MEDWIN PUBLISHERS
Committed to create value for Researchers

Medical Journal of Clinical Trials & Case Studies
ISSN: 2578-4838

Pregnancy and Pheochromocytoma

Merve K, Emre K* and Hakan D

Department of Obstetrics and Gynecology, Bilecik State Hospital, Turkey

***Corresponding author:** Emre Köle, Department of Obstetrics and Gynecology, Bilecik State Hospital, Bilecik, Turkey, Email: drmehmetcelik@hotmail.com

Research Article

Volume 3 Issue 3

Received Date: May 13, 2019

Published Date: June 07, 2019

DOI: 10.23880/mjccs-16000223

Abstract

Determining the etiology of Hypertensive Disorders of Pregnancy (HDPs) is important to reduce maternal and fetal mortality. Pheochromocytoma is included in the differential diagnosis of hypertension during pregnancy, which is a rare neuroendocrine tumor but has a high mortality. Pheochromocytoma may not present a specific symptom or finding during pregnancy and may be detected just before birth. Characteristic paroxymal attacks such as palpitations, sweating, headache and severe hypertension attacks may indicate pheochromocytoma. In pregnant women who are considered to have an increased risk of developing a pheochromocytoma, 24-hour urinary fractionated metanephrines and catecholamine levels are measured for diagnosis. To detect tumor localization, ultrasonography and Magnetic Resonance Imaging (MRI) are used as imaging method. Although surgical removal is the main treatment of pheochromocytoma, alpha-blockers are used for hypertension. In pregnant women, the timing of tumor surgery varies according to gestational age, the severity of maternal symptoms and the risks of termination of pregnancy. In hypertensive cases during pregnancy Pheochromocytoma is a rare, potentially life-threatening tumor that should be kept in mind. Today in these patients, fetal and maternal mortality can be reduced with appropriate treatment. For the proper management and treatment of pheochromocytomas, multidisciplinary team working is essential in the tertiary health centers.

Keywords: Pregnancy; Hypertension; Pheochromocytoma

Abbreviations: HDPs: Hypertensive Disorders of Pregnancy; MRI: Magnetic Resonance Imaging; Aıs: Adrenal Incidentalomas; CT: Computed Tomography.

Introduction

Pheochromocytoma is a metabolically active neuroendocrine tumor that originates from chromaffin cells, 90 % of which is located in the adrenal medulla [1]. The incidence of pheochromocytomas is approximately 0.2 to 0.9 case per 100.000 individuals per year, and the malignant forms account for approximately 10% of all cases [2-8]. Approximately 0,4 % of the patients with adrenal incidentalomas (AIs) are pheochromocytoma. The prevalence of pheochromocytoma is 0.2 % to 0.4 % among hypertensive patients. May cause severe and fatal hypertensive crises [3] . Before week 20 of gestation, pheochromocytoma should be kept in mind as a differential diagnosis in patients with severe hypertension or accompanied hypertension, palpitation, headache and excessive sweating. If pheochromocytoma is not treated adequately and timely during pregnancy, maternal and fetal mortality rate may reach up to 50% [4,5]. With early diagnosis and appropriate treatment, decreases to less than 5% for maternal mortality and less than 15% for fetal mortality [4,6]. Pheochromocytoma is rare during pregnancy and diagnosis of it is often hard;

may not give any findings until birth. The patient might haveno symptoms until delivery time. Wrong treatment and management may lead to undesired results. The most common symptom is resistant or paroxysmal hypertension; only 5-15 % of the patients are normotensive [7,9]. 90% of symptomatic patients have headache [10].

Paroxysmal hypertension during pregnancy mimics gestational hypertension, the most common cause of elevated blood pressure during pregnancy is gestational hypertension. Therefore, if there is no high index of clinical suspicion, it may be difficult to diagnose pheochromocytoma. Maternal and fetal mortality rates are high in patients, particularly in those who are not diagnosed until delivery. A systematic review by Biggar and Lennard of 77 pregnancies in women with pheochromocytoma showed the maternal and fetal mortality rates were 8 % and 17 %, respectively [11]. Pheochromocytoma with an endocrinological stimulation, causes excessive catecholamine release and then leads to paroxysmal hypertension. A thorough investigation of the patient's hypertension history should be obtained.

While gestational hypertension is considered primarily in patients with a history of hypertension in previous pregnancies and a family history of hypertension in pregnancy, pheochromocytoma should be considered in the differential diagnosis of patients resistant to antihypertensive therapy. Endocrinological laboratory tests help to determine whether hypertension is secondary or related to pregnancy. Abdominal ultrasonography and MRI are used in patients with a high level risk for pheochromocytoma. If diagnosis of pheochromocytoma can be made during the antenatal period, maternal and fetal complications decrease to a considerable extent. Increased intra-abdominal pressure during pregnancy; fetal movements, uterine contractions, vaginal or surgical delivery, general anesthesia can make pheochromocytoma clinically overt in pregnancy [12]. The enlarged uterus leads to increased intra-abdominal pressure and direct compression of the tumor leading to catecholamine release from the tumor and thus an increase in blood pressure. Since metastatic lesions are endocrinologically active, any stimulation bears a huge risk of unwanted release of catecholamine, resulting in hemodynamic complications [13].

The main purpose of the treatment of pheochromocytoma is prevention of hypertension attacks. At the time of diagnosis, during the preoperative period patients should get alpha blockade for at least 10-14 days before surgery [14]. Phenoxybenzamine (pregnancy Class C) is preferred as alpha blocker as the best treatment in pregnancy. This drug crosses the placenta and reaches the fetus. It may cause perinatal depression and neonatal transient hypotension as side effect [15]. Treatment of choice for pheochromocytoma is surgery. The surgery time depends on factors such as gestational age of pregnancy, the accessibility of the tumor for surgery, and fetal condition and clinical response to treatment [7,16]. Based on our review of 5 case reports on table 1, we can analyze appropriate treatment modalities of phechromocytoma in last five years.

Authors	Year	Age	Pregnancy week	Symptoms, signs	Surgery	Complications and Outcome
Sonali Shah, et al.	2017	26	35	Paroxymal hypertension and headache	After 38 week of gestation ; C/S , then postpartum six weeks ; L/S adrenalectomy	No recurrence
Shuzhong Liu, et al.	2017	26	34	Paroxymal hypertension , numbness, back pain, urinaary incontinance	After C/S, biopsy and RT ; then surgery	Multiple metastases
Felipe de Almedia e Paula, et al.	2017	32	22	Headache; facial flushing, sweating	L/S adrenalectomy (24.week of gestation) ; then 29.week of gestation C/S	Newborn die due to plasental abruption
Seyedeh Nosushin Ghalandorpoor Attar et al.	2018	24	37	Left flank pain , Diabetes Melltus,	After C/S at 40 week of gestation , L/S adrenalectomy	No recurrence
Monika Lubinska, et al.	2018	30	12	High blood pressure despite antihypertensive treatment	At 17.week of gestation; L/S adrenalectomy	No recurrence ; normal fetal devolopment

Table 1: Clinical review of previously published phechromacytoma in pregnancy at 5 case reports in last five years [17-21].

Discussion

In one 20 year a review of 30.246 pregnant women, the incidence of pheochromocytoma was found to be 0.007% [22]. Autopsy studies suggest a higher incidence [23]. Pheochromocytoma in pregnancy can cause fatal hypertensive crisis that can be stimulated by vaginal or caesarean delivery, general anesthesia, enlarging of the uterus, uterine contractions, or fetal movements and this may cause morbidity and mortality for the fetus. Hypertensive crises can lead Extreme vasoconstriction in the uteroplacental circulation and this may result in intrauterine hypoxia and premature placental abruption [2].

Symptoms may occur for the first time in pregnancy due to increased vascularity of the tumor or mechanical factors such as pressure from the enlarging uterus or fetal movements, which can stimulate catecholamine secretion [24]. In 98% of the cases, pheochromocytoma come to existence with hypertension. Other findings are, orthostatic hypotension, palpitations, headaches, sweating, anxiety attacks, and anxiety attacks. Hypertension occurring during pregnancy may lead to the pheochromocytoma to be mistaken for pre-eclampsia. High-risk patients should undergo 24-hour urinary fractionated metanephrines and catecholamines measurements (sensitivity = 98%, specificity = 98%). Biochemical confirmation of the diagnosis are followed by radiological evaluation of the tumor's location, using Computed Tomography (CT) and Magnetic Resonance İmaging (MRI). Approximately 95% of the tumors are located within the abdomen and pelvis. In addition to the imaging methods, Iodine -123 metaiodobenzylguadine (MBIG) scintigraphy can be performed. Genetic testing can be used to confirm a diagnosis. Von Hippel Lindau Syndrome, Multiple Endocrine Neoplasia, Neurofibromatosis type 1 are genetic diseases associated with pheochromocytoma. Ultrasonography and MRI are the most reliable radiological imaging methods in pregnant women.

In order to be successful in the treatment of pheochrocytoma, alpha adrenergic blocker should be started in order to regulate preoperative blood pressure. Phenoxybenzamine (2 * 10-40 mg) and doxazosin (2 * 4-16 mg) are frequently used as alpha-adrenergic blockers [25]. According to recent studies, doxazosin has been used more frequently. Although it passes the placenta, the fetal drug concentration remained lower than the maternal concentration. Neonatal hypotension and respiratory depression were not reported [26]. Pre-surgical preparation with this class of drugs is one of the main reasons why surgical mortality has decreased over the last 30 years to <3% [6]. In case of tachyarrhythmias, beta-adrenergic blockade should only be started after some days of appropriate alpha adrenergic blockade [2]. In emergency hypertensive pregnancies, treatments such as intravenous phenoxybenzamine, sodium nitroprusside, nicardipine and magnesium sulfate can be administered. The timing of tumor surgery depends on the gestational age of the pregnant woman, the severity of the symptoms and the fetal development at the time of diagnosis.

Since organogenesis is incomplete and miscarriage is highly likely and the enlarged uterus in the first trimester and last trimester complicates adequate access to the surgical site, surgical intervention is not recommended [27]. The ideal time for surgical intervention is the second trimester and surgical removal is recommended before 24 weeks of gestation. After 24 weeks of gestation, the patient can be treated with the appropriate alpha-adrenergic blockade until the fetus is viable, when the tumor can be removed after an elective cesarean section [28].

In the general population, laparoscopic surgery is preferred because of lower postoperative complications for adrenalectomy. However, in a study involving 18 pregnant patients, laparoscopic adrenelectomy in the second trimester yielded positive results in 16 patients [11]. Laparoscopic surgery is the first choice for tumors below 7 cm [5] and the complication rate is less than 8%. Since it is performed without entering the peritoneal cavity, the retroperitonescopic approach for adrenelectomy is a better alternative than the laparascopic transperitoneal approach, but has similar morbidity and mortality rates [29]. Laparoscopy provides less catecholamine discharge compared with open adrenelectomy. Laparoscopy is a less invasive procedure than open surgery, the hospital stay is short, it is associated with faster healing process and the risk of thromboembolic event is less [2]. Laparoscopic surgery also reduces the risk of preterm labor by providing better visibility than uterine manipulation [1,2]. Perioperative management is very important for maternal and fetal well-being. Complications that may occur during surgery should be kept in mind and should be rapidly intervened in case of emergencies. These potential occurences are hypertensive attacks, fetal distress after sudden collapse, acute pulmonary edema, myocardial infarction and hemodynamic collapse.

Recent studies have shown successful vaginal deliveries utilizing epidural analgesia in patients with pheochromocytoma [30]. Epidural analgesia, especially in

multiparous patients, shortened the 2nd stage of labor and the duration of pushing phase. However, it should be kept in mind that oxytocin and other uterotonic agents may cause hemodynamic instabilitiy (tachycardia, hypotension). Since it provides a more suitable environment for the treatment of sudden hemodynamic instability cesarean delivery is usually preferred.

Anesthesia can be epidural, spinal and general. The disadvantage of cesarean delivery is hemorrhage and catecholamine secretion with peritoneum or tumor stimulation [31].

A multidisciplinary consultation should be followed in patients diagnosed with pheochromocytoma and the treatment of the patient should be arranged with a team including the anesthesiologist, obstetrics, surgeon and endocrinologist.

Conclusion

Pheochromocytoma, although rarely seen in the etiology of hypertensive diseases in pregnancy, is a tumor that can be fatal if not diagnosed and may cause serious complications for the fetus and mother. In pregnant women presenting with hypertension, the history should be taken into consideration and differential diagnoses should be evaluated carefully. In the tertiary health institutions, the pregnant women diagnosed as pheochromocytoma should be approached multidisciplinary with a team of obstetrics, anesthesiologist, internal medicine, general surgeon and pediatrician. It should be kept in mind that with proper management and treatment, the rate of fetal and maternal mortality can be decreased.

References

1. Castilho LN, Simoes FA, Santos AM, Rodrigues TM, Santos CA (2009) Pheochromocytoma: A Long-Term Follow-Up of 24 Patients Undergoing Laparoscopic Adrenalectomy. Int Braz J Urol 35(1): 24-31.

2. Dugas G, Fuller J, Singh S, Watson J (2004) Pheochromocytoma and pregnancy: a case report and review of anesthetic management. Can J Anesth 51(12): 134-138.

3. Karagiannis A, Mikhailidis DP, Athyros VG, Harsoulis F (2007) Pheochromocytoma: an update on genetics and management. Endocr Relat Cancer 14(4): 935-956.

4. Santos DRP, Barbisan CC, Marcellini C, Santos RMVR (2015) Feocromocitoma e gravidez: Relato de caso e revisão atualizada. J Bras Nefrol 37(4): 496-500.

5. Oliva R, Angelos P, Kaplan E, Bakris G (2010) Pheochromocytoma in Pregnancy. A Case Series and Review. Hypertension 55(3): 600-606.

6. Lenders JWM (2012) Pheochromocytoma and pregnancy: a deceptive connection. Eur J Endocrinol 166: 143-150.

7. Sarathi V, Lila AR, Bandgar TR, Menon PS, Shah NS (2010) Phaeochromocytoma and pregnancy: a rare but dangerous combination. Endocr Pract 16(2): 300-309.

8. Kaloostian PE, Zadnik PL, Kim JE, Groves ML, Wolinsky JP, et al. (2014) High incidence of morbidity following resection of metastatic pheochromocytoma in the spine. J Neurosurg Spine 20(6): 726-733.

9. Bravo EL (1991) Pheochromocytoma: new concepts and future trends. Kidney Int 40(3): 544-556.

10. Manger WM, Gifford RW (2002) Pheochromocytoma. J Clin Hypertens (Greenwich) 4(1): 62-72.

11. Biggar MA, Lennard TW (2013) Systematic review of phaeochromocytoma in pregnancy. Br J Surg 100(2): 182-190.

12. Manger WM (2006) An overview of pheochromocytoma: history, current concepts, vagaries, and diagnostic challenges. Ann N Y Acad Sci 1073: 1-20.

13. Goodwin CR, Clarke MJ, Gokaslan ZL, Charles F, Ilya L, et al. (2016) En bloc resection of solitary functional secreting spinal metastasis. Global Spine J 6(3): 277-283.

14. Witteles RM, Kaplan EL, Roizen MF (2000) Safe and cost-effective preoperative preparation of patients with pheochromocytoma. Anesth Analg 91(2): 302-304.

15. Reisch N, Peczkowska M, Januszewicz A, Neumann HP (2006) Pheochromocytoma: presentation, diagnosis and treatment. J Hypertens 24(12): 2331-2339.

16. Griffin JB, Norman PF, Douvas SG, Martin JN, Morrison JC (1984) Pheochromocytoma in pregnancy: diagnosis and collaborative management. South Med J 77: 1325-1327.

17. Sonali S, Lindsay E, Andrew R, Amy C, Christine H, et al. (2017) Rare cause of hypertension in pregnancy: Phaeochromocytoma, Obstet Med 10(2): 83-84.

18. Ghalandarpoor-Attar SN, Ghalandarpoor-Attar SM, Borna S, Ghotbizadeh FA (2018) Rare presentation of pheochromocytoma in pregnancy: a case report. J Med Case Rep 12(1): 37.

19. Paula FA, Dos Santos RI, Ferruzzi OA, Melo RO, Takaku M (2018) Laparoscopic approach to pheochromocytoma in pregnancy: case report. Int Braz J Urol 44(3): 629-633.

20. Łubińska M, Hoffmann M, Jendrzejewski J, Kobiela P, Kobiela J, et al. (2018) Successful surgical treatment of pheochromocytoma during pregnancy. Pol Arch Intern Med 128(5): 322-323.

21. Liu S, Song A, Zhou X, Kong X, Li WA, et al. (2017) Malignant pheochromocytoma with multiple vertebral metastases causing acute incomplete paralysis during pregnancy: Literature review with one case report. Medicine (Baltimore) 96(44): e8535.

22. Harrington JL, Farley DR, van Heerden JA, RaminKD (1999) Adrenal tumors and pregnancy. World J Surg 23(2): 182-186.

23. Sutton MG, Sheps SG, Lie JT (1981) Prevalence of clinically unsuspected pheochromocytoma. Review of a 50-year autopsy series. Mayo Clinic Proceedings 56(6): 354-360.

24. Kiroplastis K, Kambaroudis A, Andronikou A, Reklou A, Kokkonis D, et al. (2015) Dealing with Pheochromocytoma during the First Trimester of Pregnancy. Case Rep Obstet Gynecol 2015: 439127.

25. Lenders JW, Duh QY, Eisenhofer G, Gimenez-Roqueplo AP, Grebe SK, et al. (2014) Pheochromocytoma and paraganglioma: an endocrine society clinical practice guideline. J Clini Endocrinol Metabol 99: 1915- 1942.

26. Versmissen J, Koch BC, Roofthooft DW, Ten Bosch-Dijksman W, van den Meiracker AH, et al. (2016) Doxazosin treatment of phaeochromocytoma during pregnancy: placental transfer and disposition in breast milk. Br J Clin Pharmacol 82(2): 568-569.

27. Kitayama K, Kashiwagi S, Amano R, Noda S, Ohira G, et al. (2015) A Case of Bilateral Pheochromocytoma During Pregnancy. BMC Surg 15: 55.

28. Podolsky ER, Feo L, Brooks AD, Castellanos A (2010) Robotic Resection of Pheochromocytoma in the Second Trimester of Pregnancy. JSLS 14(2): 303-308.

29. Conzo G, Tartaglia E, Gambardella C, Esposito D, Sciascia V, et al. (2016) Minimally invasive approach for adrenal lesions: Systematic review of laparoscopic versus retroperitoneoscopic adrenalectomy and assessment of risk factors for complications. Int J Surg 28(1): 118-123.

30. Strachan AN, Claydon P, Caunt JA (2000) Phaeochromocytoma diagnosed during labour. British J Anaesthesia 85: 635-637.

31. Cammarano WB, Gray AT, Rosen MA, Lim KH (1997) Anesthesia for combined cesarean section and extra-adrenal pheochromocytoma resection: a case report and literature review. Int J Obstetric Anesthesia 6: 112-117.