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Case Report

Complete hydatidiform mole with massive intrauterine hemorrhage in an adolescent girl

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Abstract: Hydatidiform mole (HM) is a premalignant proliferative trophoblastic disorder. Vaginal bleeding is the most common presenting symptom in women with HM. A 17-year-old nulliparous adolescent girl presented with progressive lower abdominal pain and pronounced nausea and vomiting of about a week's duration. Her gestational age was 12 weeks and 4 days according to her last menstruation date. Pelvic examination revealed a closed cervical os and no uterine bleeding. Subsequent ultrasound and magnetic resonance imaging (MRI) depicted a T2-hyperintense, huge intrauterine mass, numerous cystic spaces, and massive peri-lesional hemorrhage. Immediately after introducing a forcep into the uterine cavity for suction curettage, a large amount of trophoblastic tissue was expelled and sudden gushes of blood with clots were passed. Histological examination and p57 immunohistochemistry resulted in a final diagnosis of complete hydatidiform mole. Massive intrauterine concealed hemorrhage in an adolescent is a rare complication of complete hydatidiform mole.

Keywords: Complete hydatidiform mole, massive intrauterine hemorrhage, abdominal pain

Introduction

Hydatidiform mole (HM) is a proliferative disorder of placental trophoblastic cells. It may result from an aberrant fertilization process, and is more common in women younger than 20, older than 40, or in women with prior molar gestations. Approximately one fourth of patients that develop HM are adolescents [1]. Signs and symptoms include vaginal bleeding, anemia, excessive vomiting, transvaginal expulsion of grape-like vesicles, excessive uterine size, hyperthyroidism, and preeclampsia [2]. HM is classified as complete or partial based on histopathologic and genetic features. Progression to gestational trophoblastic neoplasia (GTN) occurs in 5-15% of cases of complete mole and in 1-3% of cases of partial mole [3]. Here, we report an unusual presentation of complete hydatidiform mole, which exhibited prominent features, such as, extremely high human chorionic gonadotropin (HCG) levels, excessive uterine size, and hyperthyroidism with massive intrauterine concealed hemorrhage without obvious vaginal bleeding in an adolescent.

Case presentation

A 17-year-old nulliparous adolescent girl presented with progressive lower abdominal pain with pronounced nausea and vomiting of duration around one week. She was referred to our hospital for further evaluation of a huge abdominal mass, and had no significant medical, surgical, or obstetric history. The patient was alert, afebrile, and hemodynamically stable (BP 110/70 mmHg, HR 74 bpm), and her chest X-ray and electrocardiogram were unremarkable. A pregnancy test was positive and her last menstrual period was 12^{+4} weeks prior to presentation. The abdomen was distended and a huge mass was palpable above the umbilicus. Pelvic examination with a speculum showed no blood in the vagina and a closed cervical os. However, subsequent ultrasound revealed a distended endometrial cavity containing a

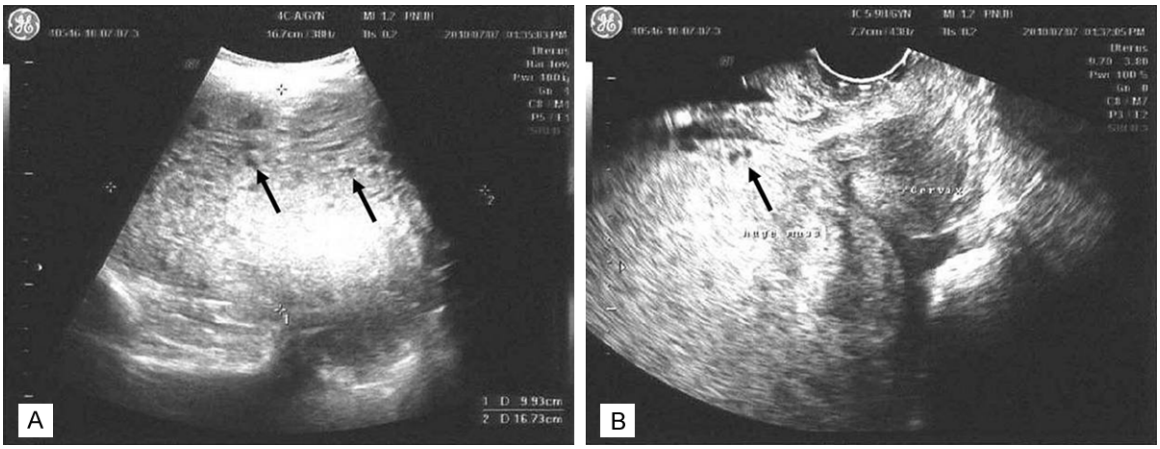

Figure 1. Transabdominal (A) and transvaginal (B) ultrasound of the uterus demonstrating the sonographic appearance of a hydatidiform mole. A heterogenous, complex echogenic, solid mass containing tiny, hypoechoic cystic spaces (arrows) characteristic of hydropic villi was noted within the endometrial cavity.

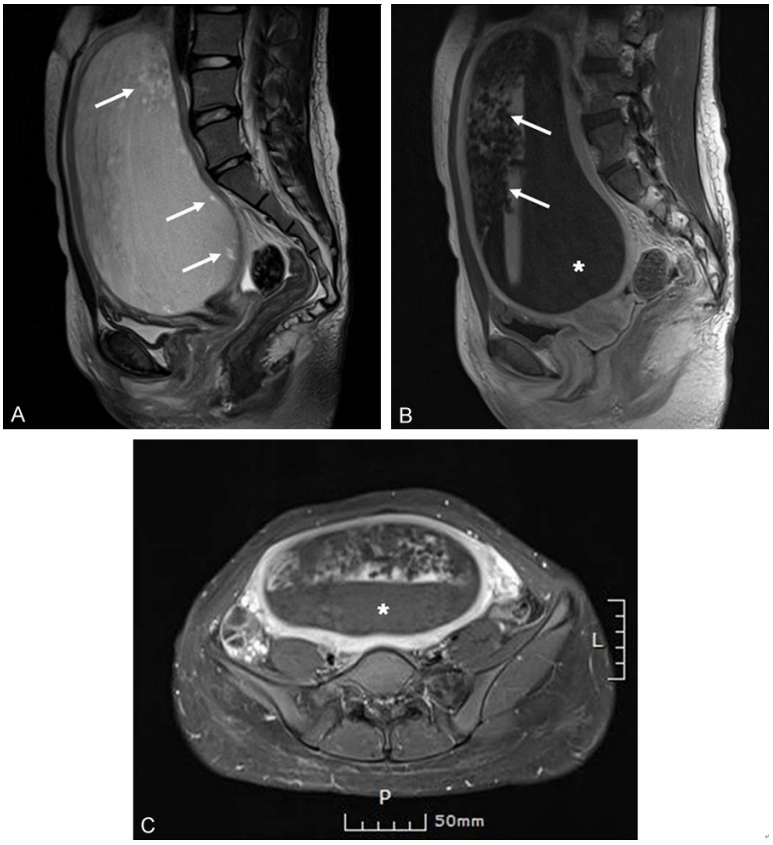

Figure 2. MRI findings of complete hydatidiform mole. A. Sagittal T2-weighted image showing a hyperintense intrauterine mass that distended the endometrial cavity. Numerous cystic spaces (arrows) were present in the mass. B. Sagittal contrast-enhanced T1-weighted image showing the enhancement and the "bunch of grapes" appearance (arrows), representing hydropic swelling of trophoblastic villi. C. In the supine position, the upper half of the uterus showed molar tissues and the lower half massive peri-lesional hemorrhage (*).

huge, heterogeneous solid mass with multiple hypoechoic cysts suggestive of molar pregnancy (**Figure 1**).

Upon admission, hemoglobin was 7.0 g/dL, hematocrit was 20.9%, and HCG was highly elevated (1,741,487 mIU/mL). Thyroid function test (TFT) showed elevated triiodothyronine (T3) and free thyroxine (FT4) levels, and a diminished thyroid-stimulating hormone (TSH) level. Despite a hyperthyroidic state, as determined by laboratory findings, she was asymptomatic and had a normal heart rate, and thus, no further treatment was needed. MRI was performed to ascertain the presence of a coexisting or extrauterine disease. T2-weighted images depicted a hyperintense intrauterine mass that distended the endometrial cavity and contained numerous cystic spaces. Contrast-enhanced T1-weighted images showed enhancement with a "bunch of grapes" appearance, representing hydropic swelling of trophoblastic villi. Massive

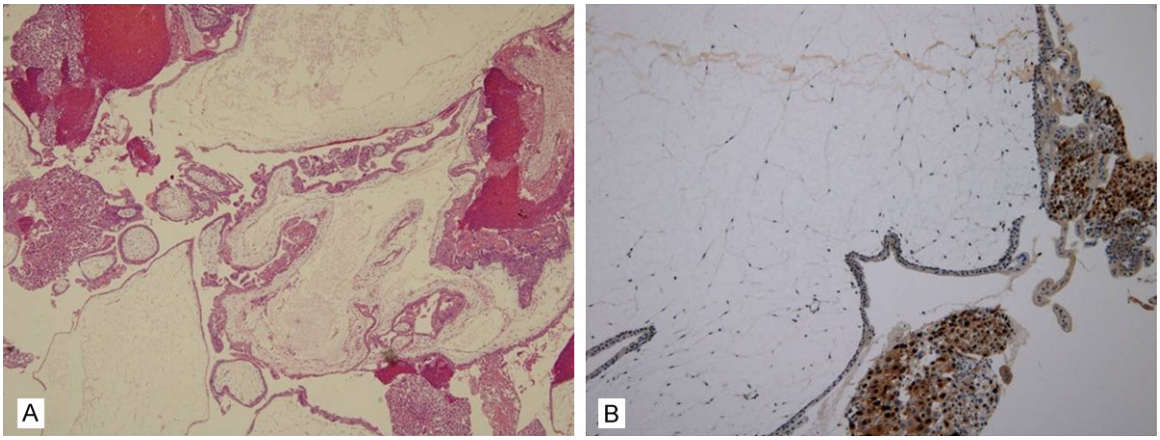

Figure 3. A. Complete hydatidiform mole containing a mixture of edematous villi and relatively normal-appearing villi. Edematous villi were enlarged, irregularly shaped and exhibited central cavitation (H&E, ×40). B. Villous stromal cells and cytotrophoblasts were negative for p57, but extravillous intermediate trophoblastic cells were positive and served as internal positive controls (p57, ×200).

peri-lesional hemorrhage and theca lutein ovarian cysts were also observed (**Figure 2**).

At time of laminaria insertion for suction curettage, no bleeding was observed, but immediately after forcep introduction into the uterine cavity, a large amount of trophoblastic tissue and sudden gushes of blood with clots (~1,300 ml in total) were passed. The amount of bleeding spontaneously decreased without active bleeding. After uterine decompression, the uterus was fully evacuated without further significant hemorrhage. On gross examination, molar specimens consisted of bloody fluid with clots admixed with grape-like vesicles, which weighed 866.8 g. Microscopically, the mass was composed of a mixture of edematous and relatively normal villi. The edematous villi were irregular in shape and showed central cavitation. Immunohistochemical staining for p57 was negative for villous stromal cells and cytotrophoblasts (**Figure 3**). Histological examination resulted in a final diagnosis of complete HM. Serum HCG declined to 466,442 and 9,118 mIU/mL on days 1 and 7, respectively, after evacuation. Plateaued or rising HCG levels were observed at 2, 3, and 4 weeks after evacuation (2,093, 3,068, and 6,298 mIU/mL, respectively). Metastatic work up demonstrated no lesions in other sites. Three courses of chemotherapy with methotrexate (MTX) were administered and hCG decreased to normal at approximately 10 weeks and has remained at this level ever since.

Discussion

The described case exhibited an unusual presentation of complete HM with prominent clinical features, which included an extremely high HCG level, huge enlargement of the uterus, hyperthyroidism, and a rare massive intrauterine concealed hemorrhage. Major risk factors for HM are the upper and lower extremes of maternal age and prior molar pregnancy. Markedly elevated HCG levels are commonly associated with hyperemesis gravidarum, hyperthyroidism, theca lutein ovarian cysts, and even preeclampsia [4]. However, these classic symptoms and signs are now infrequently encountered because of the availabilities of sensitive HCG assays and the early use of high resolution ultrasound during obstetrical care.

The clinical characteristics of molar pregnancy in adolescents have been previously described by Braga et al., and its most common symptom at presentation is vaginal bleeding. Complete moles are more common than partial moles in adolescents. However, the risk of progression to GTN is significantly lower in adolescents. On the other hand, HCG levels and median gestational ages at diagnosis are similar in adults and adolescents [1].

Disruption of maternal vessels by chorionic villi causes bleeding into the uterine cavity and retained blood presents as vaginal bleeding in most cases of HM [3]. Although vaginal bleed-

ing remains the most common presentation in women with complete HM, its prevalence is gradually declining due to earlier diagnoses. Recent studies have shown that vaginal bleeding is presented in 46% and 98% of cases in the UK and Philippines, respectively, and its incidence has been reported to differ in geographic regions [5, 6]. Gestational trophoblastic disease is considered a vascularized tumor and hemorrhagic complications are the most common cause of mortality associated with this disorder. Vaginal bleeding may become aggravated or life-threatening during medical or surgical procedures, but massive intrauterine hemorrhage associated with HM as an initial presentation prior to a suction evacuation procedure has rarely been reported. However, a case of partial HM with massive intraplacental hemorrhage resulting in a hemoglobin level decrease at 28th week of gestation has been reported [7]. In the present case, no obvious vaginal bleeding was observed at initial presentation. In addition, the cervix was closed and no bleeding was encountered during laminaria insertion. However, immediately after introducing a forcep into the uterine cavity, sudden gushes of blood were passed, which probably originated from intrauterine concealed hemorrhage rather than ongoing hemorrhage. Nonetheless, after a large amount of blood had been expelled the bleeding spontaneously decreased, and the uterus was fully evacuated without further significant hemorrhage.

Elevated serum HCG in HM may activate thyroid cells due to structural homology between HCG and TSH, which results in free T4, free T3, total T3, and total T4 increases and a subsequent TSH decrease [8]. The prevalence of hyperthyroidism among HM patients has been reported to be 7-35% [8, 9]. Our case showed biochemical hyperthyroidism, but was asymptomatic and did not require treatment.

Ultrasound is the modality of choice for diagnosing localized gestational trophoblastic disease. Molar pregnancy is characteristically observed as an enlarged uterus containing a hyperechoic, solid, heterogenous mass, with many anechoic spaces representing dilated, hydropic villi. Bilateral ovarian theca lutein cysts are present in 30-50% of cases. MRI appearance of HM may be relatively nonspecific, although pelvic MRI is sometimes used to assess the depth of myometrial invasion and extrauterine spread in complicated cases. In addition, MRI may play an important role in patients with confusing clinical features. Our patient with severe iron-deficiency anemia had a huge, heterogenous, endometrial mass with no apparent vaginal bleeding, and MRI demonstrated HM with no myometrial invasion, massive intrauterine hemorrhage, and the absence of necrotic and inflammatory lesions and of coexistent trophoblastic tumors.

Diagnosis can be made based on histopathological criteria in most cases. However, diagnosis based on morphological features alone is insufficient in around 10% of cases and subject to interobserver variability. Thus, ancillary investigations, such as, p57 immunohistochemistry or molecular genotyping, may be required. Furthermore, these investigations accurately classify HM as complete or partial. p57 immunostaining is helpful for the identification of complete mole, and genotyping provides a means of differentiating complete and partial HM in diagnostically challenging cases [10] and is appropriate for clinical management and assessing the risk of persistent gestational trophoblastic disease. Our case appeared to be partial mole morphologically, but p57 immunostaining was negative, which is diagnostic of complete mole.

Suction curettage is the treatment most commonly used to manage HM, and its cure rate for partial mole is approximately 84%. Serial quantitative serum HCG measurement after suction evacuation is needed to diagnose persistent trophoblastic neoplasia early in all patients. This condition occurs in 5-15% cases of complete mole and in 1-3% cases of partial mole and requires further treatment [3].

The gestational age of patients diagnosed with HM has continuously declined over the last two decades [6]. It has been reported diagnosis of complete HM at earlier gestation was not associated with a reduced risk of postmolar GTN or the subsequent need for chemotherapy [11]. Adolescents are more likely to develop HM at a later gestational age in some countries [12], in adolescents HM is associated with higher rates of vaginal bleeding and anemia, and greater uterine sizes than indicated by dates [13]. Thus early diagnosis is essential as delayed detection may expose adolescents to an increased

risk of serious complications. Furthermore, adolescents tend to visit hospital late because they are incautious about symptoms and are unaware of the seriousnesses of their conditions. This case highlights that complete mole may have an unusual presentation with massive intrauterine concealed hemorrhage and no obvious vaginal bleeding in adolescents.

Disclosure of conflict of interest

None.

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