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Internal Medicine Insights

CASE REPORT

The pulseless pregnancy: A predictable outcome

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Abstract

Takayasu arteritis (TA) is known to affect young women of reproductive age. Pregnancy is not uncommon in TA patients, and the goal is to avoid complications in order to achieve a good pregnancy outcome.

We present two patients with TA for which both of them had 3 pregnancies with 2 successful deliveries. Both of our patients had not been properly prepared before pregnancy. They had hypertension, termination of pregnancy, spontaneous miscarriage, one small for gestational age baby and the majority of the deliveries required an elective caesarean section. However, both of them had stable disease activity and were maintained with low dose steroid and azathioprine throughout their pregnancies. Although the pregnancies were eventful, each of them managed to deliver two healthy babies.

Keywords: *takayasu arteritis, pregnancy, maternal outcome, fetal outcome, disease activity*

Introduction

Takayasu arteritis (TA) is a type of large vessel vasculitis characterized by chronic inflammation of the aorta and its main branches. Less commonly, the pulmonary arteries can also be affected. It was first described by the Japanese ophthalmologist, Mikito Takayasu in 1908 [1]. It is most common in Asia, particularly Japan, and in the Orient [2,3]. The annual incidence is 1-3/million in most populations. In Malaysia, Khor et al. reported a total of 40 patients with TA from April 2006 to September 2013, with a female-to-male ratio of 12:1 [4].

Inflammation of the blood vessels usually results in stenosis or occlusion, although aneurysms may also develop. Histologically, it is described as "granulomatous pan-arteritis", affecting all layers of the arterial wall [5]. The prevalence is highest among women of childbearing age, which is why it is also known as ''young female arteritis''.

Case Presentation

Case 1

A 37-year-old woman was diagnosed with Takayasu arteritis in April 2011. She first presented in 2004 to a private clinic with reduced effort tolerance, and was treated for idiopathic dilated cardiomyopathy secondary to post viral myocarditis. Her blood pressure (BP) was within normal range and her echocardiogram (ECHO) showed a dilated left ventricle with a poor ejection fraction (EF) of 30%. One year later, she was noted to have hypertension and further investigation revealed bilateral renal artery stenosis with a shrunken right kidney at 8.1 cm. She underwent a renal angiogram, which showed subtotal occlusion of the right renal artery and proximal left renal artery stenosis of 70%, followed by angioplasty and stenting of the left renal artery. Post stenting, her blood pressure was still difficult to control. A repeat renal angiogram was performed 7 months later, which showed progression of the stenosis with complete occlusion of the right renal artery and 50% in-stent restenosis (ISR) in the left renal artery. Her serum creatinine level was 113 µmol/L. She was referred to a urologist for further treatment, but no further surgical intervention was offered at that time because her renal function was stable. Her clinical condition, blood pressure and serum creatinine level were continued to be monitored.

Four years later, she was found to have unequal BP in her upper limbs and bruits in both carotids and left renal artery. Doppler ultrasound (USG) of neck arteries showed increased velocity in the left vertebral and right subclavian arteries, possibly due to stenosis. Computed tomographic angiography (CTA) showed bilateral renal artery stenosis with a shrunken right kidney, blocked proximal celiac artery, stenosed proximal superior mesenteric artery (SMA), but normal cerebral arteries. This was followed by a positron emission tomography (PET) scan, which confirmed increased accumulation of fluorodeoxyglucose (FDG) in the right carotid artery, aortic arch, pulmonary trunk, abdominal aorta, and SMA, suggestive of Takayasu arteritis. She was then referred to us for further evaluation and treatment.

Upon further questioning, she denied history of limb claudication, angina, Raynaud's phenomenon, carotidynia, unexplained gastrointestinal or neurologic symptoms. Her BP was controlled with the maximum dose of prazosin, hydrochlorothiazide, metoprolol, and methyldopa. Her erythrocyte sedimentation rate (ESR) was 41 mm/hr, c-reactive protein (CRP) 42.20 mg/L, creatinine 86 µmol/L, globulin 33 µmol/L, albumin 35 µmol/L, and hemoglobin 11.4 g/dL. She had an insignificant positive antinuclear antibody (ANA) of 1:40, nucleolar pattern. Other serology tests including double-stranded DNA (dsDNA), extractable nuclear antigen antibody (ENA), and antineutrophil cytoplasmic antibody (ANCA) were negative. She was treated with prednisolone at 0.5mg/kg/day as she worried about steroid side effects at a higher dose. Methotrexate (MTX) was administered and the dose was optimized slowly. Following that, her condition was stable.

At 6 months after initiation of therapy, she had a repeat CTA and a PET scan examination, which showed no progression and uptake in the arteries, indicating a resolution of the inflammation. Her ESR had improved significantly to 11 mm/hour. At this point, the patient and her husband expressed their wish to have a baby. In order to properly assess her risk, she was then referred to the cardiology team. Her angiogram showed complete occlusion of the right coronary artery (RCA) with collaterals from the left coronary artery (LCA), occlusion of the right vertebral, left subclavian, celiac, SMA, and ISR of the left renal artery. Stenting of the RCA and left renal artery was planned. However, she was found to be pregnant and upon further questioning, she had actually discontinued her MTX for 1 month prior. A multidisciplinary team discussion was held with her cardiologist and obstetrician. As her pregnancy was considered to be a high risk, she was advised for termination of pregnancy. She was also counselled for an appropriate contraceptive method thereafter and her MTX and prednisolone were continued.

Within that year, due to the erratic blood pressure control, angioplasty of the left renal artery was attempted twice but failed. She was once again advised against pregnancy. Unfortunately, she did not come for her follow-up with us subsequently. Two years later, the patient went to another centre for left renal angioplasty, which was successfully done. This had resulted her to have a better BP control and one of her antihypertensive medications was ceased. Three months after the angioplasty, she was pregnant and had self-stopped her MTX for the previous 4 months. As a result, azathioprine (Aza) was commenced, all her anti-hypertensive treatments were switched to pregnancy compatible medications, and aspirin was initiated. A repeat echocardiogram showed left ventricular hypertrophy with a dilated left ventricle and EF was 40-45%. After discussion with the cardiology

team and based on the previous angiogram finding, we decided to allow a high-risk pregnancy with frequent monitoring. Both the patient and husband were counselled. Her BP was difficult to control throughout her antenatal period, but there were no other complications and her serial feotal scans were good. She delivered a 2.7 kg baby girl at 38 weeks via elective lower segment cesarian section (LSCS).

Her disease was stable for 3 years until she came to our clinic with a positive urine pregnancy test (UPT). We faced the same problem in controlling her BP during this pregnancy but fortunately, she again went through the pregnancy safely. She delivered a 2.57 kg baby boy at 36 weeks via elective LSCS. After delivery, she was switched to an appropriate contraceptive method. Her disease was stable and prednisolone was discontinued in March 2019. She was maintained on Aza.

Case 2

A 31-year-old woman gave a history of recurrent syncopal attacks since 2014 but was not properly investigated. She was hospitalized for delivery of her first child and had a hypotensive episode after delivery. On examination, she was found to have no pulses in both radial and brachial arteries and a bruit over the left carotid artery. Her BP were not measurable in both upper limbs. Her blood tests showed high inflammatory markers and negative ANA, ANCA, thrombophilia screening and biohazards screening. Her CTA chest and abdomen showed uniform circular arterial wall thickening of the ascending, arch, and descending aorta, irregular wall thickening of the right brachiocephalic, left carotid arteries causing mild to moderate narrowing and complete occlusion of the left subclavian artery. Her renal arteries were spared. Her echocardiogram showed a left ventricular EF of 61 % without regional wall motion abnormalities.

She was diagnosed to have TA, and steroid and Aza were initiated. Magnetic resonance angiography (MRA) of the brain was performed to assess the extent of disease involvement, which confirmed the absence of the right common carotid artery, and right internal carotid artery and the proximal right subclavian artery were small and poorly visible. The large artery in the neck, lateral and posterior to the left common carotid artery was most probably a collateral artery. Her BP was controlled with single antihypertensive treatment. We were unable to perform a PET scan until 17 months after treatment because she was breastfeeding her baby, which showed no signs of active vasculitis. Her serial ESR levels following treatment also improved.

In May 2020, the patient had a spontaneous miscarriage at the 7th week of gestation. The couple expressed their wish to have another baby soon after. However, she was advised to hold her pregnancy until after assessment by the cardiology team.

However, two months later, she informed us that she was pregnant. A repeat echocardiogram showed an EF of 63 % and a mildly dilated left atrium. A multidisciplinary meeting was held, and the team had decided to allow pregnancy with close monitoring in view of the previous successful delivery after the onset of TA. The goal was to optimize the BP and to monitor disease activity. During her antenatal follow up, she had several episodes of high BP, but these were controlled by optimizing her antihypertensive treatment. A foetal scan however revealed a small for gestational age baby. She had no evidence of disease flare throughout. Eventually, she delivered a 2.4 kg baby at 37 weeks via elective LSCS. After delivery, her disease was stable on low dose steroid and Aza. She opted for an intrauterine device as her contraceptive method.

Discussion

Management of TA patients when they are pregnant is challenging and there are no proper guidelines established. Most guidelines for the management of pregnant women with TA come from small studies and case reports. Many studies have actually shown favourable pregnancy outcomes [6].

The main concerns are the impact of TA on pregnancy, especially on maternal and foetal complications, TA disease activity during pregnancy, and most importantly, the choice of treatment during pregnancy. Since the most ideal time for pregnancy in a TA patient is when the disease is in remission, preconception counselling is of utmost importance in all patients of reproductive age. The counselling should involve all the managing teams, patients and their partners. The main goal is to evaluate disease activity and assess the risk of existing comorbidities, both of which are important in determining the success rate of pregnancy. Some medications may need to be adjusted [7,8]. Unfortunately, in the case of our two patients, we did not manage to prepare them properly prior to conception. However, both patients and their partners were informed of all possible risks and complications when they were found to be pregnant.

Obstetric complications that may occur include gestational hypertension, preeclampsia, eclampsia, medical abortion, and higher rate of caesarean section [9,10]. As for the foetus outcome, baby of a TA patient has higher risk for intrauterine growth retardation (IUGR), intrauterine death (IUD), miscarriage, preterm delivery, and abruptio placenta [9-12]. As for our two cases, each patient had 3 pregnancies with only 2 successful deliveries, 1 spontaneous miscarriage and 1 termination of pregnancy due to medical reasons. Three out of the 4 deliveries were complicated by hypertension and required elective LSCS. One of these 4 babies was small for gestational age.

Assessment of TA disease activity during pregnancy is difficult. Some symptoms related to mechanical stress may mimic ischemic symptoms in TA, making it difficult to distinguish between them. Inflammatory markers such as ESR is not reliable because it is known to be increased during pregnancy. Doppler ultrasound is not easy to perform in patients with renal artery involvement, as it can be compromised as gestation progresses [6]. Another concern is the exposure of radiation and the safety of MRI and PET scan when a patient is pregnant. During the follow up, monitoring of blood pressure during pregnancy is not easy because in patients with arterial occlusion, blood pressure may be lower than the actual pressure.

The management of TA patients who are pregnant requires a multidisciplinary approach. The patient and foetus require more frequent antenatal visits, serial monitoring of BP in all 4 limbs, renal function, assessment of cardiac status, preeclamptic screening, and foetal growth monitoring [6,7]. Blood pressure must be closely monitored and treated from early pregnancy because it is associated with favourable pregnancy outcomes [6,13]. In patients who develop active disease during pregnancy, high-dose steroids must be considered. In refractory cases, biologic agents such as anti-TNF and certolizumab may be considered [6,13,14]. To date, no study has identified an optimal time for delivery, but most studies suggest that treating physicians should aim for a normal vaginal delivery if possible [13]. During delivery, consider shortening the second stage of labour as blood pressure can increase significantly during this phase. In the postpartum period, BP monitoring should continue for at least 24–48 hours after delivery, because of hemodynamic changes in the postpartum period may affect the blood pressure [2,9,15].

Conclusion

Pregnancy in a TA patient has a predictable outcome, provided the patient is properly counselled and screened before conception. Planning for pregnancy during disease remission is necessary to reduce maternal and foetal risks and must be managed with a multidisciplinary team. The most important treatment measure is to control blood pressure appropriately during pregnancy through the judicious use of antihypertensive drugs and to keep the disease in remission throughout pregnancy.

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