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Complete hydatidiform mole in a 52-year-old postmenopausal woman: A case report and literature review

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ABSTRACT

Benign gestational trophoblastic disease generally occurs in women of reproductive age and is extremely rare in postmenopausal women. Here, the authors describe a case of complete hydatidiform mole in a 52-year-old postmenopausal woman with a history of lower abdominal bloating and vaginal bleeding. The paper summarizes the clinical manifestations, physiopathology, diagnosis, and treatment options for gestational trophoblastic disease in postmenopausal women. This study highlights that gestational trophoblastic disease can occur in postmenopausal women and that it is important to include it in the differential diagnosis of postmenopausal bleeding, to prevent delay in treatment.

1. Introduction

Gestational trophoblastic disease (GTD) is an uncommon group of pregnancy-related disorders, with a course of trophoblastic proliferation, including hydatidiform mole (HM), invasive and metastatic mole, choriocarcinoma, placental-site trophoblastic tumor, and epithelial trophoblastic tumor [1]. HM is an abnormal pregnancy caused by genetic fertilization disorders that often occurs in women of reproductive age (13 to 49 years) [2]. Pregnancy at an older age is uncommon and is more likely to result in spontaneous abortion or to be a molar pregnancy [3]. However, it frequently represents a malignant disease in women older than 50 years [4]. HM is categorized into two separate entities, complete hydatidiform mole (CHM) and partial hydatidiform mole (PHM) according to morphology and cytogenetics, with a ratio from 3:1 to 1:1 [5]. The incidence of CHM and PHM is 1 and 3 per 1000 pregnancies and 3 per 1000 pregnancies, respectively [6]. CHM is extremely rare in postmenopausal women: only approximately 14 cases of CHM have been reported in the world literature since its first description in 1973 [7]. This reports describes the case of a 52-year-old woman with benign CHM noted more than two years after amenorrhea.

2. Case Presentation

A 52-year-old postmenopausal woman (gravida 5, para 3, abortion 2) whose last menstrual period was two years previously presented with a 15-day history of lower abdominal bloating and vaginal bleeding. The patient denied drug allergies, systemic diseases, and any personal or family history of malignancy. The gynecologic examination of the vulva and vagina was normal, the size of the uterus was appropriate for 20 weeks of gestation, and she had mild bleeding. Transabdominal pelvic ultrasound showed an enlarged uterus (16.4 cm × 14.2 cm × 8.9 cm) and a heterogeneous mass (15.2 cm × 10.5 cm × 7.4 cm) occupying the whole uterine cavity. Laboratory tests showed a decreased hemoglobin level (81 g/L, reference range: 115–150 g/L) and an elevated serum levels of beta-human chorionic gonadotropin (β-HCG) (1239.0 mIU/mL, reference range: 0–3.0 mIU/mL) and carbohydrate antigen 125 (CA125) (52.0 U/mL, reference range: 0–35.0 U/mL). Due to the high level of β-HCG, gestational trophoblastic neoplasm was considered in the differential diagnosis, alongside ectopic pregnancy, resulting in gynecooncology consultation. In addition to abdominal sonography, thoracic and cranial tomographic examinations were performed to identify potential lung, liver, and brain metastases. No clear evidence of metastatic lesions was observed in the diagnosis images. As HM is occasionally complicated by hyperthyroidism or increased thyroid function, which may require treatment, thyroid function tests were also performed. Serum concentrations of free triiodothyronine (FT3), free thyroxine (FT4), and thyroid-stimulating hormone (TSH) were 6.57 pg/mL, 3.13 ng/dL, and < 0.01mIU/L, respectively, and therefore the patient was treated with thiamazole.

The findings, in combination with the patient's clinical presentation,

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confirmed the diagnosis of molar pregnancy. Suction evacuation was performed after arranging two units of whole blood. The operation was successful, and the intraoperative blood loss was approximately 200 mL. Macroscopic examination revealed blood clots and large edematous villi with multiple grapelike transparent vesicles measuring up to 5 mm in diameter (Fig. 1). Microscopic examination revealed generalized hydropic villi with cisterns and trophoblast proliferation, confirming the diagnosis of CHM (Fig. 2). Immunostaining for p57 was negative in the nuclei of cytotrophoblasts and villi mesenchyme (Fig. 3), which further supported the CHM diagnosis. The serum β-HCG level fell to 127.4 mIU/mL on the third day after suction. The patient underwent total laparoscopic hysterectomy and bilateral salpingo-oophorectomy given the postmenopausal state and was discharged from the hospital on the fourteenth postoperative day, when her serum β-HCG level had dropped 3.6 mIU/ml. She was followed up regularly and did well. Quantitative serum β-HCG level testing over follow-up followed a steady downward trend to the normal range. The final evaluation was postmenopausal non-invasive complete mole.

3. Discussion

GTD covers a spectrum of benign and malignant conditions arising from pregnancies with highly abnormal trophoblastic tissue development. As early as 1973, Jequier and Winterton reported 109 patients with GTD, ranging in age from 50 to 59 years, two of whom were postmenopausal and had been diagnosed with a benign mole more than one year earlier [7]. Tsukamoto *et al.* reported 20 women of GTD (≥ 50 years), none of whom were diagnosed with CHM [8]. In China, Feng *et al.* reviewed 38 cases of GTD in women aged 50 years or more, of whom 19 had invasive moles, five were HM patients, 12 were choriocarcinomas patients, and two had placenta-site trophoblastic disease [9]. There are about 14 cases [3,7,10–21] in the global literature concerning CHM in the postmenopausal period (Table 1). Based on these cases, the most common symptoms of CHM in postmenopausal women are vaginal bleeding (approximately 80%), uterine enlargement (100%), abdominal pain (42%), and nausea and vomiting (25%), as well as markedly elevated serum β-HCG levels.

However, postmenopausal women with amenorrhea for more than one year may not have their β-HCG level checked because the possibility of pregnancy is often overlooked or denied [22]. Menopause is a turning point in every woman's life, the final episode of menstrual bleeding associated with cessation of the activity of the ovarian follicle, resulting in the permanent cessation of menstruation [23]. The aging ovaries continue to produce some estrogen and androgens for at least ten years after the start of menopause [24]. However, at menopause, the number of follicles in the ovaries decreases, and estrogen production continues to fall. Therefore, ovulation may cease or frequently may become irregular when a level incompatible with the induction of a surge in luteinizing hormone (LH) is reached. Clinically, this is associated with irregular cycles and a shortened luteal phase, or anovulatory cycles with unopposed estrogen stimulation and endometrial hyperplasia. Sometimes anovulatory cycles may be interspersed with ovulatory cycles. For example, a period of amenorrhea with elevated follicle-stimulating hormone and LH may mimic menopause but is followed a few months later by an anovulatory cycle and average gonadotropin level. This transitional period of progressive loss of ovarian function and irregular ovulatory cycles explains molar pregnancy in the 52-year-old woman reported here.

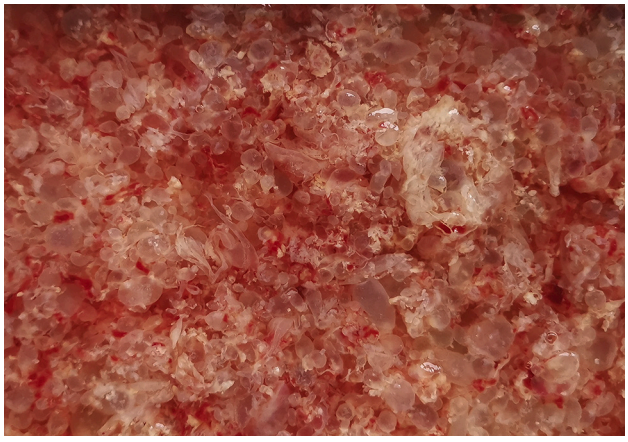

Fig. 1. Macroscopic view of the molar tissue.

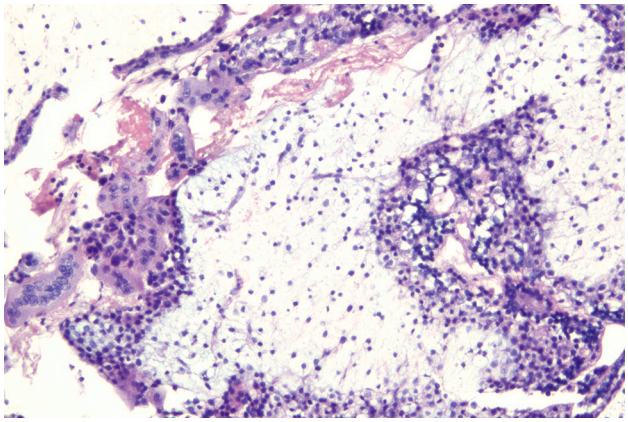

Fig. 2. Hydropic villi with circumferential hyperplastic trophoblast (hematoxylin-eosin, 100 ×).

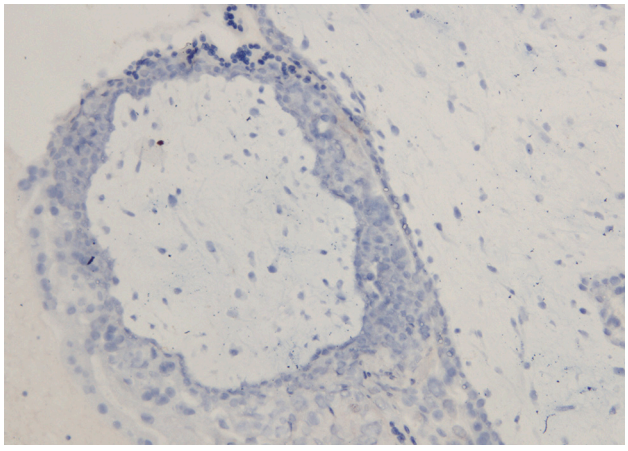

Fig. 3. Immunohistochemical staining for p57 was negative in cytotrophoblasts and villi mesenchyme (100 ×).

HM is a benign trophoblastic tumor and accounts for about 80% of GTDs [25]. HM is associated with abnormal gametogenesis and fertilization, with the incidence ranging from 1 per 1000 pregnancies to 1 per 500 pregnancies. HM's risk factors include old age, ethnicity, genetic basis, spontaneous miscarriage, and nutrient restriction [26]. The most consistently demonstrated risk factor for CHM is maternal age, with an increased relative risk of a molar pregnancy of up to 519 for women over 50 years [27]. Women with a history of prior spontaneous miscarriage have a two- to three-fold greater risk of molar pregnancy compared with the general population [28]. Some women with a history of molar pregnancy have a 10- to 20-fold risk of repeat molar pregnancy [29].

Due to hydropic degeneration in chorionic villi known as the "snowstorm" appearance, a characteristic vesicular pattern on ultrasonography is the most sensitive diagnostic method [30]. Depending on age, desire for fertility, and willingness to be followed up after molar

Table 1
Literature concerning CHM in the postmenopausal period.

Reference	Age (years)	Amenorrhea time (years)	Clinical manifestations	β-HCG (IU/mL)	Uterus (cm) /(weeks)	Treatment	Recurrence
[3]	52	5	Vaginal bleeding, loss of appetite	400	20 × 15 × 15	Hysterectomy	unknown
[7]	50	1.5	Abdominal swelling, vaginal bleeding	no	20	Dilatation and curettage, and hysterectomy	no
	54	10	Vaginal bleeding		no	Dilatation and curettage	
[10]	56	5	Abdominal pain, nausea and vomiting	188,000 (diluted)	14.3 × 9.5	Hysterectomy and bilateral; salpingo-oophorectomy	no
[11]	57	1.25	Abdominal pain, nausea and vomiting	100	15 × 13 × 10	Hysterectomy and bilateral; salpingo-oophorectomy	unknown
[12]	55	9	Vaginal bleeding	290	14	Hysterectomy and bilateral; salpingo-oophorectomy	unknown
[13]	57	2	Vaginal bleeding	193	no	Hysterectomy and bilateral; adnexectomy	unknown
[14]	61	1	Vaginal bleeding	>200	12.2 × 6.7 × 9.6	Endometrial curettage and hysterectomy and bilateral salpingo-oophorectomy	no
[15]	55	1.5	Breakthrough bleeding	96.4	Slightly bulky	Hysterectomy and bilateral, salpingo-oophorectomy with pelvic node dissection	unknown
[16]	60	2.5	Abdominal swelling and pain, vaginal bleeding	262	24	Suction evacuation, hysterectomy and bilateral; salpingo-oophorectomy	no
[17]	58	8	Vaginal bleeding, abdominal pain, nausea and vomiting	157	14 × 12 × 9	Hysterectomy and bilateral; salpingo-oophorectomy	unknown
[18]	52	2	Abdominal pain vaginal bleeding	450	16	Hysterectomy	no
[19]	51	3	Acute lower abdominal pain	29,000 (2 weeks after surgery)	7 cm irregular right adnexal mass	Total hysterectomy with bilateral salpingo-oophorectomy, omentectomy, and appendectomy	no
[20]	59	–	Vaginal bleeding	128.6	–	Transabdominal hysterectomy and bilateral oophorosalpingectomy	unknown
[21]	55	2	Vomiting and irregular bleeding	65,000	18	Total abdominal hysterectomy with bilateral salpingo-oophorectomy	no

evacuation, treatment can be suction curettage, chemotherapy, or hysterectomy. Prophylactic chemotherapy can effectively prevent distant metastasis of hydatidiform mole, so it is necessary for patients over 50 years [9]. Owing to the high rate (56.3%) of malignant sequelae after the evacuation of molar tissue in women aged over 50 years, a primary hysterectomy for treating hydatidiform mole in this age group is recommended [1]. Although CHM is extremely rare in postmenopausal women, it should be included in the differential diagnosis of postmenopausal bleeding, especially with an ultrasound picture of cystic endometrial changes. Additionally, continuous monitoring of serum levels of β-hCG is crucial for CHM diagnosis in postmenopausal women.

Contributors

The two authors contributed equally to this case report's conception and writing, and both saw and approved the final manuscript.

Conflict of interest

The authors declare that they have no conflict of interest regarding the publication of this case report.

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Patient consent

Obtained.

Provenance and peer review

This case report was peer reviewed.

References

[1] J.R. Lurain, Gestational trophoblastic disease II: classification and management of gestational trophoblastic neoplasia, Am. J. Obstet. Gynecol. 204 (1) (2011) 11–18.
[2] G. Coukos, et al., Complete hydatidiform mole: a disease with a changing profile, J. Reprod. Med. 44 (8) (1999) 698–704.
[3] J. Begum, P. Palai, S. Ghose, Complete molar pregnancy in postmenopausal women, J. Midlife Health. 7 (2) (2016) 91–93.
[4] S. Yen, B. MacMahon, Epidemiologic features of trophoblastic disease, Am. J. Obstet. Gynecol. 101 (1) (1968) 126–132.
[5] R.A. Fisher, E.S. Newlands, Gestational trophoblastic disease molecular and genetic studies, J. Reprod. Med. 43 (1) (1998) 87–89.
[6] J.Q. Cao, et al., A case of unplanned pregnancy at 2 months after uterine curettage in a patient with a hydatidiform mole, J. Int. Med. Res. 48 (6) (2020), 030006052092596.
[7] A.M. Jequier, W.R. Winterton, Diagnostic problems of trophoblastic disease in women aged 50 or more, Obstet. Gynecol. 42 (3) (1973) 378–387.
[8] N. Tsukamoto, et al., Gestational trophoblastic disease in women aged 50 or more, Gynecol. Oncol. 20 (1) (1985) 53–61.
[9] F.Z. Feng, et al., Clinical characteristics and management of gestational trophoblastic disease in women aged 50 years or more, Chinese J. Obst. Gynecol. 40 (9) (2005) 605–608.
[10] F. Abike, et al., Postmenopausal complete hydatidiform mole: a case report, Maturitas. 59 (1) (2008) 95–98.
[11] H. Camuzcuoglu, et al., Complete mole hydatidiform in a postmenopausal woman, Eur. J. Obstet. Gynecol. Reprod. Biol. 142 (1) (2009) 85–86.
[12] A.S. El-Agwany, H.A. Rady, H.M. Hegab, Complete molar pregnancy in postmenopausal woman, Indian J. Surg. Oncol. 8 (2) (2017) 185–187.
[13] J. Fatusic, I. Hudic, Complete molar pregnancy in posmenopausal woman-a case report, Mediev. Archaeol. 73 (6) (2019) 436–437.
[14] M. Garcia, R.L. Romaguera, C. Gomezfernandez, A hydatidiform mole in a postmenopausal woman. A case report and review of the literature, Arch. Pathol. Lab. Med. 128 (9) (2004) 1039–1042.
[15] J. Hirst, A. Ferrier, Postmenopausal bleeding: Hydatidiform mole a rare cause, Aust. N. Z. J. Obstet. Gynaecol. 44 (5) (2004) 462–463.
[16] S. Mehrotra, U. Singh, S. Chauhan, Molar pregnancy in postmenopausal women: a rare phenomenon, BMJ Case Rep. 2012 (2012) bcr2012006213.
[17] S. ÖZdemir, et al., Bilateral adnexal torsion due to postmenopausal hydatidiform mole, J. Obstet. Gynaecol. Res. 37 (4) (2011) 359–362.

[18] K.K. Roy, et al., Post-sterilization molar pregnancy in a 52 year old menopausal woman, Acta Obstet. Gynecol. Scand. 79 (8) (2000) 716–717.
[19] S. Stolnicu, et al., Ectopic Complete Hydatidiform Mole Presenting as an Adnexal Tumor in a Postmenopausal Patient, Int. J. Surg. Pathol. 22 (5) (2014) 470–472.
[20] J. Rabczyński, et al., Hydatidiform mole in 59-years-old woman: a case report, Ginekol. Pol. 71 (3) (2000) 152–154.
[21] R. Malik, et al., Molar Pregnancy in a 55-Year-Old Woman, J. Gynecol. Surg. 25 (4) (2009) 163–164.
[22] L.C. Bandy, D.L. Clarke-Pearson, C.B. Hammond, Malignant potential of gestational trophoblastic disease at the extreme ages of reproductive life, Obstet. Gynecol. 64 (3) (1984) 395–399.
[23] A.M. Malutan, et al., Proinflammatory and anti-inflammatory cytokine changes related to menopause, Prz. Menopauzalny 13 (3) (2014) 162–168.
[24] D.R. Meldrum, et al., Changes in circulating steroids with aging in postmenopausal women, Obstet. Gynecol. 57 (1998) 624–628.
[25] R. Nadhan, et al., Insights into dovetailing GTD and Cancers, Crit. Rev. Oncol. Hematol. 114 (2017) 77–90.
[26] K.Y. Loh, N. Sivalingam, M.Y. Suryani, Gestational trophoblastic disease, Med J Malaysia 59 (5) (2004) 697–703.
[27] S.A. Davidson, J. Gottesfeld, F.G. La Rosa, Molar pregnancy in a 60-year-old woman, Int. J. Gynaecol. Obstet. 56 (1) (1997) 53–55.
[28] F. Parazzini, et al., Risk factors for gestational trophoblastic disease: a separate analysis of complete and partial hydatidiform moles, Obstet. Gynecol. 78 (6) (1991) 1039–1045.
[29] F. Ning, et al., Understanding and management of gestational trophoblastic disease, F1000Res 8 (2019). F1000 Faculty Rev–428.
[30] D.J. Fowler, et al., Routine pre-evacuation ultrasound diagnosis of hydatidiform mole: Experience of more than 1000 cases from a regional referral center, Ultrasound Obstet. Gynecol. 27 (1) (2006) 56–60.