Obstetrics and Gynecology Reports

Case Report ISSN: 2515-2955

Challenges in managing a pregnancy with underlying renal fibromuscular dysplasia

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Abstract

Renal Fibromuscular Dysplasia (RFD) is the most common complication of Fibromuscular dysplasia (FMD). FMD is a non-atherosclerotic arterial disease which usually presents as beaded lesions in medium or small-sized arteries. RFD can be defined as renal artery stenosis secondary to abnormal cellular proliferation and disrupted arterial wall structure which leads to reno-vascular hypertension. FMD has prevalence of 5.8% based on Cardiovascular Outcomes in Renal Atherosclerotic Lesions trial and 75% of FMD have been shown to have RFD. In Australia, as of 2018, 41 patients have been registered in FMD Registry.1 Pregnancy with underlying RFD has significant adverse effect to both foetus and mother if it has not been managed appropriately.

This case report is aimed to be a quick guiding tool for the practitioners who are in rural and remote setting when they come across this group of women. We will discuss management dilemmas from preconception until postpartum in a woman with underlying RFD who had bilateral renal stenting done prior to pregnancy.

Introduction

Renal Fibromuscular Dysplasia (RFD) is also known as renal artery stenosis and defined as narrowing of renal arteries leading to hypertension. In older population, renal artery stenosis is mainly caused by atherosclerosis. Whereas, in young population renal artery stenosis is commonly due RFD. RFD arises from Fibromuscular Dysplasia (FMD) [1]. FMD is defined as inflammatory pathology of arterial walls which affects small and medium sized arteries segmentally causing stenosis [1]. FMD most commonly affects renal artery causing RFD followed by carotid artery. RFD usually presents with hypertension in age lesser than 30 years old and appears to be more prevalent among females. CT-Angiography and MR-Angiography are the gold standard in diagnosing RFD. Revascularization via renal artery surgery or balloon PTA with or without stenting remains the cornerstone treatment for it.

Pre-Eclampsia (PE) is defined as hypertension in pregnancy affecting one or more maternal organs with or without affecting the foetus [3]. Chronic hypertension is strongly linked to the diagnosis of PE in pregnancy. PE in those who have underlying chronic hypertension is called as superimposed preeclampsia when one or more of the systemic features and foetal effects of PE develops after 20 weeks of gestation [3]. Pregnancy with underlying RFD puts one at high risk of developing PE. Hence, it is crucial to take necessary management to prevent PE. Initial step should start with preconception counselling followed by multidisciplinary approach between renal and obstetric team during both antenatal and postnatal period. In this case report, we will discuss challenges faced in managing Mrs. X who has RFD and had PTA with stenting done prior to pregnancy, looking at initial stages of preconception counselling until postpartum period.

Case

Mrs. X is a 37 years old primigravida who has RFD with bilateral renal artery stenting, hyperprolactinaemia and hypertension related white matter changes. Bilateral renal stenting were done when she was 24 years old. She migrated to Australia 6 years later and has been under Royal Darwin Hospital Renal team's follow up since then. Her hypertension was managed with Olmesartan and Nifedipine along with Aspirin 100mg. Otherwise, she had normal renal function with absent proteinuria. Olmesartan was switched to Labetolol when she decided to conceive. She also has hypertension related white matter changes which was picked up when she had MRI brain as part of the hyperprolactinaemia investigations. Apart from that, she had normal echocardiogram and carotid artery Doppler.

She was unable to conceive after trying for 2 years. Upon further investigating her subfertility, she had hyperprolactinaemia with serum prolactin of 1700mU/L and was managed with bromocriptine. There aren't any pituitary masses identified from the MRI brain. Other investigations for subfertility were normal with BMI of 23. She was also screened negative for autoimmune diseases. Subsequently, she conceived through IVF. She had her dating scan at 7 weeks of period of gestation (POG) with normal antenatal blood investigations and she was low risk for aneuploidy from first trimester combined screening test.

She attended her first appointment at the high-risk pregnancy unit RDH at 10 weeks POG. Her blood pressure was within normal range < 140/90mmHg on Labetolol 400mg BD and Nifedipine 60mg BD. Her renal function test was normal with urine protein-creatine ratio (PCR) of 8.0mg/mmol. Her aspirin dose was increased to 150mg with addition of Calcium 1.2 gm. A week later she was reviewed with home blood pressure monitoring and labetolol dose was increased to 600mg TDS

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Received: July 13, 2021; **Accepted:** July 22, 2021; **Published:** July 29, 2021

as she had suboptimal blood pressure control. A third antihypertensive agent which is Methyldopa 250 mg BD was added during her third visit at 11weeks 5days POG. At 14 weeks POG, she had positive urine PCR with 32 mg/mmol. Her renal function and liver function tests were normal. She didn't have any features of haemoconcentration or thrombocytopenia. At 18 weeks POG, methyldopa was ceased as she had symptomatic hypotension. Labetolol was reduced to 400mg TDS at 31 weeks of POG. Subsequently, her blood pressure was managed with labetolol 400 mg TDS and Nifedipine 60mg BD until delivery.

In terms of monitoring, she was reviewed every fortnightly until 28 weeks and weekly after that. She also had serial foetal growth scans for 28 weeks. Foetus started manifesting early signs of intrauterine growth restriction at 32 weeks when the estimated foetal weight reduced from 24% to 11%. At 36 weeks growth scan, estimated foetal weight dropped further to 4%. Otherwise, foetus had normal umbilical artery Doppler and amniotic fluid index.

Hence, delivery was planned at 37 weeks. Cervical ripening was achieved with Cook's catheter followed by artificial rupturing of membrane and induction with syntocinon. However, she had abnormal CTG with reduced variability soon after induction. She subsequently delivered via emergency caesarean section and baby was delivered with Apgar Score 9 in 1 min and 9 in 5 min. The baby weighed 2.2 kg with normal blood gas.

She had unremarkable post Caesarean recovery. She was discharged with T. Labetolol 200 mg TDS and T. Nifedipine 60 mg BD with postpartum review in 2 weeks.

Discussion

Question 1: Where do we start in these group of patients?

Answer: Preconception counselling is the best point to start. Primary health care system should identify women who are in their reproductive age with underlying RFD and refer them for preconception counselling with the obstetrics team.

Question 2: What are the issues to be discussed in preconception counselling?

Answer: Anti-hypertensive drugs should be revised. Angiotensin-converting enzyme (ACE) inhibitor and angiotensin receptor blockers (ARBs) are contraindicated. Beta-blockers, calcium channel blockers or alpha blockers are preferred agents in pregnancy. If blood pressure is not well controlled with single agent, combination of beta-blockers with calcium channel blockers shown to be effective [4].

Question 3: What are the investigations to be organised during preconception counselling?

Answer:

- Renal function test and Urine Protein Creatinine Ratio

Renal function test and proteinuria are important as abnormalities of these parameters later in pregnancy will be diagnostic of superimposed preeclampsia [3].

- Echocardiogram

Pre-pregnancy echocardiogram is beneficial as pre-existing cardiac dysfunction increases risk of complications in pregnancy [5]. Thus, abnormal pre-pregnancy echocardiogram will require close monitoring and cardiology input.

Question 4: What additional interventions are needed during initial antenatal visit?

Answer:

- High dose Aspirin and calcium supplement before 16weeks.

Initiation of aspirin before 16weeks reduces risk of preeclampsia, preterm birth, baby born small for gestational age and foetal and neonatal death [6]. Moreover, high dose calcium supplements are shown to reduce risk of preeclampsia for those who has high risk for pre-eclampsia [7].

Question 5: How to pick up Superimposed pre-eclampsia in this group?

Answer: Development of systemic features of preeclampsia such as worsening proteinuria, blood pressure, oligohydramnios or abnormal umbilical artery doppler after 20 weeks gestation will be diagnostic of superimposed preeclampsia [3].

Question 6: How often do they need to be reviewed?

Answer: Development of systemic features of preeclampsia after 20 weeks gestation will be diagnostic of superimposed preeclampsia.

Question 7: When is delivery indicated?

Answer: A Cochrane review on early planned induction of labour in those with mild to moderate hypertensive disorder before 37 weeks of gestation has shown reduction on composite maternal and morbidity, however it also increases composite infant mortality and morbidity [8]. Unless there are signs suggestive of worsening blood pressure or foetal compromise, delivery should be planned after 37 weeks of gestation [9].

Question 8: What is the next step after delivery?

Answer:

- Blood pressure optimisation

Blood pressure should be monitored daily until sixth day of post-delivery. Drugs which block renin-angiotensin-aldosterone system with combination of calcium channel blocker, diuretics and beta-blockers can be used to manage chronic hypertension secondary to RFD [10]. Among drugs which block renin-angiotensin-aldosterone system, only ace-inhibitors are deemed safe in breastfeeding [11]. Hence, changing to ace-inhibitor with combination of calcium channel blockers or beta-blockers and titrate with the goal of maintaining blood pressure (systolic < 140 and/or diastolic < 90) mmHg [12].

Conclusion

Given the rarity of RFD, this could pose challenges in managing pregnancy with underlying RFD. Pre-existing reno-vascular hypertension secondary to RFD predisposes to superimposed preeclampsia [2]. Apart from focusing on pregnancy, concurrently we have to look out for other cardiovascular complications such as left ventricular hypertrophy, carotid artery stenosis and stroke [1]. Thus, the ultimate goal is to manage the RFD and preventing from worsening cardiovascular status of the woman. Concurrently, we need to watch out for early manifestation of pregnancy related complication such as superimposed preeclampsia followed by planning for induction.

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