CASE REPORT

An Adverse Obstetric Event Following Conversion of DAPT to a Single Antiplatelet Agent in a Pregnant Woman with Coronary Artery Disease Treated by Angioplasty: A Case Report

Vignesh Durai[1], Poojitha K Kanikaram[2], Paapa Dasari[3]

Received on: 03 August 2022; *Accepted on:* 14 July 2023; *Published on:* 25 November 2023

Abstract

Aim: To describe the adverse fetal outcome at term due to discontinuation of clopidogrel before delivery in woman with coronary artery disease who was on dual antiplatelet therapy (DAPT) for 5 years.

Background: Acute myocardial infarction (MI) during pregnancy is reported more often than pregnancy outcomes in woman with coronary artery disease (CAD). The recommendation regarding the mode of delivery in women with preexisting CAD is not uniform, and the role of continuing DAPT before delivery is a matter of debate in the literature.

Case description: A 38-year-old primigravida with a history of CAD for 5 years was hospitalized at 37 weeks for safe confinement. She was a tailor by occupation and was diagnosed with CAD 5 years ago, for which she underwent primary percutaneous transluminal angioplasty with an everolimus-eluting stent of the left anterior descending (LAD) artery. She has been taking tablet (Tab) aspirin, Tab clopidogrel, β-blockers, and statins since then. She was married for 20 years and was investigated for primary infertility. Her cycles were irregular, and she was diagnosed with polycystic ovary syndrome (PCOS), treated with oral ovulogens without success, and stopped further fertility treatment when diagnosed with CAD. She recognized herself as pregnant only at 32 weeks. She was scheduled to be delivered by elective cesarean section (CS) at 38 weeks. The cardiologist and the anesthesiologist advised her to stop clopidogrel 1 week before CS. She suffered from sudden intrauterine fetal demise (IUFD) the day before the scheduled CS and went into labor. She was delivered by emergency cesarean, and the stillborn baby weighed 3.4 kg.

Conclusion: Discontinuing DAPT in pregnant women with CAD may lead to IUFD.

Clinical significance: Continuing DAPT from pregnancy till delivery or substituting with heparin to prevent thrombosis is essential, possibly preventing sudden intrauterine death. The benefits should be weighed against the risk of bleeding when such therapy is stopped.

Keywords: Acute coronary syndrome, Case report, Coronary artery disease, Intrauterine fetal death, Myocardial infarction, Postprimary percutaneous transluminal angioplasty, Primary infertility.

International Journal of Infertility and Fetal Medicine (2023): 10.5005/jp-journals-10016-1321

Background

Pregnancy in women with coronary heart disease (CAD) is associated with a 3 to 4-fold higher risk of myocardial infarction (MI), and maternal mortality ranges from 4.5 to 7.3%.[1–3] Acute MI during pregnancy is reported in literature more often than pregnancy outcomes in a woman with CAD. CAD is said to complicate 0.01% of all pregnancies,[4] and the recommendation regarding the mode of delivery and antiplatelet agents are not uniform and should be individualized. This case is reported due to its rarity, adverse fetal outcome and controversies in management.

Case Description

A 38-year-old primigravida with a history of CAD of 5 years was hospitalized at 37 weeks for safe confinement. She was married for 20 years and was investigated for primary infertility. Her cycles were irregular, and she was diagnosed with polycystic ovary syndrome (PCOS), received oral ovulogens for conception without success, and stopped further fertility treatment when she was diagnosed with CAD. Her body mass index was 30.6 (class I obesity). She has given up hope of having a baby after being diagnosed with CAD. There was no family history of CAD, stroke, or sudden death.

Her past history revealed that she was a tailor by occupation and experienced sudden chest pain and giddiness while working, and her electrocardiogram showed anterior wall MI. She was found to have elevated serum cholesterol levels (227 mg/dL), but no other workup for young CAD was done. The coronary angiography revealed single vessel disease with complete occlusion of the proximal part of the left anterior descending (LAD) artery. The rest of the artery was filled by collaterals from the right coronary artery. She underwent primary percutaneous transluminal angioplasty

[1–3]Department of Obstetrics and Gynaecology, Jawaharlal Institute of Postgraduate Medical Education & Research (JIPMER), Puducherry, India

Corresponding Author: Paapa Dasari, Department of Obstetrics and Gynaecology, Jawaharlal Institute of Postgraduate Medical Education & Research (JIPMER), Puducherry, India, Phone: +91 9442566883, e-mail: dasaripapa@gmail.com

How to cite this article: Durai V, Kanikaram PK, Dasari P. An Adverse Obstetric Event Following Conversion of DAPT to a Single Antiplatelet Agent in a Pregnant Woman with Coronary Artery Disease Treated by Angioplasty: A Case Report. Int J Infertil Fetal Med 2023;14(3):143–147.

Source of support: Nil

Conflict of interest: None

Patient consent statement: The author(s) have obtained written informed consent from the patient for publication of the case report details and related images.

with everolimus-eluting stenting of the LAD artery and was started on dual antiplatelet therapy (DAPT), β-blockers, and statins. She was well-compliant with the cardiac medications and had three monthly follow up for 1 year, followed by six monthly follow-ups in the subsequent years with the cardiologists. She has not revealed or discussed her amenorrhea with the cardiologist.

She did not realize that she was pregnant till 32 weeks of gestation and had not consulted any doctor for her amenorrhea as she thought it was due to irregular cycles. She did not experience early pregnancy symptoms, such as nausea and vomiting and was busy with her tailoring occupation. She has taken [tablet (Tab) aspirin 150 mg, Tab clopidogrel 75 mg, Tab atorvastatin 40 mg, and Tab bisoprolol 2.5 mg] throughout the pregnancy. Her first antenatal visit to our hospital was at 34 weeks, and she was advised to get a cardiac evaluation after an obstetric assessment which was normal. She was completely asymptomatic, New York Heart Association class 1 from her prepregnancy. Her subsequent antenatal visits were at 35 and 36 weeks of gestation and are summarized in Table 1. She was hospitalized at 37 weeks for safe confinement, and fetal surveillance was done with a daily nonstress test and fetal kick count. An obstetric ultrasound at 37 weeks by a consultant obstetrician showed a live fetus in a cephalic position with an estimated fetal weight (EFW) of 2.7 kg, with no gross anomalies, and the amniotic fluid index was 15 cm. The placenta was in the posterior wall of the upper segment. The Doppler study revealed an umbilical artery pulsatility index of 1.1 and a middle cerebral artery pulsatility index of 1, the cerebroplacental ratio was <1, and the biophysical profile was 10/10. The Doppler study was repeated on alternate days, and she received antenatal corticosteroids for fetal lung maturity.

Table 1: Antenatal visits

Period of gestation	*Obstetric findings and advice given*
34 weeks	*Vitals* Pulse rate (PR): 88/minute, blood pressure (BP): 122/80 mm Hg *Obstetric findings* The uterus was 32 weeks, cephalic, relaxed, with average liquor, and had a normal fetal heart rate. *Obstetric ultrasound* Single live intrauterine gestation of 33 weeks in cephalic presentation with an EFW of 2 kg without gross congenital anomalies. The liquor was average, and the placenta was in the posterior wall of the upper segment. Adviced to get a cardiology consultation. Cardiologists advised electrocardiogram (ECG) and echocardiogram (Echo). They opined to continue aspirin and to stop clopidogrel 1 week before the expected delivery date. Restart clopidogrel once the patient is out of risk of bleeding.
35 weeks	*Vitals* PR: 80/minute, BP: 124/88 mm Hg *Obstetric findings* The uterus was 34 weeks, cephalic, relaxed, with average liquor, and had a normal fetal heart rate. Adviced to continue the same medications and review after 1 week.
36 weeks	*Vitals* PR: 84/minute, BP: 118/76 mm Hg *Obstetric findings* The uterus was 36 weeks, cephalic, relaxed, with average liquor, and had a normal fetal heart rate. Adviced to continue the same medications and review after 1 week.
37 weeks	*Vitals* PR: 78/minute, BP: 126/76 mm Hg *Obstetric findings* The uterus was term size, cephalic, relaxed, average liquor, and had a normal fetal heart rate with an estimated weight of 3 kg. Adviced for admission and repeat cardiology opinion as planned for elective CS. Cardiology opinion: to stop clopidogrel 1 week before CS.

Her hematological investigations are summarized in Table 2. She was counseled regarding vaginal and cesarean delivery and decided to undergo a cesarean section (CS) at 38 weeks. The anesthesiologist did the preoperative assessment and advised to stop clopidogrel 1 week before the planned CS. Initially, the cardiologist also suggested the same. She was taking aspirin, but clopidogrel was stopped. Her fetal heart could not be located the day before the scheduled CS, which was confirmed by ultrasound. There was no evidence of a retroplacental clot or any other finding and she was informed about the fetal demise. A repeat cardiology opinion was obtained after the fetal demise regarding the mode of delivery. They opined that she could tolerate normal labor and delivery under standard cardiac risk as her left ventricular ejection fraction was 60%. She went into spontaneous labor on the same day and underwent emergency CS under spinal anesthesia due to a maternal request though the choice of vaginal delivery was given. A stillborn baby was delivered, which weighed 3.4 kg. At CS, the liquor was clear, the placenta, umbilical cord, and fetus were grossly normal, and there was no postpartum hemorrhage. The placenta was not sent for histopathological examination. The option of the fetal autopsy was not given as the neonatologist felt that the ultrasound was normal, and there was no protocol for autopsy in the presence of maternal disease.

She was managed postoperatively in the obstetric intensive care unit. She was started on low molecular weight heparin for thromboprophylaxis after 6 hours of surgery, and her regular medication was restarted after 24 hours. She was given a lactation suppressant and discharged on the 7th postoperative day with the advice to continue thromboprophylaxis for 6 weeks and to review with a complete thrombophilia workup.

Discussion

Pregnancy causes profound hemodynamic alterations resulting in increased heart rate and cardiac output due to circulatory overload. These changes increase the myocardial oxygen demand and require increased myocardial perfusion. In cases with CAD, there is compromised blood flow due to the atherosclerotic plaque in the coronaries causing ischemic damage to the myocardium. Moreover, the coronaries get perfused during the diastolic phase of the cardiac cycle. A fall in systemic vascular resistance in pregnancy may further reduce the blood flow in the under-perfused atherosclerotic arteries. MI more commonly involves the anterior wall due to the common involvement of the LAD artery. The risk factors for CAD during pregnancy are similar to that in a nonpregnant state, including hypertension, diabetes, hypertriglyceridemia, hyperlipidemia, smoking, obesity and immobility.[5] The reproductive risk factors include early and late menarche, polycystic ovarian syndrome, infertility, and fertility treatment.[6] In our patient, prolonged infertility and fertility treatment could have been a significant risk factor in addition to dyslipidemia. An expert opinion and a thorough cardiovascular evaluation antenatally are mandatory in women with preexisting CAD. Screening for gestational diabetes and preeclampsia should be done as these women are at increased risk.

The presence of hypertriglyceridemia in our patient could be due to the changes in the lipid metabolism during pregnancy,[7] as

Table 2: Investigations

Laboratory tests	*Values*	*Normal*
Prepregnancy		
Lipid profile		
Total cholesterol (mg/dL)	196	<200
Triglycerides (mg/dL)	142	<150
LDL (mg/dL)	122	<100
Very LDLs (VLDL) (mg/dL)	28	<30
High-density lipoproteins (HDL) (mg/dL)	56	>40
34 weeks of gestation		
Hemoglobin (g/dL)	10.6	12.5–15.5
Glucose challenge test (mg/dL)	112	<140
Thyroid-stimulating hormone (mIU/L)	2.27	0.5–3.5
ECG	Sinus rhythm, Normal axis and lead III–Q waves and T wave inversion	
Echo	No regional wall motion abnormalities. Left ventricular ejection fraction 60%	
37 weeks of gestation		
Complete hemogram		
Hemoglobin (g/dL)	11.4	12.5–15.5
Total counts (/mm^3)	14,430	4,000–11,000
Platelet (/mm^3)	2.85 lakh	1.5–4.5 lakh
Renal and liver function tests		
Urea (mg/dL)	13	17–43
Creatinine (mg/dL)	0.4	0.5–0.9
Sodium (mEq/L)	136	136–146
Potassium (mEq/L)	5	3.5–5.5
Total bilirubin (mg/dL)	0.55	0.3–1.2
Direct bilirubin (mg/dL)	0.11	0–0.2
Aspartate transaminase (U/L)	15	0–35
Alanine transaminase (U/L)	8	0–35
Total protein (g/dL)	6.6	6.6–8.3
Albumin (g/dL)	3.6	3.5–5.2
Lipid profile		
Total cholesterol (mg/dL)	178	<200
Triglycerides (mg/dL)	283	<150
LDL (mg/dL)	103	<100
VLDL (mg/dL)	57	<30
HDL (mg/dL)	48	>40
Coagulation profile		
Prothrombin time (seconds)	10.7	10–15
Activated partial thromboplastin time (seconds)	28	25–35
Thrombin time (seconds)	13.2	12–15
International normalized ratio	0.98	1–1.2
Bleeding time (minutes)	4	2–5
Clotting time (minutes)	7	5–8
Urine routine	No bacteria, casts, crystals	
Urine culture	Sterile	
Postpartum period		
Thrombophilia panel		
Anti-nuclear antibody	Negative	Negative
Anti-cardiolipin antibody immunoglobulin (Ig) IgG/IgM	Negative	Negative
β-2 glycoprotein IgG/IgM	Negative	Negative

her prepregnancy lipid profile (Table 2) was not grossly deranged as she was on statins. However, she did not achieve the low-density lipoprotein (LDL) target. Hyperlipidemia is the second most common cause of CAD, and significantly elevated triglycerides are implicated in the same.[8]

Pharmacotherapy with DAPT is generally indicated in post-angioplasty patients. Low-dose aspirin (category B) is considered safe in pregnancy, but the studies on clopidogrel are controversial. It is suggested that prescribing clopidogrel (category C) during pregnancy should be individualized and used for a short period whenever necessary due to limited data on fetal safety.[9] A systematic review by Nana et al.[10] also describes the acceptable fetal risks in women exposed to clopidogrel. Statins are category X drugs, which should ultimately be avoided during pregnancy. It is not the hypolipidemic drug to be considered due to the associated risk of fetal anomalies. Our patient was on atorvastatin and continued during the pregnancy till the term. Atorvastatin could have been changed to pravastatin which has a relatively lower risk of congenital defects.[11] Gross anomalies were looked in the third-trimester scan as she realized to be pregnant only in the third trimester.

The mode of delivery should be individualized, and the pregnancy can be terminated by 39 weeks of gestation in women with stable cardiac status.[12] It also depends on the obstetric factors and myocardial stability. Vaginal delivery is preferred in women with preexisting ischemic heart disease. Intrapartum, adequate labor analgesia should be given, and Valsalva is not contraindicated in patients having uncompromised cardiac status.

Pregnancy in women with preexisting coronary artery disease is considered very high risk, and only 21% of women had a completely uncomplicated pregnancy.[13] Cardiovascular complications can occur in 32% of women with CAD, including ischemic cardiovascular complications in 9%, maternal mortality in 2%, and future recurrence in 9%.[13] Spontaneous rupture of coronary arteries in the peripartum period has been reported due to hemodynamic and hormonal changes.[14] A retrospective study[15] of 43 women with preexisting CAD/acute coronary syndrome/MI before pregnancy reported ischemic cardiac events in 26% and adverse pregnancy outcomes in 16% of the individuals. Preeclampsia and postpartum hemorrhage were common. Fetal adverse outcomes occurred in 30%, of which preterm delivery and spontaneous abortion were common. Intrauterine fetal demise (IUFD) occurred in 2% of the individuals.[15] Replacing clopidogrel with low molecular weight heparin 1 week before planned delivery was reported to be safe in preventing IUFD.[16] However, this wasn't done in our case. In another case, DAPT was continued throughout pregnancy without any adverse effects being reported.[17] Though continuing DAPT beyond one year increases the bleeding tendency, it decreases the risk of future ischemic attacks.[18] Early cessation of DAPT in patients with coronary angioplasty has an increased risk of stent thrombosis.[19] The decision to continue clopidogrel during the perioperative period must be individualized.[20]

Proper counseling before planning conception, lifestyle modifications, absolute compliance to cardiac medications, risk stratification and close surveillance of the mother and fetus during the antepartum and intrapartum period are required for a good maternal and fetal outcome. Involvement of the pregnancy heart team[10] consisting of obstetricians, maternal-fetal medicine specialists, family physicians, internal medicine physicians, cardiologists, and obstetric anesthesiologists is essential in decision-making in a tertiary care center.

A complete thrombophilia panel of investigations should be done for young CAD patients to determine the cause. Apart from the antiphospholipid antibodies profile, thrombophilia panel like factor V Leiden mutation, protein C and S deficiency, prothrombin gene mutation, antithrombin III activity, and homocysteine levels could not be performed due to nonavailability at our institute, and she could not afford the cost of these tests at private lab. Our patient was young with dyslipidemia, belonging to class II of the World Health Organization maternal cardiovascular risk categorization. A sudden IUFD could be due to acute microthrombi formation in the placental vasculature secondary to single antiplatelet therapy before delivery.

Conclusion

Discontinuing DAPT in pregnant women with CAD may lead to IUFD.

Clinical Significance

Continuing DAPT from pregnancy till delivery or substituting with heparin to prevent thrombosis is essential, possibly preventing sudden intrauterine death. The benefits should be weighed against the risk of bleeding when such therapy is stopped.

Informed Consent

Written informed consent was obtained from the patient to publish their clinical details.

Acknowledgments

The authors want to acknowledge the Department of Anesthesiology and Critical Care and the Department of Cardiology, Jawaharlal Institute of Postgraduate Medical Education & Research.

References

1. Ladner HE, Danielsen B, Gilbert WM. Acute myocardial infarction in pregnancy and the puerperium: a population-based study. Obstet Gynecol 2005;105(3):480-484. DOI: 10.1097/01.AOG.0000151998.50852.31
2. James AH, Jamison MG, Biswas MS, et al. Acute myocardial infarction in pregnancy: a United States population-based study. Circulation 2006;113(12):1564–1571. DOI: 10.1161/CIRCULATIONAHA.105.576751
3. Smilowitz NR, Gupta N, Guo Y, et al. Acute myocardial infarction during pregnancy and the puerperium in the United States. Mayo Clin Proc 2018;93(10):1404–1414. DOI: 10.1016/j.mayocp.2018.04.019
4. Frenkel Y, Barkai G, Reisin L, et al. Pregnancy after myocardial infarction: are we playing safe? Obstet Gynecol 1991;77(6):822–825. PMID: 2030850.
5. Pathak LA, Shirodkar S, Ruparelia R, et al. Coronary artery disease in women. Indian Heart J 2017;69(4):532–538. DOI: 10.1016/j.ihj.2017.05.023
6. O'Kelly AC, Michos ED, Shufelt CL, et al. Pregnancy and reproductive risk factors for cardiovascular disease in women. Circ Res 2022;130(4):652–672. DOI: 10.1161/CIRCRESAHA.121.319895
7. Butte NF. Carbohydrate and lipid metabolism in pregnancy: normal compared with gestational diabetes mellitus. Am J Clin Nutr 2000;71(5 Suppl):1256S–1261S. DOI: 10.1093/ajcn/71.5.1256s
8. Benjamin EJ, Muntner P, Alonso A, et al. Heart Disease and Stroke Statistics-2019 Update: A Report From the American Heart Association. Circulation 2019;139(10):e56–e528. DOI: 10.1161/CIR.0000000000000659
9. Regitz-Zagrosek V, Roos-Hesselink JW, Bauersachs J, et al. ESC Guidelines for the management of cardiovascular diseases during pregnancy. Eur Heart J 2018;39(34):3165–3241. DOI: 10.1093/eurheartj/ehy340

10. Nana M, Morgan H, Moore S, et al. Antiplatelet therapy in pregnancy: a systematic review. Pharmacol Res 2021;168:105547. DOI: 10.1016/j.phrs.2021.105547
11. Janion-Sadowska A, Sadowski M, Kurzawski J, et al. Pregnancy after acute coronary syndrome: a proposal for patients' management and a literature review. BioMed Res Int 2013;2013:957027. DOI: 10.1155/2013/957027
12. American College of Obstetricians and Gynecologists' Presidential Task Force on Pregnancy and Heart Disease and Committee on Practice Bulletins—Obstetrics. American College of Obstetricians and Gynecology Practice Bulletin No. 212: pregnancy and heart disease. Obstet Gynecol 2019;133(5):e320– e356. DOI: 10.1097/AOG.0000000000003243
13. Lameijer H, Burchill LJ, Baris L, et al. Pregnancy in women with pre-existent ischaemic heart disease: a systematic review with individualised patient data. Heart. 2019;105(1):873–880. DOI: 10.1136/heartjnl-2018-314364
14. Vijayaraghavan R, Verma S, Gupta N, et al. Pregnancy-related spontaneous coronary artery dissection. Circulation 2014;130:1915–1920. DOI: 10.1161/CIRCULATIONAHA.114.011422
15. Burchill LJ, Lameijer H, Roos-Hesselink JW, et al. Pregnancy risks in women with pre-existing coronary artery disease, or following acute coronary syndrome. Heart 2015;101(7):525–529. DOI: 10.1136/heartjnl-2014-306676
16. De Santis M, De Luca C, Mappa I, et al. Clopidogrel treatment during pregnancy: a case report and a review of literature. Intern Med 2011;50(16):1769–1773. DOI: 10.2169/internalmedicine.50.5294
17. Tello-Montoliu A, Seecheran NA, Angiolillo DJ. Successful pregnancy and delivery on prasugrel treatment: considerations for the use of dual antiplatelet therapy during pregnancy in clinical practice. J Thromb Thrombolysis 2013;36(3):348–351. DOI: 10.1007/s11239-012-0830-7
18. Levine GN, Bates ER, Bittl JA, et al. 2016 ACC/AHA Guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease: a report of the American college of cardiology/American heart association task force on clinical practice guidelines: an update of the 2011 ACCF/AHA/SCAI Guideline for percutaneous coronary intervention, 2011 ACCF/AHA Guideline for coronary artery bypass graft surgery, 2012 ACC/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the diagnosis and management of patients with stable ischemic heart disease, 2013 ACCF/AHA Guideline for the management of ST-elevation myocardial infarction, 2014 AHA/ACC Guideline for the management of patients with non-ST-elevation acute coronary syndromes, and 2014 ACC/AHA Guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery. Circulation 2016;134(10):e123–e155. DOI: 10.1161/CIR.0000000000000404
19. Quiñones JN, Cox D, Smolinski WJ, et al. Pregnancy in women after coronary revascularization. Obstet Med 2014;7(4):168–170. DOI: 10.1177/1753495X14546434
20. Udell JA, Bonaca MP, Collet JP, et al. Long-term dual antiplatelet therapy for secondary prevention of cardiovascular events in the subgroup of patients with previous myocardial infarction: a collaborative meta-analysis of randomized trials. Eur Heart J 2016;37(4):390–399. DOI: 10.1093/eurheartj/ehv443