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The Importance of Early Diagnosis: A Case Report of Uterine Rupture in Molar Pregnancy

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Abstract: Gestational trophoblastic disease (GTD) is a heterogeneous spectrum of diseases with abnormal trophoblastic proliferation ranging from benign to malignant state. It has varying degree of spread from local invasion to distant metastasis. These disease are characterized by a reliable tumor marker, which is the β-subunit of human chorionic gonadotropin (β-hCG), and have varied tendencies for local invasion and spread. Benign lesions consist of hydatidiform moles, complete and partial, whereas malignant lesions consist of invasive moles, placental-site trophoblastic tumors (PSTT), epithelioid trophoblastic tumors (ETT), and choriocarcinoma. Although GTNs commonly follow a molar pregnancy, they can occur after any gestational event, including induced or spontaneous abortion, ectopic pregnancy, or term pregnancy. Hydatidiform mole or what is called a molar pregnancy, is histologically characterized by chorionic villous abnormalities consisting of trophoblastic proliferation and villous stromal oedema. The incidence of hydatidiform mole is increasing every year. It may be categorized as either complete or partial moles on the basis of gross morphology, histopathology, and karyotype. The classical presenting symptoms and signs of patients with complete and partial molar pregnancy are vaginal bleeding, excessive uterine size, and sign of toxemia. Ultrasonography has replaced all other radiographic means for diagnosis of hydatidiform mole. Molar tissue typically is identified as a diffuse mixed echogenic and vesicular pattern replacing the placenta.

In this case report, the patient is a 44-year-old woman with a diagnosis of gravida 14-15 weeks and acute abdomen suspected of ruptured ectopic pregnancy. The patient has signs of acute abdomen, hemodynamic disorders, anemia, and increased β-hCG. Ultrasound examination showed vesicular patterns and intraperitoneal bleeding. The patient underwent stabilization, fluid resuscitation, and molar tissue evacuation management with laparotomy surgery, and a rupture was seen in the anterior uterine wall and mola tissue was obtained.

Keywords: Molar Pregnancy, GTD, β-hCG

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Introduction

Gestational trophoblastic disease (GTD) is a heterogeneous spectrum of diseases with abnormal trophoblastic proliferation ranging from benign to malignant state. It has varying degree of spread from local invasion to distant metastasis. These disease are characterized by a reliable tumor marker, which is the β-subunit of human chorionic gonadotropin (β-hCG), and have varied tendencies for local invasion and spread.[2] Benign lesions consist of hydatidiform moles, complete and partial, whereas malignant lesions consist of invasive moles, placental-site trophoblastic tumors (PSTT), epithelioid trophoblastic tumors (ETT), and choriocarcinoma. Although GTNs commonly follow a molar pregnancy, they can occur after any gestational

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event, including induced or spontaneous abortion, ectopic pregnancy, or term pregnancy.

Hydatidiform mole or what is called a molar pregnancy, is histologically characterized by chorionic villous abnormalities consisting of trophoblastic proliferation and villous stromal oedema. The incidence of hydatidiform mole is increasing every year. It may be categorized as either complete or partial moles on the basis of gross morphology, histopathology, and karyotype. The classical presenting symptoms and signs of patients with complete and partial molar pregnancy are vaginal bleeding, excessive uterine size, and sign of toxemia. Ultrasonography has replaced all other radiographic means for diagnosis of hydatidiform mole. Molar tissue typically is identified as a diffuse mixed echogenic and vesicular pattern replacing the placenta.

Epidemiology

The incidence of molar pregnancy in Japan (2:1,000 pregnancies) is reported to be about threefold higher than the incidence in Europe or North America (about 0.6 to 1.1 per 1,000 pregnancies). In Taiwan, 1 in 125 pregnancies are molar, while in the United States the incidence is 1 in 1,500 live births. The incidences of complete and partial hydatidiform moles in Ireland were investigated by reviewing all products of conception from first- and second-trimester abortions. Based on a thorough pathologic review, the incidence of complete and partial hydatidiform moles was 1:1,945 and 1:695 pregnancies, respectively.

Features	Complete Mole	Partial Mole
Fetal or embryonic tissue	Absent	Present
Hydatidiform swelling of chorionic villi	Diffuse	Focal
Trophoblastic hyperplasia	Diffuse	Focal
Scalloping of chorionic villi	Absent	Present
Trophoblastic stromal inclusions	Absent	Present
Karyotype	46, XX (90%); 46, XY	Triploid

Table 1: Features of complete and partial hydatidiform moles

While variations in the worldwide incidence of molar pregnancy may result in part from reporting population-based versus hospital-based data, a number of studies suggest that the high incidence in some populations can be attributed to socioeconomic and nutritional factors. Maternal age and reproductive history influence the rate of molar pregnancy. Women older than 40 years have a 2- to 10-fold greater risk of having a complete mole, while one in three pregnancies in women older than 50 years results in a molar gestation. Similarly, adolescents have a sevenfold increased risk of developing a complete mole.

Limited information is available concerning risk factors for partial molar pregnancy. The epidemiologic characteristics of complete and partial moles appear to differ significantly. The risk for partial moles is associated with the use of oral contraceptives and a history of irregular menstruation, but not with dietary factors. Nor does there appear to be a strong association between maternal age and the risk for partial moles.

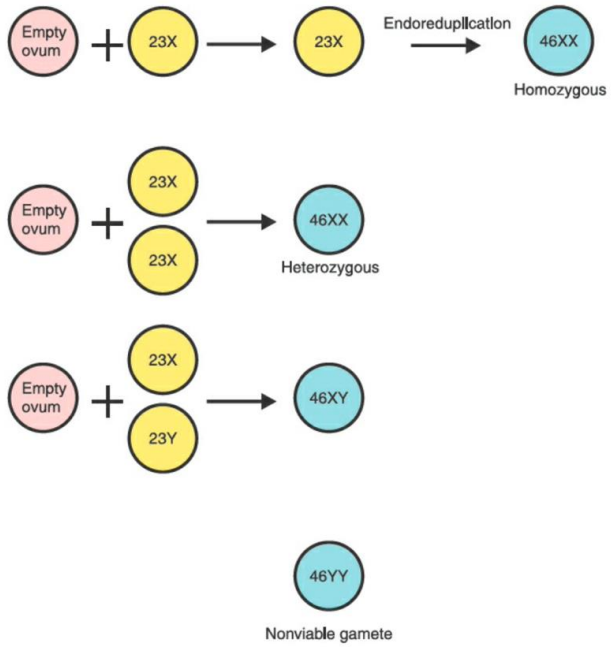

Figure 1: The karyotype of complete hydatidiform mole

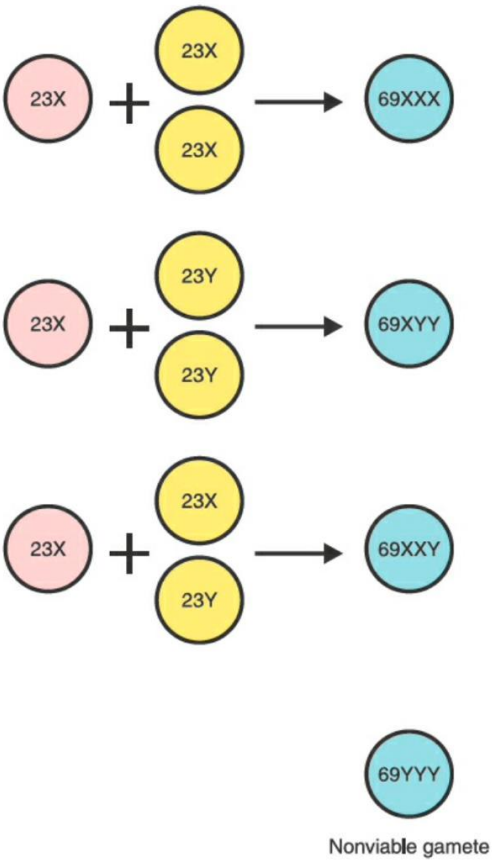

Figure 2: The karyotype of a partial hydatidiform mole

Clinical Features

Complete Hydatidiform Mole

Vaginal Bleeding. Vaginal bleeding is the most common symptom causing patients to seek treatment for complete molar pregnancy. It is reported to occur in 46% of patients, rather than the previous reports of 97% of cases. Molar tissues may separate from the decidua and disrupt maternal vessels, and large volumes of retained blood may distend the endometrial cavity. Because vaginal bleeding may be considerable and prolonged, in the past one-half of these patients had anemia (hemoglobin <10 g/100 mL). Anemia is typically present in only 5% of patients.

Excessive Uterine Size. Excessive uterine enlargement relative to the gestational age is one of the classic signs of a complete mole, although it was present in only about half of patients. Excessive uterine size occurs in only 28% of patients. The endometrial cavity may be expanded by chorionic tissue and retained blood. Excessive uterine size is generally associated with markedly elevated levels of hCG, because uterine enlargement results in part from trophoblastic overgrowth.

Preeclampsia. Preeclampsia was observed in 27% of patients with a complete hydatidiform mole. Preeclampsia is reported in only 1 of 74 patients with complete mole at the initial visit. Although preeclampsia is associated with hypertension, proteinuria, and hyperreflexia, eclamptic convulsions rarely occur. Preeclampsia develops almost exclusively in patients with excessive uterine size and markedly elevated hCG levels. Hydatidiform moles should be considered whenever preeclampsia develops early in pregnancy.

Hyperemesis Gravidarum. Hyperemesis requiring antiemetic or intravenous (IV) replacement therapy historically occurred in one-fourth of women with a complete mole, particularly those with excessive uterine size and markedly elevated hCG levels. Severe electrolyte disturbances may develop and require treatment with parenteral fluids. Typically 8% of patients have hyperemesis.

Hyperthyroidism. Clinically evident hyperthyroidism was observed in 7% of patients with a complete molar gestation. These women may have tachycardia, warm skin, and tremor, and the diagnosis can be confirmed by detection of elevated serum levels of free thyroxine (T4) and triiodothyronine (T3). Clinical evidence of hyperthyroidism with complete mole is rare.

Partial Hydatidiform Mole

Patients with partial hydatidiform mole usually do not have the dramatic clinical features characteristic of complete molar pregnancy. These patients have the signs and symptoms of incomplete or missed abortion, and a partial mole is diagnosed after histologic review of the tissue obtained by curettage.

In a survey of 81 patients with a partial mole, the main initial sign was vaginal bleeding, which occurred in 59 patients (72.8%). Excessive uterine enlargement and preeclampsia were present in 3 patients (3.7%) and 2 patients (2.5%), respectively. No patient had theca lutein ovarian cysts, hyperemesis, or hyperthyroidism. The initial clinical diagnosis was an incomplete or missed abortion in 74 patients (91.3%) and hydatidiform mole in 5 patients (6.2%). Pre- evacuation hCG levels were measured in 30 patients and were higher than 100,000 mIU/mL in 2 patients (6.6%).

The true incidence of GTD developing outside the uterine cavity approximates 1.5 per 1 million births. More than 90 percent of suspected cases will reflect an overdiagnosis of florid extra villous trophoblastic proliferation in the fallopian tube. As with any ectopic pregnancy, initial management usually involves surgical removal of the conceptus and histopathologic evaluation.

Diagnosis

Ultrasonography is a reliable and sensitive technique for the diagnosis of complete molar pregnancy. Because the chorionic villi exhibit diffuse

hydropic swelling, complete moles produce a characteristic vesicular ultrasonographic pattern as early as the first trimester.

Ultrasonography may contribute to the diagnosis of partial molar pregnancy by demonstrating focal cystic spaces in the placental tissues and an increase in the transverse diameter of the gestational sac. When these criteria are present, the positive predictive value for a partial mole is 90%.

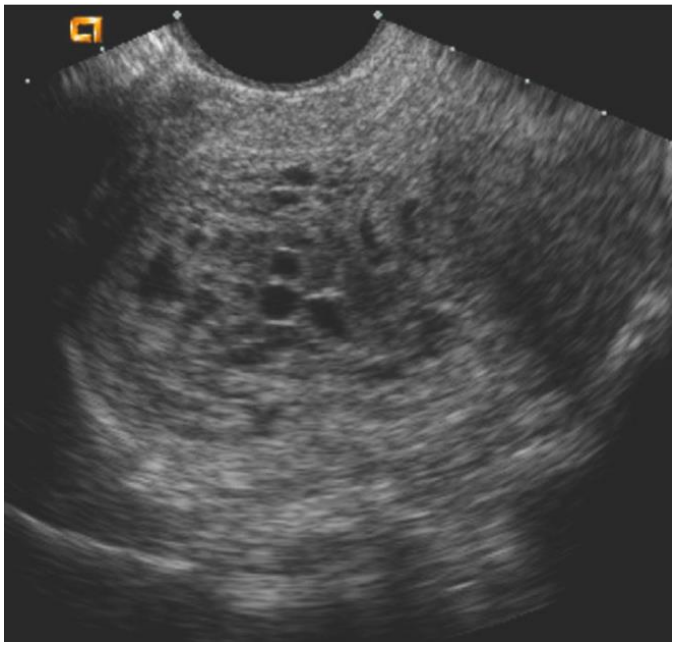

Figure 3: Ultrasonogram of a uterus showing a typical pattern of a complete hydatidiform mole.

Treatment

When molar pregnancy is diagnosed, the patient should be evaluated for the presence of associated medical complications, including preeclampsia, hyperthyroidism, electrolyte imbalance, and anemia. After the patient's condition is stabilized, a decision must be made concerning the most appropriate method of evacuation.

a. *Suction curettage*.

Suction curettage is the prefereed method of evacuation, regardless of uterine size, for patients who desire to preserve fertility.

b. *Hysterectomy*.

If the patient desires surgical sterilization, a hysterectomy may be performed with the mole in situ. The ovaries may be preserved at the time of surgery, even in the presence of prominent theca lutein cysts. Large ovarian cysts may be decompressed by aspiration. Hysterectomy does not prevent metastasis; patients still require follow-up with assessment of hCG levels.

c. *Prophylactic Chemotherapy*.

The use of prophylactic chemotherapy at the time of molar evacuation is controversial. The debate concerns the wisdom of exposing all patients to potentially toxic treatment when only about 20% are at risk of developing persistent tumor. In a study of 247 patients with complete molar pregnancy who prophylactically received a single course of actinomycin D (ActD) at the time of evacuation, local uterine invasion developed in 10 patients (4%), and no patients experienced metastasis. All 10 patients with local invasion achieved remission after one additional course of chemotherapy. Prophylactic chemotherapy, prevented metastasis and reduced the incidence and morbidity of local uterine invasion. In two prospective randomized studies of prophylactic chemotherapy in patients with a complete mole, a significant decrease in persistent tumor was detected in patients with high-risk moles who received prophylactic chemotherapy (47% and 50% vs. 14%).

Follow-Up

Human Chorionic Gonadotropin

After molar evacuation, patients should be monitored with weekly determinations of a-subunit hCG levels until these levels are normal for 3 consecutive weeks, followed by monthly determinations until the levels are normal for 6 consecutive months. The average time to achieve the first normal hCG level after evacuation is about 9 weeks. After achieving nondetectable serum hCG levels, the risk of developing GTN approaches zero. If these findings are confirmed, it is possible that postmolar hCG surveillance could be safely abbreviated.

Contraception

Patients are encouraged to use effective contraception during the entire interval of hCG follow-up. Because of the potential risk of uterine perforation, bleeding, and infection, intrauterine devices should not be inserted until the patient achieves a normal hCG level. If the patient does not desire surgical sterilization, either oral contraceptives or barrier methods should be used. It appears that oral contraceptives may be used safely after molar evacuation during the entire interval of hormonal follow-up.

Case Illustration

A 44 year old woman was referred from the Bima Regency Regional Hospital with G4P2012 Gestational age 14-15 weeks and acute abdomen suspected of a ruptured ectopic pregnancy with a differential diagnosis of molar pregnancy, the patient

with the main complaint of acute abdomen in the first trimester of pregnancy (14-15 weeks) with vaginal bleeding . This is the fourth pregnancy with a history of 2 spontaneous deliveries and 1 previous miscarriage. On physical examination, signs of acute abdomen and hemodynamic disturbances were found. Laboratory examination showed a positive pregnancy test, moderate anemia (7.3) and increased β-hCG. On ultrasound examination, a "Vesicular Pattern" and intraperitoneal bleeding were found.

The patient underwent general condition stabilization, fluid resuscitation, and management of molar tissue evacuation with laparotomy surgery. During the operation, massive hemoperitoneum (around 600 cc) was found and evaluation of the intra-abdominal organs showed a large uterus corresponding to 20 - 22 weeks, visible rupture of the anterior uterine wall with the presence of molar tissue. A total hysterectomy was performed with removal of the right tube and removal of the left tube-ovary. The results of the removal of the uterus are then cut and the molar tissue is visible and then a histopathological examination is carried out. Histopathological examination result was Hydatidiform Mole.

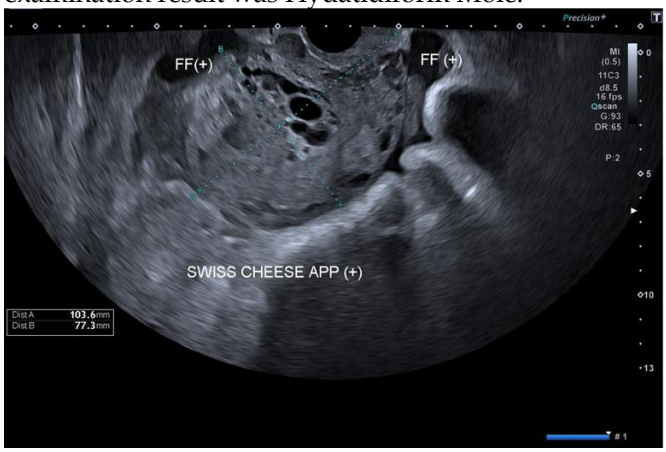

Figure 4: Ultrasound showed by this patient a "Vesicular Pattern" with intraperitoneal bleeding characterized by free fluid / FF

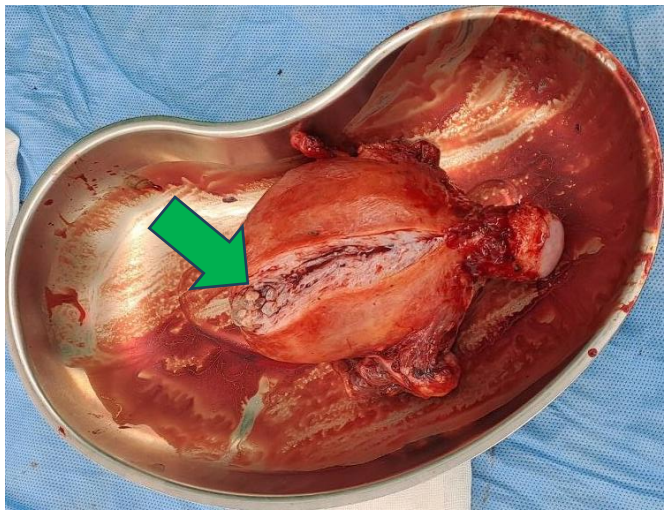

Figure 5: The results of uterine removal are evaluated for the presence of molar tissue

Discussion

Hydatidiform mole is the most common gestational trophoblastic disease. The prevalence of hydatidiform mole is higher in Asia, Africa and Latin America than in Western countries. The highest incidence rate is in women aged less than 20 years and more than 45 years, low socioeconomic status, and lack of protein, folic acid and carotene intake. Hydatidiform mole therapy consists of 4 stages, namely: Improving the general condition, removing the mole tissue, prophylactic therapy with cytostatic, and follow-up. Death in molar cases is caused by bleeding, uterine perforation, infection, sepsis, pulmonary embolism, or thyrotoxicosis. In developed countries, mortality due to mole almost no longer exists, but in developing countries it is still quite high, namely around 2.2 – 5.7%.

Uterine rupture caused by molar pregnancy is a rare but serious complication. The incidence is low, as molar pregnancies are uncommon, occurring in approximately 1 in 1,000 pregnancies in most populations. Uterine rupture in the context of molar pregnancy typically arises in cases of invasive mole (a form of gestational trophoblastic disease), where molar tissue invades the uterine wall, leading to significant thinning and potential rupture. Uterine rupture is also more commonly reported in developing countries, where early diagnosis and management of molar pregnancy may be delayed. Thus, Early detection and treatment of molar pregnancy through suction evacuation and close monitoring of β-hCG levels are critical to prevent complications such as uterine rupture.

Conclusion

Patients with pregnancies under 20 weeks who have signs of acute abdomen and vaginal bleeding should be suspected of an obstetric emergency. Rupture in a molar pregnancy can occur if early detection and

treatment is not carried out immediately. However, this incident can be prevented by evaluating the history, physical examination and appropriate supporting examinations, one of which is ultrasound. Early detection in cases of obstetric emergency can help in appropriate and fast treatment so that morbidity and mortality rates can be reduced.

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