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CASE REPORT

Markedly Elevated hCG Levels in a Patient with Partial Hydatidiform Mole: An Extremely Rare Presentation

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Abstract

In a partial molar pregnancy, the level of β-Human chorionic gonadotropin (β-HCG) is often within a large spectrum. An extremely high level of β-HCG levels (>1.000.000) is only 2-3% of partial moles. Partial molar pregnancy commonly presented with mildly elevated HCG (<100,000), vaginal bleeding, abortion and rarely complicated with medical complications and theca lutein cysts. We present a case with extremely high HCG levels (1.861.011 IU / L) in the early second trimester and complicated by maternal anemia, hyperthyroidism, proteinuric hypertension, hirsutism, and enlarged bilateral theca lutein cysts. During follow-up, the patient's HCG level returned to normal after 27 weeks. Clinicians should keep in mind that partial mole hydatidiform may be presented with very high HCG levels. They should be aware of the medical conditions that may complicate this disease and adopt a multidisciplinary approach.

Keywords: β-Human chorionic gonadotropin (β-HCG); partial hydatidiform mole; theca lutein cysts; triploidy.

Herein, we present a rare case of a partial hydatidiform mole complicated with proteinuric hypertension, hyperthyroidism and bilaterally enlarged theca lutein cysts, with extremely elevated maternal β-HCG levels. Interestingly, considering serum HCG levels per week since evacuation; the period is longer than a vast majority of the published data.

Case Report

A 28-year-old woman, gravida 2 para 1, was referred to our clinic at 15+4 weeks of gestation because of an abnormal first-trimester combined screening. She had a history of a normal single-ton pregnancy with cesarean delivery at term. During antenatal investigations, the quantitative serum β-HCG level revealed extremely high at 1.861.011 IU/L. The patient's blood type was 0 Rh-positive. On examinations, the patient's blood pressure was noted 140/100 mmHg, with a 1+ proteinuria on urine analysis. The maternal blood investigations showed as follows: Hemoglo-bin: 11.7 g/dl, Hematocrit: 34.9%, WBC: 9000/mm^3, Platelets: 166000/mm^3, Creatinine: 0.63 mg/dl, cancer antigen (CA) 125: 154 U/ml, Thyroid-stimulating hormone (TSH): 0.0029 mIU/ml (normal range: 0.35-4.94 mIU/ml), free thyroxine: 3.06 ng/dl (normal range: 0.7-1.48 ng/dl), Total testosterone: 4.17 ng/ml (normal range: 0.13-1.08 ng/ml), DHEASO4: 251.8 ug/dl, 1.25(OH)2-D vitamin: 13.96 pg/ml (normal range: 16-65 pg/ml), Alpha-fetoprotein (AFP): 987.77 ng/ml. First trimester combined screening results were as follows: nuchal translucency (NT): 5.50 mm, free β-HCG: 410 ng/ml (12.20 MoM), PAPP-A: 3.4 mIU/ml (0.85 MoM). Ultra-sonographic examination revealed large bilateral multilocular masses (the left ovary 11*9*10 cm, the right ovary 10*9*12

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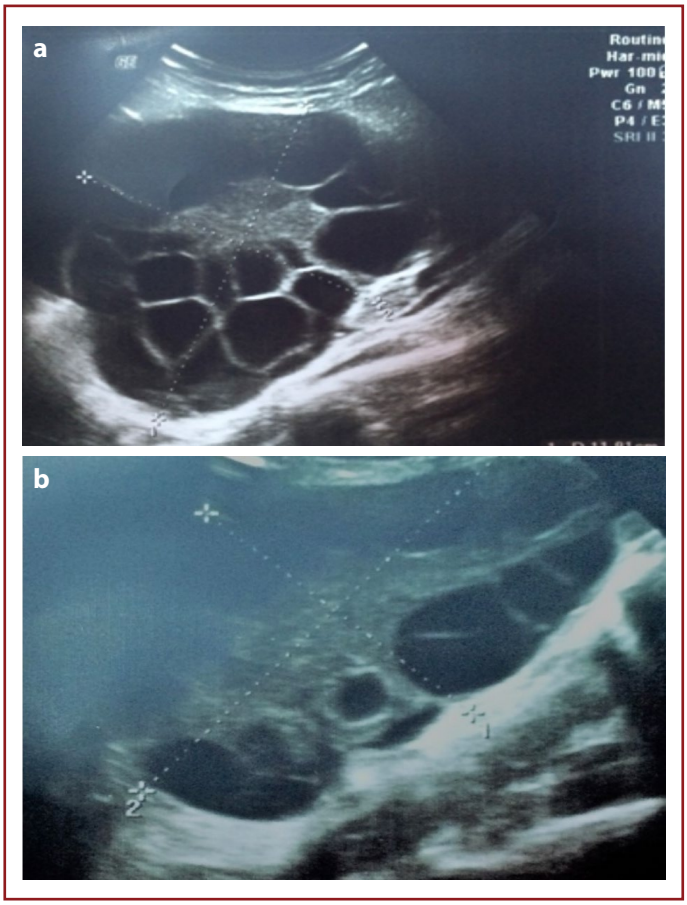

Figure 1. Bilaterally enlarged theca lutein cysts **(a)** right ovary; **(b)** left ovary).

cm) (Fig. 1). In addition, fetal severe structural malformations detected, including hyperechogenic bowel, pericardial effusion, tricuspid regurgitation (100 cm), left multicystic dysplastic kidney, double umbilical artery, bilateral pes equinovarus, skin edema, anterior located hydropic enlarged placenta and millimetric cystic spaces (Fig. 2). The diagno-sis of partial mole with type 1 triploidy was considered and the parents were informed. After counseling the patient, an amniocentesis procedure was performed. Fetal karyotyping confirmed triploidy (69, XXY). Medical termination was carried out using prostaglandin E1 followed by suction curettage. Postmortem macroscopically examination; the placenta was measured as 160 mm × 160 mm × 50 mm and composed of normal appearing villous tissue intermixed with larger, distended villi (Fig. 3). Associated fetus was 120mm in crown-rump length and it's external genitals don't appear to be clearly either male or female. Microscopic examination of placenta revealed an admixture of normal immature villi and hydropic, irregularly edematous villi which have scalloped borders. After termination, the patient was discharged and advised to attend

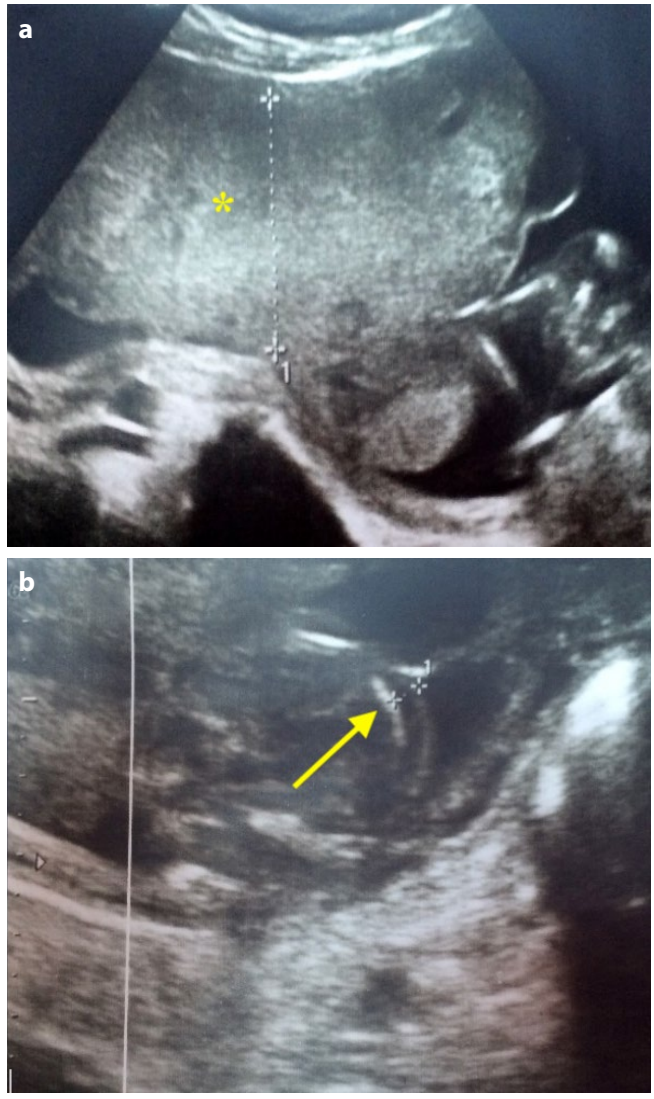

Figure 2. (a) *Anteriorly located hidropic enlarged placenta **(b)** edema on the skin.

serial follow-up cause of β-HCG monitorization. The patients β-HCG level normalized 27 weeks after evacua-tion (Fig. 4). Bilateral theca lutein cysts regressed to normal size after 19 weeks. After termi-nation, blood pressure normalized. Although thyroid function tests (TFT) showed her to be hyperthyroidic, the patient was asymptomatic throughout her pregnancy, managed conservatively. During pregnancy slightly hirsutism was observed due to elevated testosterone levels, expectant management preferred. The patient demonstrated no disease recurrence for one year.

Discussion

Hydatidiform moles are classified as complete and partial. The incidence of complete hydatidiform mole is reported about 1-3 per 1000 pregnancies and approximately 3 per

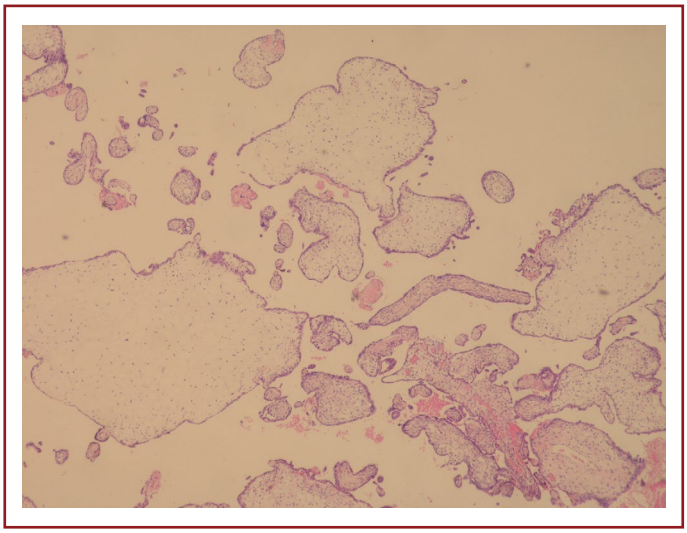

Figure 3. Small fibrotic villi and edematous villi of the case (Hematoxylin and Eosin stainX100).

1000 pregnancies for the partial hydatidiform mole in developed countries[1]. Partial molar pregnancies constitute 15-25% of the hydatidiform moles. In contrast to complete molar pregnancies, serum β-HCG levels are usually normal or slightly elevated in partial molar pregnancies. To the best of our knowledge, a value of β-HCG over 106 IU/L has been reported in only 2-3% of the partial molar pregnancies[2]. We emphasize that partial molar pregnancies may be encountered with unexpected serum HCG levels of up to 1.8 million, as in our case.

Molar pregnancy frequently complicates with hyperthyroidism due to the structural similarity and receptor homology between HCG and TSH[3]. Hershman et al. reported that thyroid function increased 25-64% of cases and clinical symptoms of hyperthyroidism were present in only 5% of the patients with gestational trophoblastic disease[4]. Several studies reported that markedly elevated HCG levels cause thyrotoxicosis due to the low receptor potency of HCG for the TSH receptor[5]. On the contrary, as in our case, even a high level of serum HCG and hyperthyroidic laboratory findings, the patient was asymptomatic throughout her pregnancy. Therefore, conservative management was preferred. One explanation that Düğeroğlu et al.[6] suggested that the stimulating effect of HCG on the thyroid gland may have a resistance at receptor levels in this euthyroid patient group despite high HCG levels.

There is a considerable amount of literature on gestational trophoblastic disease showing HCG level after evacuation in nomograms. Eysbouts et al.[7] demonstrated that 99% of partial mole pregnancies reached normal serum HCG levels within the 22nd week after evacuation. Interestingly,

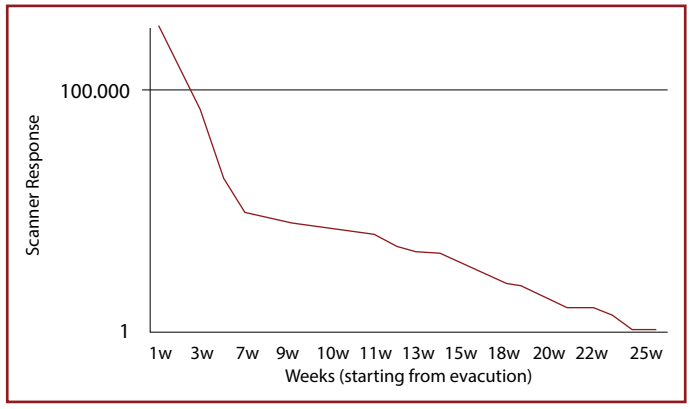

Figure 4. Serum HCG levels (mIU/ml) in log scale after evacuation.

our patient's serum HCG level was very high and returned to the normal range in the 27th week. The consideration of the normalization of serum HCG level after evacuation; the period is longer than a vast amount of the published data. Our patient's weekly serum HCG regression since the evacuation was similar to the Chale-Matsau et al.'s case[8].

In the current published data, partial hydatidiform mole rarely complicates with ovarian enlargement secondary to multiple theca lutein cysts (hyperreactio luteinalis), hyperthyroidism, increased blood pressure, proteinuria that can lead to preeclampsia. A multidisciplinary approach is required to investigate the diseases that may accompany due to excessive HCG levels.

In conclusion, clinicians should keep in mind the diagnosis of gestational trophoblastic disease in patients presenting with high HCG values. They should be aware that partial hydatidiform mole can be presented, albeit rarely, with very high HCG levels. Comprehensive further examinations should be considered in terms of other clinical conditions that may occur due to high HCG. These patients should be evaluated with a multidisciplinary team including endocrinology, genetics, perinatology, and gynecological oncology. It is essential to carefully follow up with the patient in the post evacuation period and managed accordingly.

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