CASE REPORT

An endocrine cause of acute post-partum hypertension

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Summary: This is a case of acute peri-partum hypertension secondary to Conn's syndrome. The timing of presentation offers a rare insight into the hormonal physiology of pregnancy and its impact on blood pressure regulation. This case highlights the challenges of diagnosing primary hyperaldosteronism in the peripartum period and the high index of suspicion required by the obstetric physician.

Keywords: endocrinology, general medicine, hypertension, physiology, complications

INTRODUCTION

Hypertension is a common condition encountered during pregnancy and the peri-partum period, but it is only rarely caused by hyperaldosteronism. Our case demonstrates an exceptional clinical scenario where Conn's syndrome was concealed by the physiological changes that occur during pregnancy, offering insight into the physiology of blood pressure regulation during pregnancy and the peri-partum period.

CASE REPORT

A healthy 40-year-old woman of Chinese background, pregnant by in-vitro fertilization, presented to a routine antenatal appointment at five days past her estimated delivery date with new onset hypertension (178/104 mmHg) and proteinuria. All previous antenatal blood pressure readings were less than 120/80 mmHg. Her hypertension persisted and she underwent emergency lower segment caesarean section, delivering a healthy baby girl. Postoperatively she received diclofenac 50 mg TDS for a total of four days. Her blood pressure normalized and mother and baby were discharged home.

Nine days post partum, she re-presented with dyspnoea, orthopnoea and central chest discomfort. She was hypertensive (200/110 mmHg) with mild bilateral ankle oedema. Initial investigation revealed hypokalaemia (2.8 mmol/L) with a mild elevation of troponin (0.09 μg/L) and creatine kinase (305 U/L). Electrocardiogram showed U waves (hypokalaemia) and lateral ST depression, which along with the mild troponin rise was thought more likely from left ventricular strain rather than an acute coronary syndrome. Chest X-ray revealed cardiomegaly and mild pulmonary congestion. CT pulmonary angiography excluded pulmonary embolism, but demonstrated interstitial oedema and cardiomegaly. Transthoracic echocardiogram revealed mild global systolic dysfunction with an estimated left ventricular ejection fraction of 63%.

Hypertension-induced cardiac dysfunction was diagnosed and causes of secondary hypertension were investigated. Renal artery stenosis and phaechromocytoma were excluded by renal Doppler ultrasound and normal plasma metanephrines respectively. Thyroid function was normal. A 24 hour urine collection demonstrated proteinuria (0.38 g/day [<0.15]) and excluded Cushing's syndrome. Initial aldosterone was normal (277 ρmol/L [<860]) however renin was suppressed (<0.10 μg/L/hr [1.10–8.6]). The patient was hypokalaemic (3.3 mmol/L) at time of testing. Aldosterone-renin ratio (ARR) was later repeated and revealed markedly elevated aldosterone (2083 ρmol/L [<860]) and suppressed renin levels (0.10 μg/L/hr [1.10–8.6]). Resultant ARR of 20546 [<830] was consistent with primary hyperaldosteronism. No confirmatory testing such as a saline suppression test was undertaken. A non-contrast CT revealed a 1.6cm right adrenal adenoma and adrenal vein sampling confirmed right-sided Conn's syndrome.

Initial management required 240 mmol of intravenous potassium followed by oral supplementation of 198 mmol/day. Enoxaparin 40 mg daily was administered for venous-thromboembolism prophylaxis. After careful titration she required verapamil XR 240 mg daily, prazosin 5 mg tds and hydralazine 100 mg bd until a laparoscopic right adrenalectomy was performed without complication six weeks after diagnosis. All antihypertensive medications and potassium supplements were ceased postoperatively. Histopathology confirmed a right adrenal adenoma. Repeat ARR, biochemistry and echocardiogram were normal and she remains asymptomatic and normotensive.

DISCUSSION

Primary hyperaldosteronism is rare and characterized by hypertension, hypokalaemia and metabolic alkalosis. In the majority of cases this is due to an adenoma of the adrenal cortex – Conn's syndrome.[1] Review of the literature, including

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the review by Matsumoto *et al.*[2] and subsequent reported cases, reveals 29 cases of primary aldosteronism associated with pregnancy.[2–9]

Reported complications include intrauterine growth restriction, placental abruption, preterm labour and three cases of fetal death in utero.[2,7] Maternal complications include one report each of cardiac failure, renal failure and fatal aortic dissection.[2] The majority of reported cases are associated with progressive hypertension during pregnancy (with at least six warranting urgent surgical intervention).[2,7,8] Six other cases were associated with masking of pre-existing hypertension during pregnancy followed by post-partum hypertension and hypokalaemia,[3,5,10,11] although none as severe and acute as this patient's presentation.

In pregnancy volume expansion occurs to accommodate placental perfusion. A complex interplay of hormonal mechanisms stimulate the renin-angiotensin-aldosterone system (RAAS) including placental oestrogen and progesterone secretion, local placental RAAS production and decreased vascular resistance.[1] Plasma renin activity steadily increases from early pregnancy, reaching a peak at 20 weeks gestation with levels seven-fold higher than pre-pregnancy.[12] Aldosterone levels increase ten-fold during pregnancy, roughly tripling by the eighth week of gestation and peaking at 38 weeks.[12] However, there is a net decrease in blood pressure, lowest around the 28th week of gestation and returning to pre-pregnancy levels around term.[12] This is due to high levels of circulating progesterone, which increases 17-fold.[12] Progesterone has a direct natriuretic effect in the renal proximal tubule and competitively inhibits aldosterone at the mineralocorticoid receptors in the distal tubules, interrupting its sodium-retaining activity.[2] Despite these changes the ARR remains relatively conserved and can be used for diagnosis of Conn's syndrome during pregnancy.[12]

This is a case where the clinical features of Conn's syndrome were ameliorated by the hormone changes of pregnancy. Hyperaldosteronism was overshadowed by the physiological increase in aldosterone that occurs during pregnancy and its effects were counteracted by progesterone. As our patient reached term and placental function decreased, the withdrawal of circulating progesterone enabled aldosterone to act unopposed, precipitating acute peri-partum hypertension. It is uncertain whether lactation played a role in the acuity of the presentation. Prolactin has been shown to potentiate both the antinatriuretic effects of aldosterone and vasoconstrictor effects of angiotensin in animals[13] and cause sodium retention in humans.[14] Although elevated during pregnancy, the potentiating effects of prolactin would likely be greatest post-partum, when the inhibitory effect of progesterone is lost.

Our patient's initial aldosterone level was 'inappropriately' normal in the setting of suppressed renin. Although suggestive of primary hyperaldosteronism, it was difficult to interpret given there were multiple factors that may have influenced the RAAS. Recent NSAID administration for example, can cause a false-positive ARR result. NSAIDS may have also exacerbated her hypertension and fluid overload, and should be used with caution in patients with post-partum hypertension.[15] There is evidence that enoxaparin, which our patient received, may suppress aldosterone, particulary in the first few days of administration.[16] Medications such as potassium wasting diuretics, angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers can cause false-negative results; however none were administered in this case.[17] Uncorrected hypokalaemia, and mobilisation of extracellular fluid after delivery may have also influenced the result. Repeat ARR was clearly diagnostic for hyperaldosteronism, highlighting the value of repeat testing if results are inconclusive or difficult to interpret.

Our choice of anti-hypertensive agents was influenced by an early suspicion of Conn's syndrome. Prazocin, verapamil, and hydralazine have minimal effect on measurement of ARR and therefore can be used during diagnosis.[17] We chose to continue these medications after diagnosis as a short-term measure while awaiting surgical management. Once diagnosis is established, there is a wide range of antihypertensive options available, including potassium-sparing diuretics.

CONCLUSION

This is a case of acute peri-partum hypertension secondary to Conn's syndrome. The clinical features of hyperaldosteronism were masked by the hormonal changes during pregnancy. The acute onset of symptoms in this case offers a unique insight into the hormonal physiology of blood pressure regulation in pregnancy by identifying the timing of placental hormone changes. This case highlights the complexity of presentation and diagnosis of Conn's syndrome during pregnancy and peri-partum.

DECLARATIONS

Competing interests: None declared.
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Ethical approval: Ethical approval was not required, however written consent was provided by the patient for the publication of this case.
Guarantor: IB.
Contributorship: SP and SV were involved in the diagnosis and acute and long-term management of the patient. IB and DP were involved in writing the manuscript and researching the literature review. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

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