Pheochromocytoma in ectopic pregnancy: A case report

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Summary

Objective: To study pregnancy characteristics in women with pheochromocytoma and to improve awareness of this comorbidity among obstetricians and gynecologists. *Methods:* The diagnosis and treatment of a case of ectopic pregnancy with pheochromocytoma is described. *Results:* The patient was diagnosed with a ruptured left Fallopian tube isthmus due to pregnancy, with comorbid left adrenal pheochromocytoma. *Conclusion:* Ectopic pregnancy with heavy bleeding and elevated blood pressure is indicative of pheochromocytoma. Measurement of the levels of urinary vanillylmandelic acid and urinary and serum catecholamines, as well as ultrasonography, can help diagnose this comorbidity.

Key words: Pheochromocytoma; Ectopic pregnancy; Case report.

Introduction

Pheochromocytoma is a rare tumor originating from the medulla of the adrenal gland and extra-adrenal paraganglia. Pheochromocytoma cells secrete catecholamines and cause hypertension. The incidence of pregnancy with comorbid pheochromocytoma is 2-7 per 100,000 [1, 2]. Pheochromocytoma in pregnancy is very dangerous, posing a serious risk to the lives of both mother and fetus. The reported maternal and fetal mortality of patients with undiagnosed pheochromocytoma is higher than 50% [3]. However, pheochromocytoma in ectopic pregnancy is rarely reported. Therefore, in order to increase the awareness of this condition, we report a case of ectopic pregnancy with comorbid pheochromocytoma.

Case Report

A 24-year-old woman was admitted on December 16, 2010 because of lower abdominal pain of five hours duration after intercourse and menopause for 57 days. Her previous periods were regular, lasting about three days with cycles ranging from 37 to 40 days. After the last menstruation on October 19, 2010, she did not experience symptoms of early pregnancy such as nausea and vomiting. Her urine pregnancy test conducted on December 6, 2010 was positive. Five hours before admission, the patient had lower abdominal pain after sexual intercourse with an accompanying heavy feeling in the anus. Additional symptoms experienced by the patient included dizziness, palpitation, and cold sweating, but vaginal bleeding was absent. On physical examination, her temperature was 36.4°C, pulse was 124 beats/min, respiratory rate was 22/min, and blood pressure was 92/52 mmHg. The gynecological examination showed that the vulva was normally developed. The vagina was patent with a small amount of white secretion. The cervix was smooth and soft with lifting pain. The posterior fornix was plump and tender. The uterus was in the anterior position with normal size, normal uterine motility, and tenderness. The patient had right adnexal tenderness, but without palpable masses, and left adnexal tenderness and thickening. On December 16, 2010, ultrasonography showed a normal-sized uterus with a 103 × 60 mm mixed mass just above the uterus. There was a yolk sac-like echo inside the mass, and 55 mm of fluid in the pelvic cavity. A blood workup conducted immediately after admission found that the white blood cell count was 29.2 × 10^9/l, and hemoglobin was 106 g/l. The patient underwent laparoscopic left salpingectomy under general anesthesia. During the operation, a total of 2,000 ml free blood and blood clot was cleaned from the abdominopelvic cavity. The left Fallopian was thickened, and the isthmus had ruptured. Postoperative blood pressure was 130/90 mmHg, and heart rate was 124 beats/min. The patient was extubated with full consciousness. The patient had a sudden cough with moderate amount of pink frothy sputum 1.5 h after the operation. At this time, her blood oxygen saturation was 70%, blood pressure was 168/90 mmHg, and heart rate was 162 beats/min. After treatment, these values became 100%, 140/80 mmHg, and 130-140 beats/min, respectively. She was then transferred to the intensive care unit, where her renal insufficiency was corrected and a relatively stable cardiac function was maintained for a while. However, the patient's condition subsequently deteriorated with QRS widening and ST-T variation in the electrocardiogram, significant abnormality of myocardial enzymes, heart wall motion abnormality detected by colored ultrasound images, and cardiogenic shock; the patient died after rescue. The cause of death was determined to be: (1) severe myocarditis, acute left ventricular failure, cardiogenic shock, and acute renal failure and (2) ruptured left Fallopian tube isthmus pregnancy. The autopsy result provided by the Forensic Identification Center of Sun Yat-sen University indicated that there was an 8.0 × 7.5 × 6.0 cm tumor on the left adrenal gland of the patient. Forensic pathological diagnosis (B6624) showed: (1) left adrenal pheochromocytoma, (2) postresection of the left Fallopian tube, (3) suppurative tonsillitis, (4) congestion and edema of the brain and lung, and (5) congestion of the liver, spleen, kidney, pituitary, ovary, and uterus.

Discussion

Pheochromocytoma is a tumor of the catecholamine-producing chromaffin cells of the adrenal medulla and the extra-adrenal paraganglion system. It secretes large amounts of norepinephrine and epinephrine, prompting a significant increase in blood catecholamine levels. This causes severe systemic small vessel spasms and leads to a series of symptoms, including increased blood pressure, cardiac arrhythmia, and metabolic disorders [4]. The

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onset of the disease often occurs during pregnancy, delivery, or trauma operations and poses a high risk of death if not handled properly.

Various stress factors during pregnancy may exacerbate the disease. Patients may present with heart failure or cardiac arrhythmia because of an overloaded cardiovascular system, as well as cerebral ischemia, hypoxia, or cerebral vascular hemorrhage in the central nervous system. Most pregnant patients die during delivery or several days after delivery because of hypertensive crisis, severe cardiac arrhythmia, and heart failure. The placental tissue may be damaged by hypoperfusion, ischemia, and hypoxia, and in severe cases, even infarction, necrosis, and placental abruption. Pheochromocytoma may result in poor fetal growth, spontaneous abortion, fetal distress, or fetal death; the mortality rate is high for both the mother and fetus. During pregnancy, hypertension may occur as a sudden increase in blood pressure from normal level or as paroxysmal increases on the basis of persistent hypertension. Blood pressure fluctuations are related to sudden changes in posture and sudden increases of intra-abdominal pressure and do not respond to general anti-spasmodic and anti-hypertensive therapies. In this case, the patient had paroxysmal hypertension despite massive loss of blood and a heart rate higher than 120 beats/min. Therefore, the possibility of pheochromocytoma should have been considered in this case. As pregnancy does not change the catecholamine levels in blood and urine, elevated levels of blood and urine catecholamines, norepinephrine, epinephrine, and metanephrine can be indicative of pheochromocytoma. The catecholamine levels in fetal cord blood, however, will be normal despite the increased catecholamine levels in maternal blood [5]. This is a result of monoamine oxidase activity, which degrades catecholamines, in the placenta. B-ultrasound scanning and magnetic resonance imaging can also be used for the diagnosis of pheochromocytoma. These procedures are safe for the fetus, and the accuracy of B-ultrasound scanning can be as high as 89-97% [6, 7]. However, in the case of late pregnancy, the enlarged uterus can often affect the ultrasound scan. Radiological examination in early pregnancy can cause fetal malformations, mental retardation, and abortion and is generally considered undesirable. Examinations using radioactive nuclides like metaiodobenzylguanidine (MIBG) should also be performed carefully. MIBG has a small molecular size and can pass through the placental barrier, making it unsuitable for pregnant patients, unless the patient decides to terminate pregnancy because of suspected extra-adrenal tumors whose location is difficult to determine.

Pregnancy with pheochromocytoma can be easily misdiagnosed as severe gestational hypertension. In cases of pheochromocytoma, the onset of hypertension is accompanied by headache, palpitations, and hyperhidrosis, which are critical for the diagnosis of this disease. The following tips could help discriminate the two diseases: (1) most patients with pheochromocytoma present with a sudden onset of hypertension or a sudden increase in blood pressure on the basis of persistent hypertension, and the symptoms can occur before 20 weeks of pregnancy or even before pregnancy, but most patients with gestational hypertension sustain high blood pressure with fewer fluctuations and the symptoms often occur after 20 weeks of pregnancy; (2) in pheochromocytoma, hypertension is often accompanied with palpitations, hyperhidrosis, and headache, with rare and mild edema and proteinuria, whereas patients with gestational hypertension often present with severe edema and proteinuria, with less palpitations and hyperhidrosis; (3) after the application of magnesium sulfate or the termination of pregnancy, the symptoms of pheochromocytoma are often not relieved, whereas those of gestational hypertension are often relieved or disappear; and, (4) most patients with pheochromocytoma have increased catecholamine levels in the blood and urine and increased vanillylmandelic acid (VMA) levels in 24 h urine, and a lump or lumps could be detected by imaging examinations, whereas patients with gestational hypertension do not show these changes. The patient in this case did not have significant hypertension or other discomfort and as such, the clinicians did not consider the onset of pheochromocytoma. However, the massive loss of blood and paroxysmal hypertension still suggested the possibility of this disease.

In 90% of cases of pregnancy with pheochromocytoma, the tumors are benign. Patients should receive surgery to remove the tumor shortly after diagnosis and should not wait for natural delivery with long-term drug treatment. If a patient is in the first or second trimester, she usually does not have to terminate pregnancy. If she is in the third trimester, it is relatively safe to choose cesarean section. She can choose to remove the tumor during or a few weeks after the cesarean section. Preoperative use of α-adrenergic receptor antagonists improves maternal hemoconcentration, enhances tolerance to the rapidly changing pathological and physiological states before and after the operation and eases spasms of placental arteries and improves blood supply to the placenta. Therefore, α-adrenergic receptor antagonists are conducive to the healthy development of the fetus. During the medication process, clinicians should closely monitor changes in the patient's blood pressure and heart rate and pay special attention to orthostatic hypotension. The use of α-adrenergic receptor antagonists can reduce fetal mortality from 50% to 30% and maternal mortality from 40% to 17% [1]. Although β-adrenergic receptor antagonists can quickly and effectively control symptoms such as hyperglycemia and rapid heartbeat, this type of drug can potentially retard intrauterine growth. Therefore, it should only be used in combination with α-adrenergic receptor antagonists and with close monitoring of fetal development [8, 9].

In this case, the patient received emergency surgery shortly after hospitalization and did not undergo relevant postoperative examinations. Therefore, the disease was not clearly diagnosed, and as a result, appropriate treatment was not provided. As there have been few reports

about ectopic pregnancy with pheochromocytoma, we report this case to suggest that massive blood loss in ectopic pregnancy with increased blood pressure may be an indicator of this disease. Examinations of VMA levels in urine, catecholamine levels in urine and blood, and B-ultrasound scanning should be used for diagnosing this disease. Once diagnosed, the patient should receive surgery and medication as soon as possible.

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