



Case Report

Severe hypertension complicating pregnancy, pheochromocytoma: A rare case report

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ARTICLE INFO

Article history:

Received 04-12-2019

Accepted 06-12-2019

Available online 21-02-2020

Keywords:

Pheochromocytoma
prevalence in hypertensive

ABSTRACT

Introduction: Pheochromocytoma, a rare tumor arising in the adrenal medulla, It is a catecholamine-producing tumor. It's prevalence in hypertensive patients is 0.2%, and 0.002% of pregnancies. Its clinical presentation is typically hallmarked by sustained or intermittent hypertension associated with paroxysmal symptoms. Pheochromocytoma should also be considered if a patient has labile hypertension, hypertension resistant to treat by antihypertensive therapy, or paroxysmal symptoms ("spells"). Correct diagnosis is essential as surgical resection of the tumor dramatically reverses the clinical symptoms and may cure the hypertension. Pheochromocytoma with clinical presentation was earliest reported in 1926 when Cesar Roux in Switzerland and Charles H. Mayo in the United States successfully removed pheochromocytomas to cure the catecholamine-associated symptom complex.

During pregnancy the clinical presentations can be easily confused with severe pre-eclampsia. The presentation of uncontrolled hypertension and headache not responding to medication may be misleading diagnose. It can be even more challenging if pheochromocytoma is undiagnosed. This adrenal tumor also increases the risk of adverse pregnancy outcome like abortion, still birth or pre term delivery.

We report this case from People's College of Medical Science & Research Centre a case of Pheochromocytoma with Pregnancy

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1. Introduction

Pheochromocytoma, a rare tumor arising in the adrenal medulla, It is a catecholamine-producing tumor. It's prevalence in hypertensive patients is 0.2%, and 0.002% of pregnancies. Its clinical presentation is typically hallmarked by sustained or intermittent hypertension associated with paroxysmal symptoms. Pheochromocytoma should also be considered if a patient has labile hypertension, hypertension resistant to treat by antihypertensive therapy, or paroxysmal symptoms (" spells "). Correct diagnosis is essential as surgical resection of the tumor dramatically reverses the

clinical symptoms and may cure the hypertension.¹

Pheochromocytoma with clinical presentation was earliest reported in 1926 when Cesar Roux in Switzerland and Charles H. Mayo in the United States successfully removed pheochromocytomas to cure the catecholamine-associated symptom complex.²

During pregnancy the clinical presentations can be easily confused with severe pre-eclampsia. The presentation of uncontrolled hypertension and headache not responding to medication may be misleading diagnose. It can be even more challenging if pheochromocytoma is undiagnosed. This adrenal tumor also increases the risk of adverse pregnancy outcome like abortion, still birth or pre term delivery.^{3,4}

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2. Case Report

A 26 year old Gravida 3 Para 0 Abortion 2 admitted with Amenorrhoea 4 months. She presented with palpitation, perspiration, epistaxis. She was a diagnosed case of Pheochromocytoma since 3 yrs. On admission her blood pressure was 200/120 mm of Hg. Her previous pregnancy losses were also of early pregnancy of late 1st Trimester and early second trimester and no live baby.

She was referred by Physician with history of 4 months amenorrhoea having uncontrolled hypertension. USG report showed 14 weeks 3 days with absent heart beats suggestive of intka uterine feal dimise. The anti - hypertensives given to her were Prazocin 10 mg BD and Labetalol 100mg TDS. Her blood pressure range was high (160 /110 mm of Hg) despite the medication. Her urine proteins by dipsticks was negative. All lab reports of complete blood count, liver, kidney functions and coagulation profiles were normal. Abortion was induced using prostaglandins. Dinoprostone gel 0.5 mg was instilled intra cervical and followed by misoprostol 200mg 2 doses. The induction abortion interval was 24 hrs.

The MRI scan for whole abdomen was done later which showed 5.1x 4.8x 6 cm hyperintense T1 and Hypointense T2 mass arising from right adrenal gland (Figure 1). 24 hours urine chromogranin A was 203.3 ng /ml, Metanephrine 78.47 $\mu\text{g/g}$, Normetanephrines were 10562.71 $\mu\text{g/g}$ were elevated.

Her surgery was planned after stabilizing her and after attaining adequate control of BP by the senior endocrinologist and physicians. Surgery was performed under general anesthesia. epidural catheter was additionally inserted for post operative pain relief. Invasive (intra-arterial) blood pressure (IBP) monitoring was done throughout the surgical procedure. Right side adrenalectomy was performed by team of senior surgeons. (Figure 2). Immediate post operatively the patient vitals were closely monitored under supervision of senior anesthetist, senior endocrinologist and physicians team. Her BP was controlled post operatively and she was continued on anti -hypertensive medications. Her post operative period was uneventful. Histopathology diagnosis zellballen (small nests or alveolar pattern), trabecular or solid patterns of polygonal / spindle shaped cells in rich vascular network, round / oval nuclei with prominent nucleolus confirming the diagnosis Cells have finely granular basophilic or amphophilic cytoplasm.

Upon post operatively follow up during 3rd month her 24 hour urine catecholamines and metanephrines were done and reports came to within normal levels.

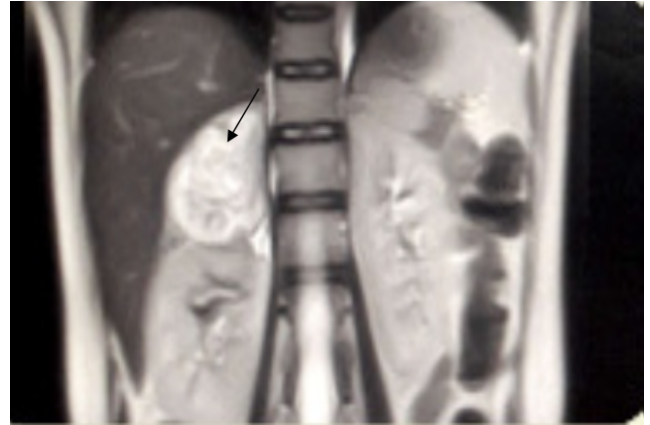


Fig. 1: MRI Image of the Mass at Right Adrenal Gland

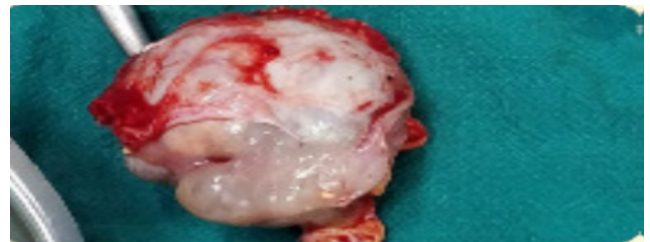


Fig. 2: Tumor Mass, Right Adrenalectomy done

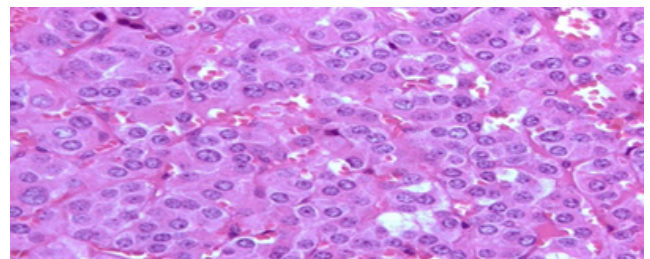


Fig. 3: Microscopic Picture of Pheochromocytoma

3. Discussion

Our 26yr old patient manifested with classical presentation of uncontrolled BP, palpitation, perspiration and epistaxis. She posed challenge in the management as presented at 14 weeks 3 days with intra uterine fetal death requiring immediate abortion.

Pirtskhalava reported A 36-yr-old previously healthy woman (gravida 4, para 3) presented to tertiary care centre at 26 weeks four days gestation with a history of labile blood pressure and severe hypertension.⁵ A two week prior to admission she began having episodes of severe headache, sweating, nausea and dizziness. She had severe hypertension with a blood pressure of 220/120 mmHg. Ultrasound showed a 11.6 cm x 9.2 cm right adrenal mass, biochemical investigations confirmed the diagnosis of pheochromocytoma.

Chmielewski G and co-workers reported two cases of pheochromocytoma in pregnancy.⁶ Their first case was a 29-year-old woman with recently diagnosed MEN2A syndrome whose tests revealed bilateral pheochromocytomas of the adrenal glands and medullary thyroid cancer. She did not consent to surgery during pregnancy and was treated conservatively during that time. Due to risk of hypertensive crisis, cesarean section was performed in the 33rd week of pregnancy. The patient underwent adrenalectomy and thyroidectomy. They reported a second case of a 29-year-old woman with history of MEN2A syndrome, whose pregnancy was discovered during preparation for adrenalectomy due to pheochromocytoma. She was treated with transabdominal adrenalectomy in the 21st week of pregnancy. The subsequent childbirth was uneventful.

Mazza, Armigliato M and co-associates described “both Pheochromocytoma (PH) and paraganglioma (PG) may be asymptomatic as 30% of cases are normotensive or have orthostatic hypotension and in these cases the 24h ambulatory blood pressure (BP) monitoring is essential to diagnose and treat HT.”⁷ “Pre-operative control of BP as part of management requires the administration of selective α 1-adrenergic blocking agents (i.e., doxazosin, prazosin or terazosin) followed by a β -adrenergic blockade (i.e., propranolol, atenolol). They suggested β -adrenergic blockade should not be started initially because blockade of vasodilatory peripheral β -adrenergic receptors with unopposed α -adrenergic receptor stimulation can cause further rise of BP. Labetalol is conventionally thought as appropriate agent due to its α - and β -adrenergic antagonism, studies do not support its use in this clinical setting. As an alternative regimen, the administration of vasodilators like calcium channel blockers (i.e., nifedipine, nifedipine) may be required to control BP. Oral or sublingual nifedipine are short acting and potentially dangerous in patients with hypertensive emergencies so they are not recommended.”

Biggar MA and Lennard TW reported 135 cases in the Systematic review.⁸ 77 pregnancies involving 78 fetuses were analyzed. Fetal and maternal mortality rates were 17 per cent. They reported better outcomes when the diagnosis of pheochromocytoma was made during the antenatal period than when it was done during labour or immediately postpartum (survival of both mother and fetus(es) in 48 of 56 versus 12 of 21 respectively; $P = 0.012$). Early diagnosis in the second trimester had a better outcome.

Quartermaine G reported nested case-control comparisons involving the UK Obstetric Surveillance System cases as well as those identified in the literature were performed for pregnancy outcome data using UKOSS controls with uncomplicated singleton ($n = 2250$) pregnancy and data from the Office of National Statistics (ONS).⁹ UK Obstetric Surveillance System study with case-control comparisons. Fifteen pregnant women were reported ten

phaeochromocytoma, three primary aldosteronism and two Cushing's syndrome. All women had severe hypertension, and in those diagnosed in pregnancy prior to conception. They also reported tumor has a significantly increased risk of adverse pregnancy outcomes, with increased rates of stillbirth, preterm labour and operative delivery. Our case also presented with previous 2 abortions and current pregnancy also was missed abortion.

Shigeo Iijima also reported fetal risks are mainly determined by the vasoconstrictive effects of maternal catecholamine on uteroplacental circulation, because the fetus is protected from the direct effects of high catecholamine levels at the placental interface.⁴ Uteroplacental insufficiency may lead to spontaneous abortion, fetal growth restriction, premature delivery, and fetal hypoxia, followed by fetal distress and/or birth asphyxia. Adrenalectomy is recommended during the second trimester.

Manoharan M and colleagues reported “Adrenal disorders may manifest during pregnancy for the first time, or present from before pregnancy as either undiagnosed or diagnosed and treated.”¹⁰ They may present as hormonal hypofunction or hyperfunction, or with mass effects or other non-endocrine effects. Adrenal disorders such as Cushing's syndrome, Addison's disease, pheochromocytoma, primary hyperaldosteronism and adrenocortical carcinoma are rare in pregnancy. Pregnancy presents special problems in the evaluation of the hypothalamic-pituitary-adrenal and renin-angiotensin-aldosterone axis as these undergo major changes during pregnancy. Diagnosis is challenging as symptoms associated with pregnancy are also seen in adrenal diseases.”

Yogish C suggested that fractionated plasma free metanephrines are more sensitive than 24-h urinary metanephrines and catecholamines in testing genetically predisposed patients for pheochromocytoma.²

Lenders JWM, Langton K, Langenhuijsen JF, Eisenhofer G. The wellbeing of mother and fetus are at stake if not diagnosed and treated antenatally and timely.¹¹ The diagnosis is frequently overlooked because of the aspecific nature of signs and symptoms and confusion with pregnancy-related hypertension. Measurements of plasma or urinary free metanephrines have the highest diagnostic accuracy. MRI is preferred over ultrasonography. The optimal time for surgical removal is before 24 weeks of gestation or at/after delivery. Laparoscopic adrenalectomy should be preceded by medical pretreatment. Cesarean delivery is preferred in these patients; vaginal delivery might be considered in selected pretreated patients.

Lenders JW in his descriptive report stated that “In pregnant patients, similar to non-pregnant patients increased plasma and/or 24-h urine (nor)metanephrine concentrations most reliably confirm the diagnosis of pheochromocytoma.”¹² MRI and ultrasound are the two imaging techniques which are safe during pregnancy to

diagnose the tumor. During pregnancy, pretreatment consists of alpha blockade as usual. Dosing of α -adrenergic receptor blockers during pregnancy is a challenge as hypertension must be treated while preserving adequate uteroplacental circulation. When diagnosed before 24 weeks of pregnancy, it is recommended to remove the tumor in the second trimester, where as removal is postponed till after delivery when the diagnosis is made in the third trimester and medical pretreatment is sufficient. laparoscopic surgery is the better approach for resection of the tumor but as per literature There is no consensus about the preferred route and timing of delivery. Therefore, their view was that decisions should be made on an individual basis by an experienced and dedicated multidisciplinary team.

Lenders further described that pheochromocytoma is potentially serious condition, which can be revealed by pregnancy. Less than 250 cases described in the literature. The rarity of this association and similarity with pregnancy-induced hypertension explains the frequency of unknown diagnoses during pregnancy.

Chmielewski G et al reported two cases of pheochromocytoma in pregnancy. They reported due to extreme rarity of pheochromocytoma in pregnancy, its impact on the mother and the fetus remains poorly understood. demands a multidisciplinary and individualized approach.^{13,14}

Thus we conclude that early diagnosis of pheochromocytoma requires high index of suspicion when patient presents with high BP, palpitation and perspiration. In addition to radio imaging, plasma free metanephrines or urinary fractionated metanephrines are mandatory for correct diagnosis. A multidisciplinary team approach involving endocrinologists, physicians, obstetricians, surgeons, anesthetist is the best approach to treat the case

4. Source of funding

None.

5. Conflict of interest

None.

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Cite this article: Kalra R, Jindal S, Dave SP, Bansal S, Loya BM, Garg N, Khare I. Severe hypertension complicating pregnancy, pheochromocytoma: A rare case report. *Indian J Obstet Gynecol Res* 2020;7(1):129-132.