International Journal of
Science Inventions Today
www.ijsit.com
ISSN 2319-5436
Review Article

MOLAR PREGNANCY OR HYDATIDIFORM MOLES CONFIRMATION DIAGNOSIS BY ULTRASOUND AND HUMAN CHORIONIC GONADOTROPIN BLOOD TEST

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ABSTRACT

Distinguishing hydatidiform moles (HMs) from nonmolar specimens and the subclassification of hydatidiform mole are important because complete hydatidiform mole (CHM) is associated with an increased risk of development of gestational trophoblastic neoplasia. Complete hydatidiform mole is an abnormal pregnancy that usually presents with vaginal bleeding and markedly elevated human chorionic gonadotropin (hCG) levels. These abnormalities are established in a hypoxic environment during the first trimester of gestation. On ultrasound this mass often has a grapelike appearance, as it contains many small cysts.

Keywords: human chorionic gonadotropin; Complete molar pregnancy; Partial molar pregnancy; Hydatiform mole

INTRODUCTION

A molar pregnancy also known as hydatidiform mole. it is a rare complication of pregnancy characterized by the abnormal growth of trophoblasts, the cells that normally develop into the placenta[1]. These abnormalities are established in a hypoxic environment during the first trimester of gestation [2]. There are two distinct entities of molar pregnancy: complete molar pregnancy and partial molar pregnancy. Partial moles are characterized by the presence of fetal or embryonic tissues, chorionic villi of different sizes featured by their focal trophoblastic hyperplasia and focal swelling, and marked villous scalloping [3]. But the fetus is not able to survive, and is usually miscarried early in the pregnancy [4]. However, complete moles are characterized by the absence of embryonic or fetal tissues, diffuse trophoblastic hyperplasia and hydropic swelling of villi, and marked atypia of trophoblast at the implantation site [5]. A molar pregnancy can have serious complications including a rare form of cancer and requires early treatment [4]. The majority of complete moles present with vaginal bleeding and markedly elevated hCG values[6]. A molar pregnancy may seem like a normal pregnancy at first, but most molar pregnancies cause specific signs and symptoms, including: Dark brown to bright red vaginal bleeding during the first trimester, severe nausea and vomiting, sometimes vaginal passage of grapelike cysts, Pelvic pressure or pain [7, 8]. Sign are Rapid uterine growth the uterus is too large for the stage of pregnancy, High blood pressure, Preeclampsia a condition that causes high blood pressure and protein in the urine after 20 weeks of pregnancy, Ovarian cysts, Anemia, Overactive thyroid (hyperthyroidism)[7, 9-11].

Pathophysiology:

As described previously, hydatidiform moles arise from the gestational tissue. In whole hydatidiform moles, there is no fetal tissue presents whereas, in partial hydatidiform moles, there is some nonviable fetal tissue apparent [9]. Both are due to over-proliferation of the chorionic villi and resulted swelling[2]. They result in high levels of hCG to be produced[12]. To review, in complete moles an enucleated egg is fertilized either by two sperm or a haploid sperm that then duplicates, resulting in only paternal DNA being expressed[13]. Conversely, in partial hydatiform mole, a haploid ovum either duplicates or fertilized by normal sperm or a haploid ovum is fertilized by two sperm, resulting in both the expression of both maternal and paternal DNA.[7, 9, 14]

Histopathology:

Hydatiform moles are caused by a proliferation of the villous trophoblast accompanied by swelling of the chorionic villi [15]. As described previously, the main difference between complete and partial hydatidiform histologically is the lack of embryonic/fetal tissue in complete moles, and the presence of-of embryonic tissue in partial moles[3]. Furthermore, in a complete mole, the chorionic villi are diffusely hydropic and typically are surrounded by hyperplastic trophoblasts[16]. In a partial mole their normal chorionic villi and embryonic/fetal tissue mixed with hydropic villi. [14]

DISCUSSION

A molar pregnancy also known as hydatidiform mole[17]. It is a rare complication of pregnancy characterized by the abnormal growth of trophoblasts, the cells that normally develop into the placenta. In Europe and North and South America, hydatidiform moles are observed in Approximately 1 in every 1,000 pregnancies is diagnosed as a molar pregnancy [15]. The prevalence is 5 to 15 fold higher in East Asia [15]. In a complete molar pregnancy, an empty egg is fertilized by one or two sperm, and all of the genetic material is from the father. In this situation, the chromosomes from the mother's egg are lost or inactivated and the father's chromosomes are duplicated [4]. therefore, only paternal DNA is expressed [7]. This most often occurs when two sperm fertilize an egg, resulting in an extra copy of the father's genetic material.[4] [7, 9, 14] The karyotype of complete moles is usually 46,XX 90% of the time and 46,XY 10% of the time; the chromosomes derive completely from the father as a complete mole likely results from the fertilization of anuclear empty ovum by a haploid sperm that duplicates its own chromosomes after meiosis[3, 7, 10]. On the other hand, in partial moles, the karyotype is 90% of the time triploid and either 69,XXX or 69,XXY[1, 5, 17, 18]. This karyotype arises when a normal sperm subsequently fertilizes a haploid ovum duplicates and or when two sperms fertilize a haploid ovum. In partial moles, both maternal and paternal DNA is expressed[7]. Symptoms of a molar pregnancy may include: Abnormal growth of the uterus, either bigger or smaller than usual severe nausea and vomiting, Vaginal bleeding during the first 3 months of pregnancy [4]. Classical clinical signs of hydatidiform mole at diagnosis were vaginal bleeding, disproportionate increase in the size of the uterus, an abnormally high level of hCG for gestational age, hyperemesis gravidarum(severe nausea and vomiting), cystic enlargement of the ovaries, and eventually hyperthyroidism and pregnancy-induced hypertension [8]. The widespread use of ultrasonography in early gestation and the enhanced accuracy of hCG assays have led to earlier diagnosis of molar pregnancy and subsequently changed its classical clinical presentation[1, 2, 6, 7, 9, 11, 12, 19-22]. Complete molar pregnancies are often correctly diagnosed by ultrasound especially with the presence of characteristic placental features such as cystic changes and overt masses [16]. The ultrasound was very helpful in making the diagnosis of any patient after detecting a large intrauterine heterogeneous mass encompassing multiple anechoic spaces. As the embryo dies at an early stage, no fetal parts are seen [30]. The classic sonographic features of complete molar pregnancy include an enlarged uterus with a central heterogeneous echogenic mass that expands the endometrial canal. The mass contains multiple cystic spaces of varying size, representing the hydropic villi (Fig.1). These cystic spaces may vary in size from a few millimeters to 2 to 3 cm. In the second trimester, transabdominal sonographic diagnosis is highly accurate. In the first trimester, however, molar tissue may appear as a predominantly solid, echogenic mass on transabdominal sonography because tiny hydropic villi may not be adequately resolved. With its better resolution, transvaginal sonography may depict the hydropic villi earlier and to better advantage. In complete moles, a fetus is absent except in the rare event of a coexistent twin pregnancy; in such cases, ultrasonography is accurate in establishing the diagnosis. The ovaries may be greatly enlarged in complete molar pregnancy by multiple, bilateral theca lutein cysts. These are large, usually multilocular, and may undergo hemorrhage or torsion and can be a source of

pelvic pain. Theca lutein cysts are most marked when trophoblastic proliferation is severe. They are seen much less often in the first trimester [26, 27]. In partial molar pregnancy, the placenta is excessive in size and contains numerous cystic spaces distributed in a nonuniform manner (Fig.2) [29]. Found that a ratio of transverse to anteroposterior dimension of the gestational sac of greater than 1.5, as well as cystic changes, irregularity, or increased echogenicity in the decidual reaction/placenta or myometrium, was significantly associated with this diagnosis. Agrowth-impaired fetus is present and may show multiple anomalies. Recent studies have shown that ultrasonography is much more accurate in diagnosing complete molar pregnancy than partial molar pregnancy [28]. The diagnosis was then confirmed by the histological evaluation of the evacuated tissues [16]. Patients with complete mole usually have abnormally elevated hCG reaching greater than 100,000 milli-international units per liter in approximately half of cases [6]. Multiple pregnancy involving a partial hydatidiform mole and normal fetus is rare [4, 10, 23]. Tests done may include: Abdominal or vaginal ultrasound of the pelvis, hCG (quantitative levels) blood test, Chest x-ray, CT or MRI of the abdomen (imaging tests), Complete blood count (CBC) Blood clotting tests Kidney and liver function tests [7, 9, 10, 14]. Since the start of ultrasonography, the diagnosis of complete molar pregnancies has increased in the early stages of pregnancy, mainly during the first trimester [5, 14, 17, 18]. The most common symptom (in one study as high as 84% of patients) of a complete mole is vaginal bleeding in the first trimester which is normally due to the molar tissue separating from the decidua, resulting in bleeding[2, 9, 12]. The typical buzz word appearance of the vaginal bleeding is described as a "prune juice" appearance [19, 24]. This is secondary to the accumulated blood products in the uterine cavity and resultant oxidation and liquefaction of that blood[6]. The imaging of choice in a suspected hydatiform mole is a pelvic ultrasound. In a complete mole, the ultrasound findings include a heterogeneous mass in the uterine cavity with multiple anechoic spaces; a pregnancy ultrasound will show a snowstorm appearance with an abnormal placenta, with or without some development of a baby [7, 9, 10, 14]. These small cystic areas are typically the hydropic villi [16]. Furthermore, there is the absence of an embryo or fetus, and no amniotic fluid is present, a thick cystic placenta nearly filling the uterus or Ovarian cysts [22]. This can be detected as early as 8 or 9 weeks of pregnancy more than 50% of cases uterine size [10, 25]. In a complete mole, the uterus is usually larger than the expected gestational date of the pregnancy, whereas, in partial moles, the uterus can be smaller than the suggested date [16]. In a partial mole, there typically is the finding of a fetus which may be viable, Low amniotic fluid, and the placenta appears to have enlarged, cystic spaces (often described as "Swiss cheese" appearance)[6, 11, 21]. The presentation of a partial hydatiform mole is usually less dramatic than that of a complete mole[23]. These patients typically present as described before with symptoms similar to a threatened or spontaneous abortion including vaginal bleeding [4]. Since partial hydatiform moles have a fetal tissue, on examination, these patients may have fetal heart tones evident on Doppler [14, 18]. In a pregnant patient with vaginal bleeding, one should always obtain a serum quantitative hCG level and patient's blood type[17]. In hydatiform moles, the serum hCG levels are typically much higher than patients of the same gestational date in a normal pregnancy or ectopic pregnancy [1, 5, 24]. Complete moles tend to have very high levels of serum hCG, typically greater than 100,000 milli-international

units per liter whereas partial moles may be within normal range for gestational age or even lower than expected[6, 10, 21]. Blood type is important because most patients with complete or partial hydatiform moles present with vaginal bleeding, and therefore Rh antibody screening needs to be performed to determine whether anti-D immunoglobulin needs to be administered if the patient is Rh(D) negative[3, 4, 13, 15]. Other laboratory tests include: Complete blood count (CBC)-to evaluate for anemia and thrombocytopenia, basic metabolic panel (BMP)-to evaluate for electrolyte imbalance and renal insufficiency, Thyroid panel-if signs and symptoms of hyperthyroidism present, Liver function tests and urinalysis -if pre-eclampsia is suspected to evaluate for transaminitis and proteinuria, Coagulation profile including prothrombin time/ international normalized ratio (PT/INR) to evaluate for disseminated intravascular coagulation in severe cases[7, 12, 20]. If a molar pregnancy is diagnosed, the next step is typically a chest x-ray to determine metastasis[2]. In addition, a chest x-ray should be obtained if patient's initial symptoms include any signs of respiratory distress or increased work of breathing to evaluate for pulmonary edema.[14]

Late findings of the disease (after the first trimester around 14 to 16 weeks of pregnancy) including signs and symptoms of hyperthyroidism, Anemia including tachycardia and tremors, again caused by the high levels of circulating hCG [9, 19]. Other late sequel are pre-eclampsia In very advanced cases, patients present with severe respiratory distress possible from embolism of the trophoblastic tissue into the lungs [16, 25].

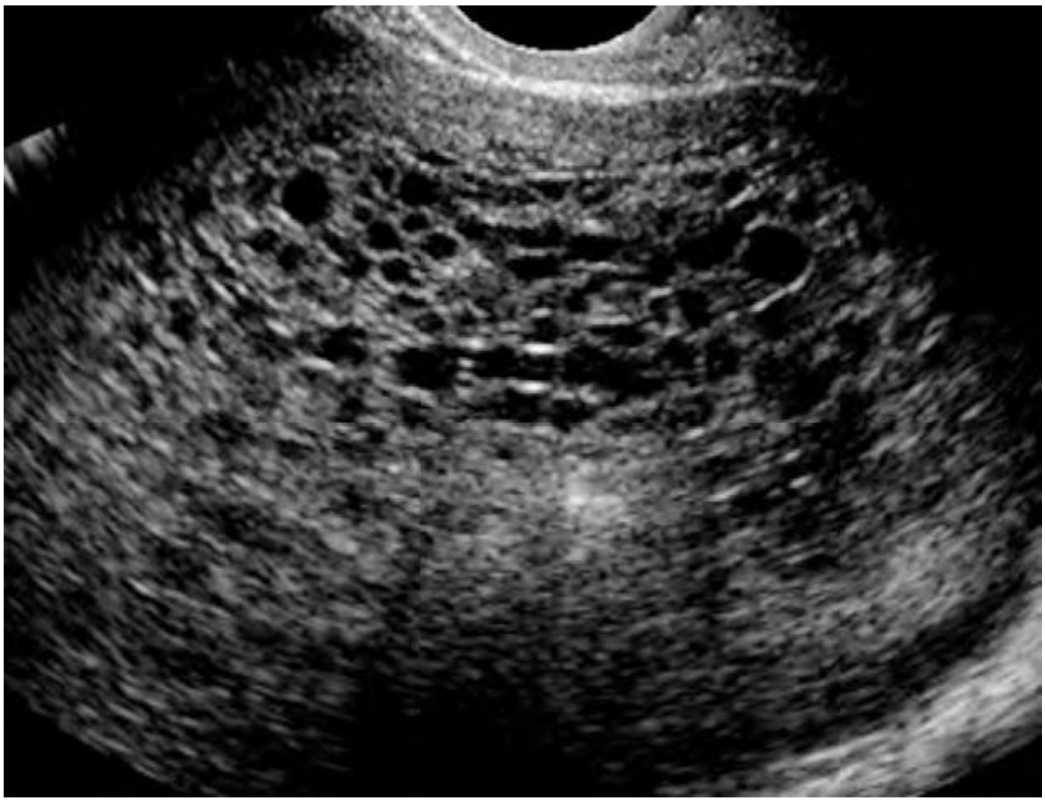

Figure 1 - Complete molar pregnancy: Transabdominal scan shows a vesicular echogenic mass distending the endometrium. The mass is filled with innumerable uniformly distributed cystic spaces that corresponded to hydropic chorionic villi at pathology.

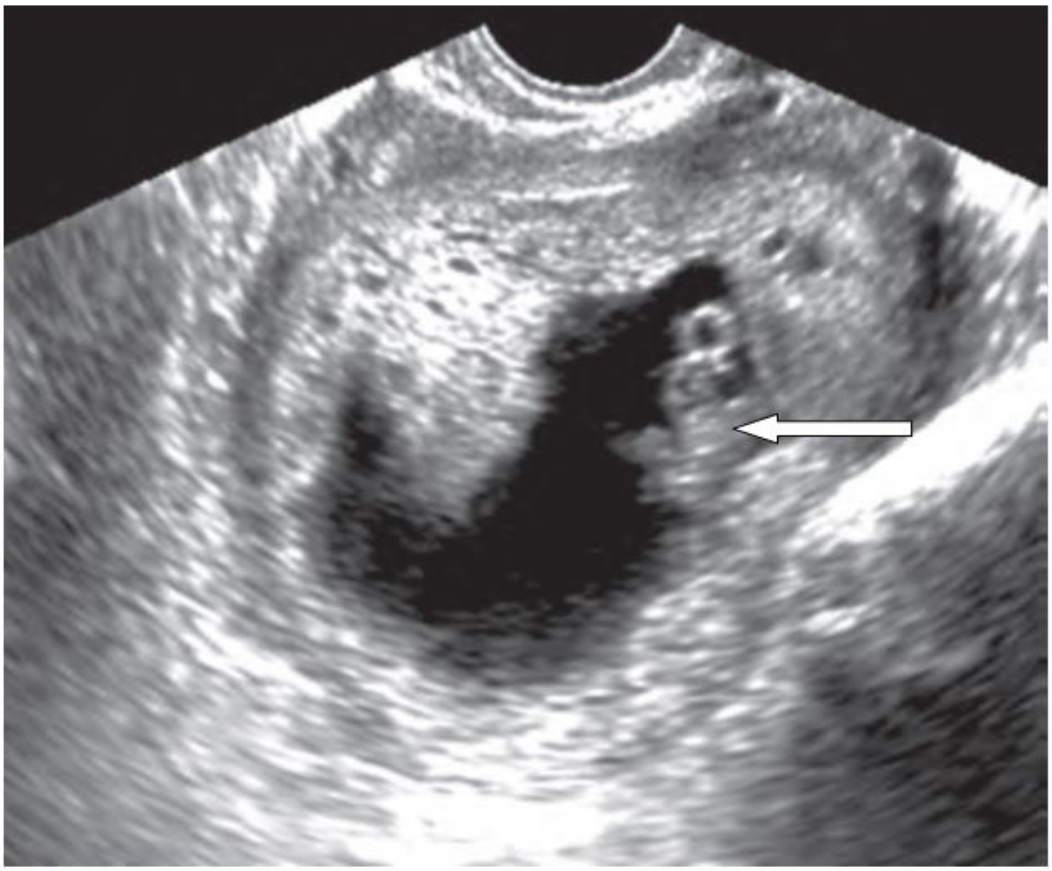

Figure 2 - Partial molar pregnancy at 8 weeks' gestation. Transvaginal scan shows a gravid uterus with a yolk sac and live 8-week embryo *(arrow).* On the right is a large placenta with multiple small cystic spaces consistent with hydropic villi. Pathology confirmed partial mole.

Treatment:

Once molar pregnancy is diagnosed, and an obstetric/gynecology consultation is obtained, patients are typically admitted to the hospital for surgery. A molar pregnancy can't continue as a normal viable pregnancy[22]. To prevent complications, the abnormal placental tissue must be removed[16]. Treatment usually consists of one or more of the following steps:

Dilation and curettage (D&C): To treat a molar pregnancy remove the molar tissue from the uterus with a procedure called dilation and curettage (D&C)[21]. A D&C is usually done as an outpatient procedure in a hospital [1, 4, 5, 13, 14, 16, 17, 21-25]. During the procedure, patient will receive a local or general anesthetic and be positioned on the operating room table on her back with your legs in stirrups. Obstetric/gynecology doctor will insert a speculum into patient vagina, as in a pelvic exam, to see the cervix[6]. Doctor will then dilate the cervix and remove uterine tissue with a vacuum device[11]. Sometimes a partial molar pregnancy can continue[23]. A woman may choose to continue her pregnancy in the hope of having a successful birth and delivery [1, 2, 5, 12, 14, 17, 22, 25]. However, these are very high-risk pregnancies[4, 14].

Hysterectomy: Rarely, if there is increased risk of gestational trophoblastic neoplasia (GTN) and there's no desire for future pregnancies, the uterus may be removed (hysterectomy).[10, 13, 18, 19, 23]. Hysterectomy (surgery to remove the uterus) may be an option for older women who DO NOT wish to become pregnant in the future[5, 17, 18].

HCG monitoring: After treatment, repeat measurements of your HCG level until it returns to normal[1, 6, 24]. If patient continue to have HCG in the blood, it is important to avoid another pregnancy and to use a reliable contraceptive for 6 months to 1 year after treatment for a molar pregnancy[10, 21]. This time allows for accurate testing to make sure there's no remaining molar tissue[4]. Women who get pregnant too soon after a molar pregnancy are at high risk of having another molar pregnancy[13]. Because pregnancy HCG levels also increase during a normal pregnancy, doctor may recommend you wait 6 months to 1 year before trying to become pregnant again[15]. Your provider will recommend a reliable form of birth control during this time[3]. Most HMs are noncancerous (benign)[7, 20]. Treatment is usually successful[12]. Close follow-up by your provider is important to ensure that signs of the molar pregnancy are gone and pregnancy hormone levels return to normal[2]. In some cases of complete HM, moles can become invasive[9]. These moles can grow deep into the uterine wall and cause bleeding or other complications[19]. In very few cases of complete HM, moles develop into a choriocarcinoma[25]. This is a fast-growing cancer[16]. It is usually successfully treated with chemotherapy, but can be life threatening[22]. Possible Complications of molar pregnancy may include: Change to invasive molar disease or choriocarcinoma , Preeclampsia, Thyroid problems Molar pregnancy that continues or comes back[16].

CONCLUSIONS

Complete molar pregnancy is associated with marked cystic changes and mass formation and is often diagnosed ultrasonographically. Partial molar pregnancy often presents with minor cystic changes of the placenta and remains underdiagnosed sonographically. However, correct prospective diagnosis was made more frequently in this study than in older reports, perhaps due to improved spatial resolution of ultrasonographic equipment.

Acknowledgement:

This work was supported by grants from the National Natural Science Foundation of China (31700736), Hubei Province Health and Family Planning Scientific Research Project (WJ2016Y07), Hubei Province Scientific and Technological Research Project (Q20171306) and the College Students Innovative Entrepreneurial Training Program in Yangtze University (2018184)

Conflicts of Interest:

The authors declare no conflicts of interest

What patient can do before appointment?

- Write down any symptoms you're experiencing, including when they first started and how they've changed over time.
- Make a note of the date of your last menstrual period, if you remember it.
- Write down key personal information, including any other medical conditions for which you're being treated.
- Make a list of all medications, as well as any vitamins or supplements you're taking
- Preparing a list of questions in advance will help you make the most of your time with your doctor. For molar pregnancy, some basic questions to ask include:
- What is likely causing my symptoms or condition?
- What kind of tests do I need?
- What needs to be done now?
- What treatment approach do you recommend?
- Do I need to follow any restrictions?
- What emergency signs and symptoms should I watch for at home?
- What are my chances for a successful future pregnancy?
- How long should I wait before trying to become pregnant again?
- Does my condition increase my risk of developing cancer in the future?

What to expect from your doctor?

- Your doctor will likely perform a physical exam and run some tests, including a blood test and ultrasound exam. He or she may also ask you a number of questions, such as:
- When was your last menstrual period?
- When did you first begin experiencing symptoms?
- Have your symptoms been continuous or occasional?
- Are you having any pain?
- Compared with your heaviest days of menstrual flow, is your bleeding more, less or about the same? Have you passed any grapelike cysts from your vagina?
- Are you experiencing any lightheadedness or dizziness?
- Have you had a past molar pregnancy?
- What chronic conditions, if any, do you have?
- Do you wish to become pregnant in the future?

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