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Choriocarcinoma on Live Pregnancy: Case Study

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ABSTRACT

Background: *Introduction: It is often difficult to diagnose choriocarcinoma on live pregnancy since it is not based on changes in blood hCG concentration. Genetic and histopathologic tests are the only two methods to determine diagnosis.*

Observation: *A clinical case is reported on a pregnant woman aged 25 years, of nulligravida, 27-week gestation, and admitted into Gia Lai Hospital in a scenario of intra-abdominal hemorrhage due to a tumor rupture at the left corner of uterine fundus. The patient had a surgery to stop bleeding and excise the tumor for histopathologic testing. The test result was placental choriocarcinoma and the patient was referred to Tu Du Hospital. The patient's blood beta-hCG was 92.715 mIU/mL. Clinical examination, chest X-ray and MRI scan found the tumor was still localized in the uterine fundus. The patient's treatment was delayed for 48 hours and cesarean section was made at 28-week and four-day gestation. The newborn's health was good.*

Discussion: *Facing a case with abnormal bleeding during pregnancy, we have to careful rule out choriocarcinoma on live pregnancy.*

Keywords

Pregnancy, Choriocarcinoma, Villi.

Introduction

Choriocarcinoma in pregnancy is a rare scenario with the incidence rate of 1/50,000 [1]. Trophoblasts will become hyperplastic, metaplastic, and invade uterine muscle, leading to loss of normal image of villi [2]. Hemorrhage and necrosis are found at the center of invaded area. The illness is often diagnosed when there is abnormal bleeding or metastatic appearances. Following is the report on the first case of choriocarcinoma on live pregnancy in Vietnam.

Clinical Case

A 25-years-old pregnant woman was referred from Gia Lai Hospital to Tu Do Hospital due to choriocarcinoma at gestational age of 27 weeks and three days.

The patient was doing business, having stable health, married for one year and primigravida (PARA 0000). Fetal growth was good during pregnancy, the pregnant woman had slight morning sickness, no medical and surgical illnesses and no abnormal hemorrhage.

On 9/15/2018 morning, the patient had a terrible pain in hypogastric area together with exhausted feeling, dazzle, dizziness, leading to her admission into Gia Lai Hospital in drowsy status, pulse rate 120 beats/min, blood pressure 90/60 mmHg, pale skin and mucous membranes, cold hands and feet, dull sound on abdominal percussion and all-abdomen pain on abdominal pressing. Sonography disclosed plentiful fluid gathering in bilateral pelvic cavities and inter-hepato-renal space. She was diagnosed of hypovolemic shock due to unknown acute intra-abdominal bleeding on 27-week gestation. Emergency operation recorded a bleeding tumor of unknown nature at the left corner of uterine fundus, management included tumor excision, anti-bleeding suture and waiting for histopathologic results. On 9/19/2018 morning, the results came out with placental choriocarcinoma, the patient was then referred to Tu Du Hospital.

On 9/19/2018 evening, Tu Du Hospital received the patient in conscious status with stable vital signs. The patient's abdomen

had a 20-centimeter-long, dry, upper midline operational scar. The abdominal wall was soft on palpation with no peritoneal reflex. Examination recorded the uterine height of 23cm, fetal heartbeat 135 beats/min, no uterine contractions, no vulvar injury, no blood in vagina, close cervix, no pain on cul-de-sac shake.

Early morning on 9/20/2018, the patient had severe abdominal pain, pulse rate 120 beats/min, blood pressure 90/60 mmHg, the abdomen was bloating and painful on palpation, emergency operation was made due to acute intra-abdominal bleeding. It was noted that there was a growth of 4x5cm at the posterior left corner of uterus, close to the large ligament, on bleeding, the tumor was excised and sutured to stop bleeding. The patient's status was stable after surgery.

By noon on 9/20/2018, the test result of blood beta-hCG was 92.715 mIU/mL, and then by re-checking of histopathologic specimen, the diagnostic result was placental choriocarcinoma invasive into uterine muscle. By sonography there was a live fetus with normal growth, it was unable to observe the uterine bottom on left corner due to abundant air in intestines. On 9/24/2018, the patient had MRI scan and the results were placental invasion into the left corner of uterine bottom, no placental invasion out of the uterus. Chest X-ray result was normal.

On 9/25/2018, diagnosing discussion at hospital level suggested treatment direction. The patient was diagnosed of placental choriocarcinoma stage I (as per FIGO 2000) on a live fetus of 28 weeks and two days and specialized treatment was pending for 48 hours with two doses of betamethasone to support fetal lung and stabilize the mother's hemodynamics.

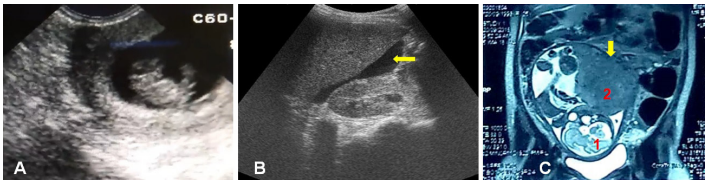

Figure 1: A: normal sonography in the first three months of pregnancy. B: fluid in inter-hemato-renal space (arrow) at this hospital admission. C: placenta invaded uterine muscle on MRI scan (1: fetal head, 2: placenta, arrow: site of placental invasion).

On 9/27/2018, the patient had cesarean section. The outcome was a male baby weighted 1200 grams, APGAR scores at 1 minutes and 5 minutes were 7 and 8 respectively, and then he was referred to Children's Hospital No. 1 due to retinopathy. The uterine fundus had vascular hyperplasia, dark purple lesion on blood oozing at the left corner, there was a dark purple lesion mass at posterior cul-de-sac peritoneum. No lymph nodes were seen in pelvis and abdomen, no macroscopic anomalies were found in other organs. The management included uterine conservation, placenta removal and excision of invaded uterine muscle area. After surgery, the diagnosis was choriocarcinoma stage II with low risk (as per FIGO/WHO 2002). On 11/5/2018, the patient's health status was stable and chemotherapy was started with Methotrexate.

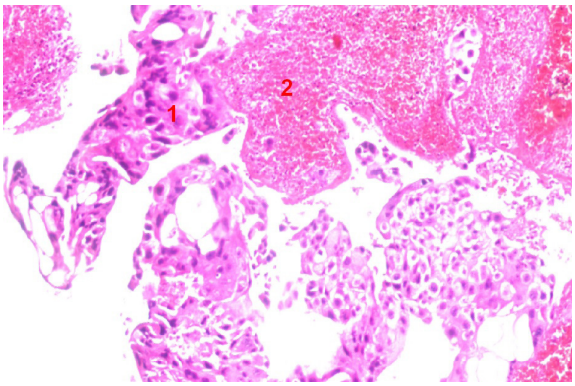

Figure 2: Histology of choriocarcinoma (1: hyperplastic and metaplastic area of trophoblasts, 2: bleeding necrosis area).

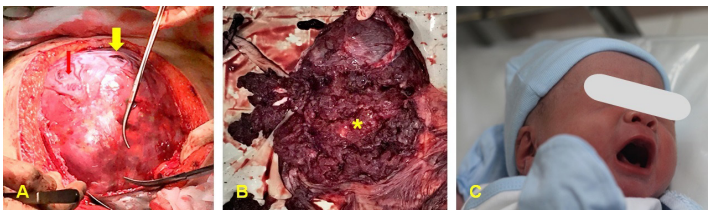

Figure 3: A: vascular hyperplasia on uterine fundus (red arrow) together with dark purple lesion (yellow arrow). B: placenta together with uterine muscle excised (asterisk). C: newborn at 40 days after birth.

Discussion

Gestational trophoblastic diseases often appear after hydatidiform mole (60%), spontaneous/induced abortion (30%) or ectopic/normal pregnancy (10%) [3-4]. Among them, choriocarcinoma in normal pregnancy is very rare. There are two hypotheses to explain this situation as (1) normal trophoblasts were transformed directly to cancer and (2) leftover trophoblasts from previous pregnancy were transformed into malignancy in this current pregnancy [5]. This clinical case is the first one in Vietnam with choriocarcinoma in pregnancy of which the outcome was a live birth and the patient had no previous pregnancies (PARA 0000). The most likely pathogenesis is thought as a direct transformation of normal trophoblasts into cancer.

The risk of illness is clearly higher in women who are more than 35 years or less than 20 years old and ever had gestational trophoblastic disease in previous pregnancy. If patients have blood groups of A, B, AB, tobacco smoking and poor animal fat and carotene eating habit, the risk of illness may be increased. The most common manifestation of disease is abnormal vaginal bleeding and signs at metastatic sites [6]. The most frequent site of metastasis is lung (60-95%), with symptoms of cough, hemoptysis, breathing distress, pleural-type chest pain [7]. On placental sonography, there may be abnormal structure (snow storm image) nested in normal placental area [8]. There are no recommendations on hCG concentration monitoring to diagnose choriocarcinoma on live pregnancy [3]. The disease is in question if there is abnormal vaginal bleeding and/or bleeding at metastatic sites, together with respiratory symptoms, neural/spinal signs, high beta-hCG concentration in blood, low serum HPL and snow storm image in placental sonography [6,8-9]. Genetic and histopathologic testing

will help to determine the diagnosis. Our patient has a risk factor of living in geographic area with poor animal fat and carotene diet (South East Asia). The woman had a good pregnancy and was admitted into hospital only when the invasive site of placenta ruptured leading to hemorrhage in abdominal cavity. The disease was thought when the test result of blood beta-hCG concentration was high and the positive diagnosis was confirmed with placental histopathologic test result.

Choriocarcinoma in pregnancy should be immediately referred to hospital with oncology department [10]. The patient was admitted into Gia Lai Hospital to stabilize bleeding condition and then referred to Tu Du Hospital when the histopathologic test result was available. Gia Lai Hospital's treatment behavior was quite reasonable. At the specialized level, the question was what treatment should be selected for the patient. If the disease is detected in early phase of pregnancy, the pregnancy should be terminated [1]. If the disease is positively diagnosed in later phase of pregnancy without complications, with genetic type, and normal sonography, the pregnancy may be maintained [3]. It the mother's condition is not good, chemotherapy can be applied and the safest time is the second or third trimester of pregnancy since it can help to reduce the risk of congenital deformity or spontaneous abortion if any [1]. It is logical that our patient was not treated with chemotherapy because the bleeding had been controlled and more disease progress was not recorded. Pregnancy should be terminated right when the fetus can be born alive and cesarean section should be made since tumor site and metastasis (if any) can be simultaneously assessed to imagine what chemotherapy plan should be used. The point in time for pregnancy termination is recommended 33 weeks and one day of gestation. If pregnancy is extended, possible benefits will not exceed potential risks [1]. In this clinical case, the pregnancy termination was made a little earlier than that in medical literature (28 weeks four days versus 33 weeks one day), the consequence was that the newborn still incurred retinopathy although it had good APGAR scores.

Choriocarcinoma is sensitive to chemotherapy so that treatment in puerperium mainly resorts to chemotherapy [3]. Patients are classified into three groups including low risk (risk score ≤6), high risk (risk score ≥7) and very high risk (risk score ≥12 plus metastasis to liver, brain or multiple sites and poor responsive to multiple chemotherapy). Low risk group should be treated with single chemotherapy of either Methotrexate or Actinomycin D [3]. Remission rate is nearly 100%. High risk group should be applied multiple chemotherapy [3]. The most frequent regimen is EMA-CO. The remission rate is 85% and five-year survival is 75-90%. In very high risk group, chemotherapy with standard regimen may result in severe marrow failure causing hemorrhage, septicemia and multi-organ deficiency [3]. Therefore, drugs should be administered at lower doses and increased more slowly than standard regimen. The use of EP/EMA or similar regimens will produce better responsive and prognosis than single EMA regimen. Our patient had cancer at stage II with low risk, and therefore, single chemotherapy was recommended with Methotrexate and drug responsive was monitored with beta-hCG. She needs to be monitored within 12 months to assess remission and during that period, a safe and effective contraceptive method is required. In future, her fecundation, pregnancy and birth delivery are not influenced [3].

Conclusion

Choriocarcinoma on live pregnancy is a rare disease. Diagnosis is often difficult if genetic and histopathologic testing is not available. Therefore, facing a case with abnormal bleeding during pregnancy, careful monitoring and assessment must be made.

When the diagnosis is determined, patients should be referred to specialized facilities for treatment. Pregnancy is preserved only when diagnosis is confirmed in later trimesters of pregnancy, no complications, with genetic type and normal sonography. Do not terminate pregnancy earlier or later than 33 weeks one day of gestation. Cesarean section should be made for full assessment.

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