Research Article

Paraganglioma: A Difficult and Threatening Ordeal of Pregnancy

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Abstract

Paraganglioma (PGL) in pregnancy is an extremely rare condition and its diagnosis is often difficult because the clinical symptoms can mimic those of preeclampsi gestational hypertension and gestational diabetes, here we report the case of a 24-year-old female primigravida with known case of hypothyroidism, presented with labile hypertension, resting tachycardia and hyperglycemia with protinuria at 27 week gestation. We suspected that she might have gestational diabetes along with hypertension and Catecholamine Secreting Tumor (CST) as her renal Doppler was suggestive of extra adrenal mass at left lumber region which confirmed on MRI abdomen pelvis and serum catecholamine levels were found to be significantly increased. She underwent laparoscopic mass removal and the pathology confirmed PGL. When typical paroxysmal hypertension and resting tachycardia is accompanied by headache, palpitation, and sweating during gestational period adrenal or extra adrenal tumor should be suspected.

Keywords: Catacholamine Secreting Tumors (CST); Paraganglinoma (PGL); Pheochromocytoma (PCC); Plasma free metanephrin; Normetanephrin; Preeclampsia

Introduction

Preeclampsia/eclampsia are one of the leading cause of maternal mortality worldwide 50,000 maternal deaths occurs every year, occurring at a rate of 1.5/100,000 live births. [1,2] Preeclampsia can be confused with many other clinical diseases including acute fatty liver, cholestasis of pregnancy, catecholamine-secreting tumors like PCC and PGL. [3]

PCC/PGL is a rare type of CST that arises from chromaffin tissues in the adrenal gland and rarely seen during pregnancy (Approximately 7 in 100,000) and PCC is more common than PGL. [4,5]90% of pregnant women have PCC or PGL symptoms just before delivery, which may lead to a delay in diagnosis and increased health risks for both the fetus and the mother. [6] (B2) PCC/PGL might be suspected in a patient by observing characteristic manifestation that is 5 H's Paroxysmal hypertension, headache, hyperhidrosis, hyperglycemia and hyper metabolism. [7]

Case History

24 year old female primigravida with 27 weeks of gestation was referred in our hospital with recently detected hypertension (Blood Pressure (BP) was 210/110 mm of mercury (hg)) with hyperglycemia (Random blood sugar was 140 mg/dl) with protinuria which initially misdiagnosed as preeclampsia and gestational diabetes.

She had history of headache, sweating and intermittent palpitation since last 2 years but relived on medications. She had labile blood pressure details mentioned in Table 1. Due to persistent symptoms and uncontrolled blood pressure patient was investigated for secondary hypertension in form of Renal Doppler it was suggestive of large well defined solid heteroechoic predominantly hypo echoiclesion measuring 62 × 66 × 70 mm (AP × TR × CC) in left lumbar region anterior to the perirenal fascia suggestive of PCC while other investigation suggestive of protinuria and hyperglycemia (only single reading of RBS was 140 all other are normal with normal glycosylated hemoglobin).

To confirm our diagnosis her MRI abdomen and pelvis was done without revealing fetus identity along with plasma free metanephrin and normetanephrin. Report was suggestive of solid round to oval shaped lesion measuring approximately 66 × 68 × 80 mm (AR × TR × CC) with smooth margin noted in retro peritoneum just anterior to left kidney suggestive of neoplastic etiology most likely extra adrenal PGL/PCC [Figures 1-3] while serum plasma free metanephrin and free normetanephrin value were higher side [Table 1] so blood parameters and radiological findings were correlated with our diagnosis of PGL.

As patient was primigravida our primary goal was mother and fetus safety with control of blood pressure. Controlling blood pressure was difficult as BP was fluctuating from systolic 210-100 mm of hg and Diastolic was 120-80 mm of hg, BP was

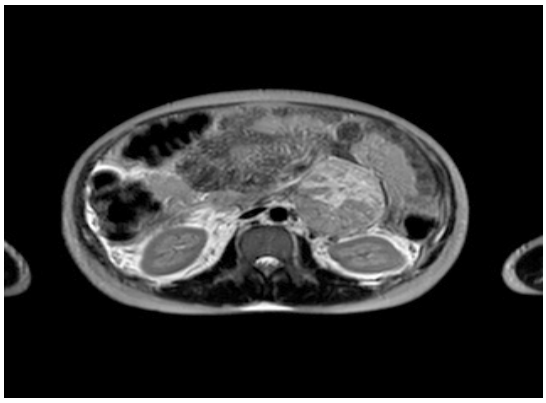

Figure 1: MRI Abdomen and pelvis.

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controlled with alpha blocker and later on addition of beta blocker. After starting medications patient was symptomatically better but after 8 days of admission she developed fetal distress in form of fetoplacetal insufficiency, As mother health was deteriorating termination of pregnancy was planned [Table 2], We can't revived fetus which delivered vaginally with help of magnesium sulphate, but mother blood pressure was under control with help of alpha blocker (prazosin) and beta blocker (lobetalol) and patient got discharge with medication.

After 1 week of discharge patient reassessment was done. At that time her blood pressure was under control with help of medications so her DOTA scan was done It was suggestive of a well-defined mass of 67 × 63 × 80 AP × TR × CC) mm with increased somatostat in receptor expression seen at left lumber region of abdomen (SUV max=6.6) located at lower pole of left kidney so finding suggestive of Neuro Endocrine Tumor (NET)-extra adrenal PGL [Figures 4 and 5]. After scan patient was planned for laparoscopic extra adrenal mass removal with multidisciplinary approach, mass removed of size 67 × 62 × 27 mm [Figures 6 and 7] and studied histo pathologically which was suggestive of PGL [Figures 8 and 9].

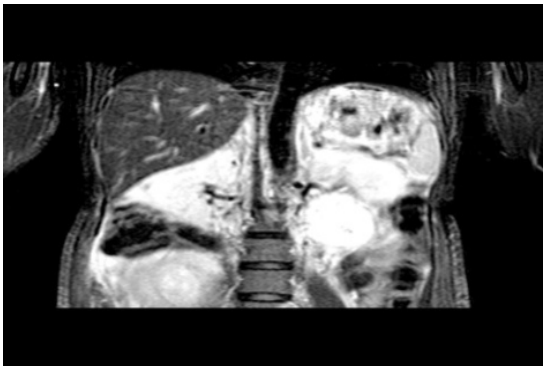

Figure 2: MRI Abdomen and pelvis.

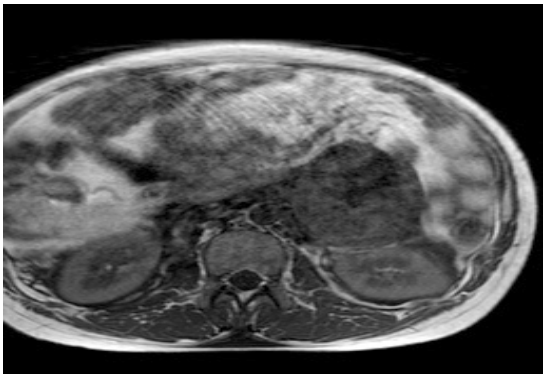

Figure 3: MRI Abdomen and pelvis.

Table 1: 24 hours Ambulatory Blood pressure and pulse rate monitoring reports.

Parameters	Average value	Maximum	Minimum
Systolic blood pressure(mm of hg)	144	170	123
Diastolic blood pressure(mm of hg)	103	119	86
Pulse Beats/minute	95	118	80

Table 2: Blood parameters of patients.

Parameters	Patient values	Normal values
Plasma free metanephrine	380 pg/ml	<65
Plasma free Normetanephrin	7196 pg/ml	<196
Total proteins	5.7 gm/dl	6.3-8.2 gm/dl
Tsh	9.8	
Serum cortisol	22.17 ug/ml	
Urinary investigations		
Urine albumin	3+	
24 Urinary proteins	4839 mg/24hr	20-140

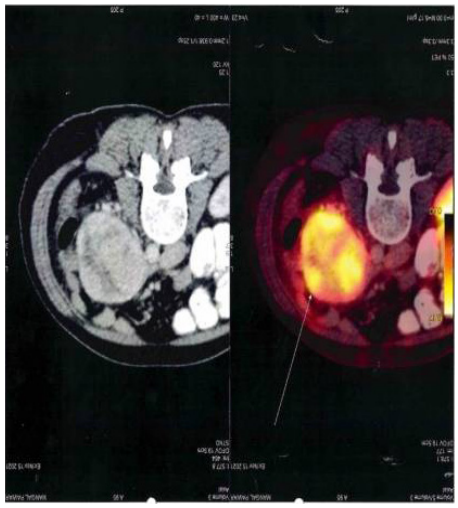

Figure 4: Gallium -68 DOTANOC PET SCAN.

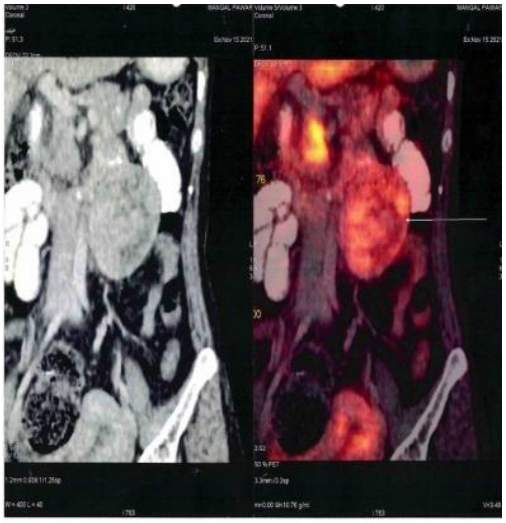

Figure 5: Gallium -68 DOTANOC PET SCAN.

Figure 6: Gross of Paraganglioma.

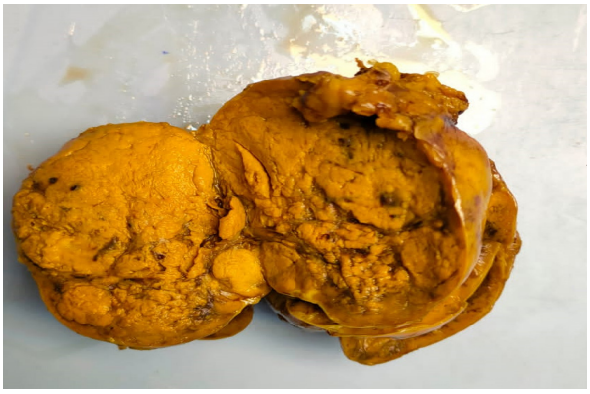

Figure 7: Gross of Paraganglioma.

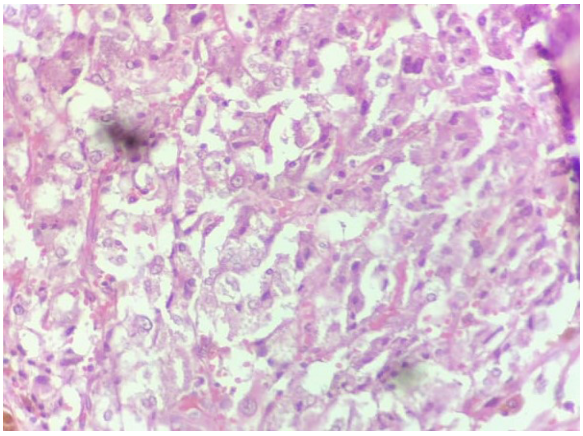

Figure 8: Histopathological examination of tumor.

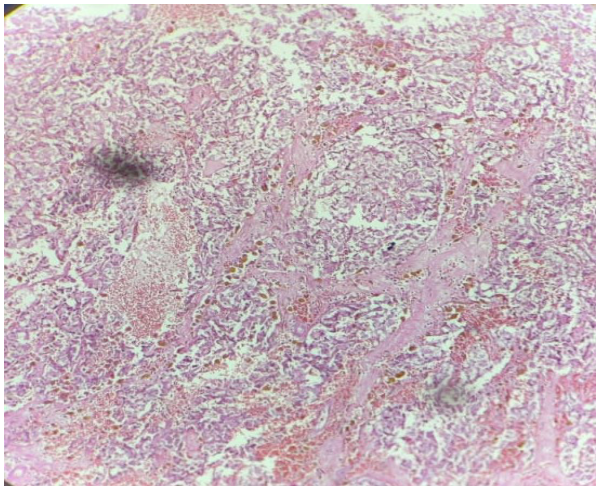

Figure 9: Histopathological examination of tumor.

It was multidisciplinary approach, after removal of mass patient was kept in the Intensive care unit for 2 days for observation. Post-operative patient had one episode of rise in blood pressure (170/100 mm of hg) along with tachycardia which was we controlled with beta blocker and patient discharged successfully without any medication.

Discussion

According to the 2017 World Health Organization (WHO) classification, Adrenal CST divided into two categories intraadrenal PGL, which is more commonly referred as PCC and extra adrenal PGL because the two tumor types cannot be distinguished based on histological characteristics, anatomical location is utilized to separate them. [8,9]

Extra adrenal PGL can develop from either sympathetic or parasympathetic paraganglia chain. Generally sympathetic PGL is catecholamine secreting functional tumor and primarily seen in the abdominal and thorax area. [10] While PGL deriving from the parasympathetic chain are catecholamine non-secreting tumors and located in neck and skull base. [11] In this case report we detected PGL in abdominal area. Many times diagnosis for CST delayed in pregnancy as it is difficult to differentiate signs and symptoms of other common disorder which observed during pregnancy that is hyper emesis gravidarum, gestational induced hypertension, preeclampsia, eclampsia and gestational diabetes mellitus. [12,13]

In this case patient presented with confusing clinical symptoms and laboratory findings in which PGL pretend to be as preeclampsia or gestational hypertension and gestational diabetes. Severe hypertension along with proteinuria in favor of severe preeclampsia, although resting tachycardia and severe sweating are not typical sign of this disease. Generally preeclampsia occurs in second trimester after 20 week of gestation as compared to CSTs which can shows symptoms and signs at any phase of gestation. [14] The fact that this patient only had first episode of paroxysmal episode of hypertension which was labile in nature associated with resting tachycardia in third trimester lead to look for PCC/PGL as a differential diagnosis. However previously asymptomatic tumor can shows symptoms for first time at late gestational age due to increased abdominal pressure due to fetal movement, uterine enlargement, uterine contraction, labor, physical and emotional stress, although catecholamine do not cross placenta but utero-placental insufficiency occurs due to paroxysmal reduction and increment of blood pressure that may lead to intrauterine hypoxia. [15]

When diagnosis of CSTs is suspected from clinical history and physical examination, immediate biochemical markers should be performed for confirmation of diagnosis. Essential test for diagnosis of CSTs is confirmation of excessive catecholamine secretions. [16] Most sensitive test for diagnosis of PCC and PGL are measurement of plasma free metanephrin, normetanephrin or urinary fractionated metanephrin but evidences suggest that plasma free metanephrin and nor metanephrin are better than urinary parameters for diagnosis of pheochromocytoma. [17] MRI without Gadolinium is diagnostic imaging test of choice in pregnancy with suspected case of PCC/PGL as it provides good visualization of abdomen and pelvis without radiation, [18] But golden test for diagnosis of PCC/PGL is MIBG (Metaidobenzylgunidine) scan but not recommended in pregnancy due to potential undesirable effect on fetus. [19]

Compared recent nucleotide (DOTA PET, FDOPA PET and FDG PET) scans MIBG and MRI scan are less sensitive [20-22] among nucleotide scan DOTA PET SCAN is more sensitive compared to others. [23]

The management of CST in pregnancy involves blood pressure control and avoidance of labile blood pressure and it requires proper equilibrium between vasodilatation and vasoconstriction to avoid fetal demises. Although surgical removal of tumor is

definitive treatment but medical management also important. [24]

Phenoxy benzamine, a non-specific, long-lasting α-adrenergic antagonist is the drug of choice even though it crosses the placenta fair neonatal outcomes after phenoxy benzamine treatment in pregnancy has been reported. [25,26] Neonatal respiratory distress and hypotension have been documented in some cases whose mothers were treated with phenoxy benzamine, it is therefore suggested neonates should be monitor after delivery whose mother was taking pheoxybenzamine for treatment. [27] Maternal tachycardia observed during use of phenoxybenzamine due to noradrenaline release from presynaptic nerve. While hypotension documented due to its prolonged half-life and irreversible blockade of α-adrenoceptors. [25] Alternatives to phenoxy benzamine include other alpha-adrenergic antagonists such as prazosin, and doxazosin, these agents produce less tachycardia with shorter duration of action when compared with phenoxybenzamine, which allow them in dose titration and decreased evidence of postoperative hypotension. [15,28] In our case patient blood pressure was under control on alpha blockers and beta blockers before surgery and all antihypertensive drug was stopped after surgery. Methyldopa which commonly used for hypertension during pregnancy may worsen the symptoms of CST hence this drug should be avoided. [29]

Traditionally it has been suggested that vaginal delivery should be avoided in pregnant women with PGL/PCC. [30] As there is high risk of hypertensive crisis during active labor but some cases are noted in literature of successful vaginal delivery without maternal and fetal mortality [31-35]. Unfortunately in our case fetus cannot be survived which was delivered by vaginally without damaging mother health as magnesium sulphate inhibits secretions of catecholamine.

In cases where the CST diagnosis is established during the third trimester, the laparoscopic approach may be difficult due to the enlarged uterus. Therefore, medical treatment is commenced with observation until sufficient fetal maturity is achieved. Delivery is then planned during final trimester, with concurrent or delayed adrenalectomy. [5,14] In our case mass was removed via laparoscopic approach after 1 week of delivery. After surgical removal of CST, careful post-surgical vital monitoring required as patient may go land up into hypovolumic shock due to sudden fall in catecholamine levels after removal of CST. [36] But in our case it was managed properly and patient was discharged without any medication for hypertension.

Conclusion

Although PGL is a rare cause of hypertension in pregnancy, it should be considered in differential diagnosis in pregnant female who presented with atypical hypertension and symptoms. A multidisciplinary team approach is important for the management of pregnancy and PGL for better outcome of patient.

Conflict of Interest

Nil

Authors Contribution

We Authors of original article Paraganglinoma: A Difficult and Threatening Ordeal of Pregnancy declare that they have no competing interests and study was not sponsored by any one for publication.

Acknowledgement

We, the undersigned, give an undertaking to the following effect with regard to our article titled Paraganglinoma: A difficult and threatening ordeal of pregnancy submitted for publication in the Journal, Indian Academy of Clinical Medicine:-

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