

CASE REPORT

A case of complete hydatidiform mole with coexistent fetus developing hypertension and acute heart failure

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Twin gestation consisting of complete hydatidiform mole with coexistent fetus (CHMCF) is a very rare entity. CHMCF is associated with serious complications, such as vaginal bleeding, intrauterine death, preterm birth, preeclampsia, and persistent gestational trophoblast disease (pGTD). Thus, management of this type of pregnancy is challenging. Here we report a case of CHMCF complicated with hypertension and acute heart failure. A 33-year-old primigravida female was clinically diagnosed with CHMCF at 12 weeks of gestation and then developed hypertension and proteinuria at 14 weeks of gestation. Elective termination of pregnancy was performed at 15 weeks of gestation and, following the procedure, she suffered from acute heart failure, suggesting peripartum cardiomyopathy. She subsequently developed pGTD, and methotrexate treatment was initiated. Since CHMCF can cause a variety of complications, its clinical management should be performed with discretion after obtaining informed consent.

Introduction

Complete hydatidiform mole with coexistent fetus (CHMCF) is very rare, arising in 1 in 22,000 to 100,000 pregnancies.^{1,2)} The management of this type of pregnancy is challenging, because it causes a predisposition to vaginal bleeding, intrauterine death, preterm birth, and preeclampsia. Furthermore, it carries a considerable risk of persistent gestational trophoblast disease (pGTD). Therefore, both the patient and physician are caught in a dilemma of whether to continue or terminate the pregnancy.

Here we describe a case of CHMCF in which the patient developed acute heart failure after the elective termination of pregnancy. The symptom of left ventricular failure was compatible with peripartum cardiomyopathy (PPCM), and this is, to the best of our knowledge, the second case of CHMCF complicated with PPCM to be reported.

Case

A 33-year-old primigravida female with an unremarkable medical history became pregnant after intrauterine insemination. At 12 weeks of gestation, she complained of slight vaginal bleeding, and transvaginal ultrasound showed a 'snow-storm' vesicular appearance, separate from a fetus with normal placenta. She was referred to our hospital on the suspicion of hydatidiform mole with coexistent fetus. Her serum β -human chorionic gonadotropin (β -hCG) level was significantly elevated (625,000 IU/l). Her initial blood pressure was 125/76 mmHg, and she had no proteinuria. Magnetic resonance imaging at 12 weeks of gestation revealed a viable fetus with normal placenta located at the anterior uterine wall, and another multicystic molar-appearing placenta located at the right side wall of the uterus. Thus, CHMCF was suspected.

The patient decided to undergo an induced abortion.

On admission to the hospital, at 14 weeks and 6 days of gestation, hypertension (144/86 mmHg), proteinuria (1+), and leg edema were observed. Transvaginal ultrasound revealed bilateral multicystic enlarged ovaries (each 8 cm) without ascites, consistent with hyperreactio luteinalis. Termination of pregnancy was achieved by cervical dilatation using laminaria sticks, and vaginal administration of the prostaglandin E1 analogue, gemeprost, at 15 weeks and 1 day of gestation. The fetus with a normal placenta and the enlarged molar placenta were delivered (Figure 1A). Histopathological examination revealed normal sized villi in the normal placental region, and edematous villi with frequent cistern formation and club-like villi in the molar region (Figure 1B). p57^{KIP2} immunohistochemical staining of cytotrophoblasts was negative in the molar region, and therefore the diagnosis of CHMCF was confirmed pathologically.

Within 15 min after evacuation, the patient complained of dyspnea and chest pain. Peripheral oxygen saturation (SpO₂) was below 93%. Her blood pressure increased to 153/98 mmHg, and severe pitting edema was observed. Chest X-ray revealed cardiac enlargement with a cardiothoracic ratio of 52% and increasing pulmonary vascular congestion. An electrocardiogram test was performed, and sinus rhythm and negative T were observed in V1–3, aVF.

Results of the laboratory examination are shown in Table 1. Levels of troponin, a specific myocardial infarction marker, were slightly elevated (0.042 ng/ml; reference range < 0.014 ng/ml). Serum levels of brain natriuretic peptide (BNP) were markedly elevated (886

pg/ml; reference range <18.4 pg/ml), indicating heart failure. The possibility of pulmonary edema and pulmonary embolism were ruled out by CT.

Transthoracic echocardiogram (TTE) demonstrated a reduced left ventricular ejection fraction (LVEF) of 37%. Her clinical profile fit the criteria for PPCM. Diuretics (loop diuretic 4 mg/day) and antihypertensive agents (angiotensin-converting enzyme inhibitors 2 mg/day) were started, to which she responded well, allowing the cessation of oxygen supplementation and early tapering of her diuretic dose. A TTE, acquired eight days after induced abortion, showed an improvement in LVEF to 53%. Serum BNP levels decreased to 160 pg/ml. Blood pressure returned to normal levels (101/51 mmHg), and proteinuria became negative, one week after the evacuation. Two months later, LVEF recovered to 69%.

After evacuation of the molar tissue, levels of serum β -hCG gradually decreased to 8,524 IU/l over a three week period; however, it began to rise to 10,851 IU/l four weeks after termination. On the suspicion of pGTD, CT was performed and multiple lung nodules were detected. Positron emission tomography (PET) revealed 18F-fluorodeoxy glucose accumulation in the uterine cavity. According to the modified World Health Organization (WHO) prognostic scoring system as adapted by International Federation of Gynecology and Obstetrics (FIGO), her score was 4 (pretreatment serum hCG < 100,000 IU/l, and number of metastases 5-8). Thus, she was classified as being in the low risk group, and a single methotrexate regimen (20 mg/day for five days, every two weeks) was administered. Serum β -hCG levels subsequently decreased steadily to under 0.5



Figure 1. Images of products of conception.

(A) Macroscopic findings of normal placenta and fetus (left) and molar placenta (right)(B) Hematoxylin-eosin section from normal placenta (left) and molar placenta (right)

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WBC	16,220 /l	CRP	1.4 mg/dl	
Hb	7.9 g/dl	CK-MB	9 U/L	
PLT	155,000 /l	BNP	886 pg/ml	
		Troponin	0.042 ng/ml	
PT	12.7 sec			
APTT	26.1 sec	Arterial Bl	Arterial Blood Gas (2I O ₂)	
Fib	304 mg/dl	рН	7.417	
D-dimer	5.7 μg/ml	pO ₂	79.4 mmHg	
AT3	74 %	pCO ₂	29.5 mmHg	
		HCO ₃ [−]	18.5 mmol/l	
AST	22 U/I	BE	– 5.2 mmol/l	
ALT	11 U/I			
Cre	0.41 mg/dl			

 Table 1. Laboratory data of the patient

reference range: CK-MB 5–6 U/L, BNP <18.4 pg/ml, Troponin <0.014 ng/ml

IU/l after the 10th course of therapy. Twelve courses of chemotherapy were performed in total, and the patient showed no evidence of residual or recurrent disease.

Discussion

Twin pregnancy with a complete hydatidiform mole and a viable fetus is uncommon, and is referred to as CHMCF. Continuation of pregnancy is an option if the pregnant woman desires it and the karyotype of the coexistent fetus is diploid. The outcome of pregnancy, however, is not necessarily satisfactory. According to a recent literature review conducted by Suksai et al., approximately 204 cases of CHMCF had been reported as of 2016. However, only 78 (38%) living newborns resulted.³⁾ They found that low levels of serum hCG (i.e., <400,000 IU/l) could be a predictor of fetal survival. Severe complications in the management of CHMCF include intrauterine death, preterm birth, and preeclampsia. Preeclampsia has long been known to be associated with molar pregnancy.⁴⁾ Preeclampsia occurs in about 20% of CHMCF cases, and can often increase in severity. Therefore, it may be an important factor that determines the pregnancy period and outcome.⁵⁾ In our case, the patient developed hypertension and proteinuria, which resolved after molar evacuation. These symptoms are consistent with those of preeclampsia, although gestational age was under 20 weeks.

Another serious concern in the management of CHMCF is pGTD. Given this significant risk, most cases of CHMCF were terminated after diagnosis. Data have been accumulating regarding the relationship between CHMCF and pGTD; however, it is still controversial due to the rarity of this disease. Several studies reported a high rate of pGTD ranging from 50 to 62.5%,^{5–8)} while other studies reported relatively low rates (19.5%¹⁾

and $25\%^{2)}$). The latter frequencies are not significantly higher than those in single complete molar pregnancies. Moreover, advanced gestational period is not associated with the development of pGTD,⁵⁾ and continuing a CHMCF pregnancy does not increase the risk of pGTD compared to first trimester termination. Thus, the termination of a CHMCF pregnancy solely due to pGTD risk might not be recommended. We informed the patient of the possible fetal and maternal complications, the rate of obtaining a live neonate, and the risk of developing pGTD, and she decided to terminate the pregnancy at 15 weeks of gestation.

PPCM is generally defined as a syndrome of unexplained heart failure resulting from left ventricular systolic dysfunction in the last month of pregnancy or within five months of delivery.⁹⁾ In the present case, the patient developed acute cardiac failure with an LVEF of 37%, which meets the criteria of PPCM, but the symptom presented at 15 weeks. However, numerous cases of cardiomyopathy developing in early gestation have been reported. Such cases are sometimes referred to as early pregnancy-associated cardiomyopathy, and are now considered to represent the same disease as PPCM.¹⁰ Therefore, we assume this case to be PPCM.

To the best of our knowledge, only three cases of molar pregnancy complicated with PPCM have been reported.^{11–13}) The first case, characterized by a family history of PPCM, developed after a molar pregnancy with hypertension and proteinuria.¹¹⁾ The second case involved preeclampsia and PPCM in a partial hydatidiform mole.¹²⁾ The third case involved CHMCF with hypertension and leg edema, followed by PPCM.¹³⁾ Based on the characteristics of these cases, including ours, we hypothesized that soluble fms-like tyrosine kinase 1 (sFlt-1), an antagonist of vascular endothelial growth factor and placental growth factor, might play a key role in the pathogenesis. It is well known that serum levels of sFlt-1 are markedly increased not only in patients with preeclampsia,¹⁴⁾ but also in those with molar pregnancy.¹⁵⁾ Furthermore, serum sFlt-1 levels are elevated in PPCM patients compared to those in control postpartum women as well.¹⁶ With this in mind, molar pregnancy, preeclampsia, and PPCM appear to be related in terms of increased sFlt-1 levels. However, sFlt-1 was not measured in the present case, and this is a limitation of our report.

In summary, we experienced a very rare case of CHMCF complicated with PPCM, which was characterized by hypertension, proteinuria, and leg edema. The patient eventually developed pGTD, and systemic chemotherapy with methotrexate was required. Since CHMCF can cause a variety of complications, the clinical management of this disease should be performed with discretion after obtaining informed consent.

Conflict of interest

None.

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