pregnancy and perinatology. 1986;7(1):1-5. [PubMed]

13. Ahmed A, Phillips JR. Teenage pregnancy with catecholaminergic polymorphic ventricular tachycardia and documented ICD discharges. Clinical Case Reports. 2016;4(4):361-365. https://onlinelibrary.wiley.com/doi/abs/10.1002/ccr3.366. [PubMed] [CrossRef]

14. Friday KP, Moak JP, Fries MH, Iqbal SN. Catecholaminergic ventricular tachycardia, pregnancy and teenager: Are they compatible? Pediatr Cardiol. 2015;36(7):1542-1547. https://link.springer.com/article/10.1007/s00246-015-1232-3. [PubMed] [CrossRef]

15. Schumer A, Contag S. Catecholaminergic polymorphic ventricular tachycardia in pregnancy: A case report. Journal of medical case reports. 2020;14(1):238. https://www.ncbi.nlm.nih.gov/pubmed/33292493. [PubMed] [CrossRef]

16. Romagano M, Quiñones J, Ahnert A, Martinez R, Smulian J. Catecholaminergic polymorphic ventricular tachycardia in pregnancy. Obstetrics and gynecology (New York. 1953). 2016;127(4):735-739. https://www.ncbi.nlm.nih.gov/pubmed/26959204. [PubMed] [CrossRef]

17. Ersbøll A, Hedegaard M, Søndergaard L, Ersbøll M, Johansen M. Treatment with oral beta-blockers during pregnancy complicated by maternal heart disease increases the risk of fetal growth restriction. BJOG : an international journal of obstetrics and gynaecology. 2014;121(5):618-626.PubMed] [CrossRef]

18. Fitton C, Fleming M, Steiner M, et al. In utero antihypertensive medication exposure and neonatal outcomes: A data linkage cohort study. Hypertension (Dallas, Tex. 1979). 2020;75(3):628-633. [PubMed] [CrossRef]

19. Duan L, Ng A, Chen W, Spencer HT, Lee M. Beta-blocker subtypes and risk of low birth weight in newborns. The journal of clinical hypertension (Greenwich, Conn.). 2018;20(11):1603-1609. [PubMed] [CrossRef]

20. Hammond BH, El Assaad I, Herber JM, Saarel EV, Cantillon D, Aziz PF. Contemporary maternal and fetal outcomes in the treatment of LQTS during pregnancy: Is nadolol bad for the fetus? Heart rhythm. 2022;19(9):1516-1521. [PubMed] [CrossRef]

21. Tester DJ, BS, Dura M, PhD, Carturan E, PhD, et al. A mechanism for sudden infant death syndrome (SIDS): Stress-induced leak via ryanodine receptors. Heart rhythm. 2007;4(6):733-739. https://www.clinicalkey.es/playcontent/1-s2.0-S1547527107002275. [PubMed] [CrossRef]

22. Larsen MK, Berge KE, Leren TP, et al. Postmortem genetic testing of the ryanodine receptor 2 (RYR2) gene in a cohort of sudden unexplained death cases. Int J Legal Med. 2012;127(1):139-144. [PubMed] [CrossRef]

23. Kohli U, Nayak HM. SIDS associated RYR2 p.Arg2267His variant may lack pathogenicity. Journal of electrocardiology. 2020;60:23-26. [PubMed] [CrossRef]

24. Roston TM, Grewal J, Krahn AD. Pregnancy in catecholaminergic polymorphic ventricular tachycardia: Therapeutic optimization and multidisciplinary care are key to success. Herzschr Elektrophys. 2021;32(2):199-206. https://link.springer.com/article/10.1007/s00399-021-00755-6. [PubMed] [CrossRef]