Case Report

**Gestational trophoblastic disease with unusually high levels of hCG: A case report**

Evdokia Karagianni1,*, Sara Mameletzi1, Eleni Bili1, Dimitrios Vavilis1

1First Department of Obstetrics- Gynecology, Aristotle University of Thessaloniki, Greece

**Abstract**

The reported incidence of gestational trophoblastic disease is 1-2:1000 pregnancies. The disease includes a) hydatidiform mole (partial and complete), b) invasive mole, c) choriocarcinoma and d) placental site trophoblastic tumors. Current management is based on several prognostic risk factors. We describe an interesting case of a 51-year-old woman who presented with abnormal vaginal bleeding and an uterine size approximately 20 weeks of gestational age. Ultrasonography revealed a mole pregnancy and serum hCG was 1.682.718mIU/ml. There was no obvious metastatic disease at the time of diagnosis. The patient underwent 8 courses of combined chemotherapy and then an abdominal hysterectomy was performed. We discuss the individualized management options of trophoblastic disease based on the extremely high levels of hCG and the other prognostic factors.

**Key Words:**

Trophoblastic neoplasia, molar pregnancy, hCG levels

**Introduction**

Gestational trophoblastic disease includes a spectrum of tumors, which are characterized by the proliferation of trophoblastic tissue associated with pregnancy, with a progressively malignant potential [1]. It is one of the possible main causes of vaginal bleeding during the first trimester of pregnancy. The disease is observed in 1-2:1000 pregnancies and histologically it is classified into a) hydatidiform mole (partial and complete), b) invasive mole, c) choriocarcinoma and d) placental site trophoblastic tumors [2, 3]. Invasive mole and choriocarcinoma are malignant by definition, while hydatidiform mole can have both benign and malignant behavior. The malignant potential is defined by the elevated levels of hCG after the evacuation of the uterus, which occurs in 15 to 20% of patients with molar pregnancy [4]. The most common locations of metastases are the lungs, the lower genital tract, the brain, the liver, the kidneys and the gastrointestinal system. According to the World Health Organization, the patient’s age, the antecedent pregnancy, the interval months from index pregnancy, the pretreatment serum hCG, the largest size of the tumor as well as the number and the site of the metastases identified, are the main factors that define the staging and the prognosis of the disease (Table 1). Moreover, the interval, the kind and the outcome of the previous pregnancy as well as any previous unsuccessful chemotherapy should be assessed [3, 5, 6]. We describe a case of gestational trophoblastic disease, which was characterized by extremely high levels of hCG (1.682.718mIU/ml) and caused dilemmas concerning the ideal method of treatment. There are no references in the literature with such high levels of hCG.
Case Presentation

A 51-year-old woman, para 1, gravida 2, presented with 12 weeks amenorrhea and abnormal (brown) vaginal bleeding since a month. She had a full term vaginal delivery and an abortion. The latter which took place six months ago. As regards her medical history, she mentioned asthma and panic attacks which were under medication. The patient was referred to our department after an ultrasonographic examination which revealed findings consistent compatible with molar pregnancy and a serum hCG 1,682,718 mIU/ml. At the time of patient’s admission, the uterus was larger than normal (approximately 20 weeks of gestational age), and the ultrasound showed a mass of (10x13) cm, with multiple cystic spaces (Figure 1). During diagnostic investigation, blood, biochemical, coagulation tests and the urine test were within normal range. The blood type of the patient was O Rh (+) and all tumor markers were negative. The findings described above led to the diagnosis of gestational trophoblastic disease. The X-ray and the CT of the thorax did not show any local lesion or pleural effusion. The MRI of the brain was normal, while the abdomen MRI revealed a nuterine lesion (differential diagnosis between complete molar pregnancy and choriocarcinoma) and absence of metastatic lesions (Figure 2). Furthermore, there was no secondary bone metastases according to the bone scan which was performed. According to the patient’s age (>40), the anteced-
ent pregnancy (abortion), the interval months from index pregnancy (6 months), the plasma levels of hCG (>100,000) and, the size of the tumor (>5cm) and the blood type of the couple, the patient was classified into the “high risk” group (total risk score=98) (Table 1). This interesting case was discussed with the Department of Oncology of our hospital in order to decide on the optimal management. The mainstay of initial treatment involves dilatation and curettage which is essential for histological diagnosis. However, the evacuation of the uterus was considered as a dangerous procedure, so initial chemotherapy (as neoadjuvant therapy) was decided. The patient received totally 8 cycles of EMA-CO regimen (Etoposide, Methotrexate, Actinomycin-D, Cyclophosphamide and Vincristine) every two weeks for the next four months.

After the second cycle of chemotherapy, the patient presented acute pelvic pain, like uterine contractions during labor and also moderate vaginal bleeding. The abdominal palpation revealed that the fundus of the uterus was at the level of the umbilicus. Two hours later, the uterine content was excreted. It included reddish-brown soft tissue of abnormal shape, sized at the largest diameter 10cm (Figure 3). Histopathologically, the findings were compatible with complete molar pregnancy. The size of the uterus was clinically decreased, while the level of hCG was 530,687mIU/ml. During the chemotherapy the patient presented anemia and neutropenia, while the levels of hCG showed a gradual decrease (1,071,455mIU/ml– 822,497mIU/ml– 80,767mIU/ml– 12,402mIU/ml– 377,52mIU/ml– 193,60mIU/ml– 66,55mIU/ml– 24,01mIU/ml– 7,32mIU/ml) and by the end of chemotherapy hCG was negative (<3,2mIU/ml). Two months after the last course of chemotherapy (hCG: 0,83mIU/ml), the patient underwent an operation of total abdominal hysterectomy with bilateral salpingo-oophorectomy. The uterus weighed 62 gr and its dimensions were 6,5x4x3cm. Histopathology revealed a nodule in the myometrium with central necrosis and remarkable lesions caused by chemotherapy, with no sign of malignancy. Postoperative period was uneventful. After 48 months of follow up in Oncologic clinic, the patient is free of symptoms without any indications of recurrence of the disease.

Figure 2.

Imaging of the uterus in pelvic MRI

Figure 3.

Spontaneous abortion of uterine cavity content
Discussion

In our case, the unusually serum hCG levels was the most impressive feature. According to the literature, 2 out of 5 patients with complete molar pregnancy, have levels of hCG >100,000mIU/mL [5]. Nevertheless, there are no references with such high levels of hCG. The case described above concerns a woman 51- year-old with amenorrhea, vaginal bleeding, uterine size larger than normal and elevated levels of hCG. The diagnosis of gestational trophoblastic disease was based on our clinical and imaging findings. According to the modified WHO prognostic scoring system as adapted by FIGO, patients are classified as “low risk” if score is 0-4, as “medium risk” if score is 5-7 and as “high risk” if score is >8 depending on the risk factors of each case [3]. The most common locations of metastases are the lungs, the lower genital tract, the brain, the liver, the kidneys and the gastrointestinal system. According to the modified WHO prognostic scoring system as adapted by FIGO, patients are classified as “low risk” if score is 0-4, as “medium risk” if score is 5-7 and as “high risk” if score is >8 depending on the risk factors of each case [3, 6] (Table 1). Despite the fact that the laboratory and the imaging results of the brain, thorax, abdomen and pelvis did not show any metastatic lesions, our medical case was classified in the group of “high risk” patients, based on the parameters mentioned above. Management options could include the evacuation of the uterus, the administration of chemotherapy followed by uterine evacuation, or the hysterectomy after an initial dose of chemotherapy. The performance of dilatation and curettage (D & C) is the optimal method of evacuating the uterus, regardless of the uterus size, especially in patients who desire to preserve their reproductive function. This procedure is related with lower risk of bleeding, infection and remaining trophoblastic tissue, compared to the administration of oxytocin and/or prostaglandins [7]. However, uUterine size (>14-16 weeks), needs extra caution during evacuation, due to higher risk of perioperational complications such as the respiratory distress syndrome (RDS) [3, 8]. In the case described above, there was no doubt about the diagnosis of trophoblastic disease according to the clinical and imaging findings. The reasons why we avoided the gold standard of D & C and an alternative management approach was followed instead, were the large uterine size and the extremely high levels of hCG. Patients who have already completed their family or who are not interested in preserving their fertility, are candidates for hysterectomy. Even though hysterectomy prevents the development of local invasion, it does not limit the metastatic disease [7]. Hysterectomy has the advantage of reducing the load/burden of the disease and probably the number of chemotherapy cycles needed in selected cases. In our case, the option of performing an initial operation (evacuation or hysterectomy), was considered as extremely risky in terms of intraoperative complications. Chemotherapeutic treatment recommendations are based on the stage, the WHO prognostic score and the histology, which usually preexists after molar evacuation [8]. A single dose of chemotherapy (methotrexate or actinomycin D) is sufficient in the group of “low risk” patients with the absence of metastatic disease. Methotrexate is the elective drug due to lower incidence of toxicity [9, 10]. In “high risk” patients, or if there are already metastatic lesions, combined chemotherapy is required [8, 10, 11]. There are several multiagent drug regimens such as MAC, CHAMOC, EMA-CO, EMA-EP, EMA-CE [12, 13, 14]. Etoposide has been associated with a higher risk of developing leukemia, while in general leucopenia grade 3-4 is the most serious toxicity of combined regimens, which appears in approximately 25% of the patients [10-12, 15, 16]. In our case, multidisciplinary approach was required in cooperation with the oncologic clinic and combined chemotherapy was considered as the ideal initial treatment. Chemotherapeutic treatment recommendations are based on the stage, the WHO prognostic score and the histology. Even though there were no obvious imaging metastatic lesions, the possibility of micro metastatic lesions was strongly supposed due to the extremely high levels of hCG. Furthermore, in case of performance an initial operation (evacuation or hysterectomy), the risk of intraoperative complications was considered as extremely high. Finally, neoadjuvant chemotherapy with EMA-CO, followed by hysterectomy, has been described in the lit-