CASE REPORT
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Laparoscopic hysterectomy as a treatment modality for gestational trophoblastic neoplasms: a report of two cases

Laparoskopska histerektomija u lečenju bolesnica sa gestacijskim trofoblastnim neoplazmama: prikaz dva slučaja

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Abstract

Introduction. Measuring the serum levels of human chorionic gonadotropin beta isoform (β-hCG) remains a crucial marker for diagnosing gestational trophoblastic neoplasms (GTNs). Choriocarcinoma is commonly diagnosed due to extremely high levels of β-hCG, but the presence of distant metastasis is not uncommon. Placental site trophoblastic tumors and epithelioid trophoblastic tumors remain an enigma because the levels of β-hCG are usually low. **Case report.** The first case report describes a 44-year-old woman, P2G3, admitted to the Clinic under the suspicion of molar pregnancy. She had vaginal bleeding with variable intensity, and her β-hCG was 1,837,787 mIU/mL. After two explorative curettages, the level of β-hCG declined, and a partial hydatidiform mole (HM) was diagnosed histopathologically. The patient was admitted to the Clinic on two occasions due to the increasing values of β-hCG. Since β-hCG failed to drop after two explorative curettages, a hysteroscopic biopsy, and one chemotherapy cycle, along with the suspicious ultrasonographic feature of metastatic GTN, and the fact that the patient has refused further chemotherapy, a total laparoscopic hysterectomy was performed. Choriocarcinoma was diagnosed after a histopathological exam was done. The second patient, a 50-year-old woman, P2G4, was admitted to the Clinic under the ultrasonographic suspicion of molar pregnancy. She was complaining of pelvic discomfort and frequent urination. Initial levels of β-hCG were 128,359 mIU/mL. Instrumental revision of the uterine cavity was performed, and partial HM was diagnosed histopathologically. Because of the increasing levels of β-hCG, ultrasonographical suspicion of the development of GTN in the uterine corpus, in accordance with the patient's age and the fact that she has regular menstrual cycles, total laparoscopic hysterectomy was performed, and a histopathological exam made the diagnosis of the placental site trophoblastic tumor. **Conclusion.** Laparoscopic hysterectomy could be a treatment of choice for the chemotherapy-resistant GTNs but also for choriocarcinoma in patients who have finished their reproductive activity and refuse to be treated with chemotherapeutics.

Key words:
choriocarcinoma; gestational trophoblastic disease; hysterectomy; laparoscopy; trophoblastic neoplasms; trophoblastic tumor, placental site.

Apstrakt

Uvod. Određivanje koncentracija beta izoforme humanog horionskog gonadotropina (β-hCG) u serumu predstavlja značajan marker gestacijskih trofoblastnih neoplazmi (GTN). Zbog izrazito visokih vrednosti β-hCG-a, horiokarcinom se obično dijagnostikuje, ali prisustvo udaljenih metastaza nije neuobičajeno. S druge strane, trofoblastni tumor placentnog ležišta i epitelioidni trofoblastni tumor ostaju velika enigma, s obzirom na to da su koncentracije β-hCG-a kod tih tumora često niske. **Prikaz bolesnika.** U prvom prikazu opisana je žena od 44 godine, P2G3, koja je primljena na Kliniku zbog sumnje na molarnu trudnoću. Žalila se na vaginalno krvarenje varijabilnog intenziteta. Inicijalna vrednost serumskog β-hCG-a iznosila je 1 837 787 mIU/mL. Nakon dve eksplorativne kiretaže došlo je do pada β-hCG-a, a histopatološki je dijagnostikovana parcijalna hidatidna mola (HM). Zbog ponovnog rasta β-hCG-a, bolesnica je u dva navrata hospitalizovana. S obzirom na to da nije došlo do pada vrednosti β-hCG-a posle dve instrumentalne revizije materične duplje, histeroskopije sa ciljanom biopsijom, jednog ciklusa hemioterapije, uz ultrazvučni nalaz visoko sumnjiv na metastatsku GTN u zidu uterusa, kao i činjenice da je bolesnica odbila dalju hemioterapiju, urađena joj je totalna laparoskopska histerektomija, sa konzervacijom adneksa. Histopatološkom analizom dijagnostikovan je horiokarcinom. U drugom prikazu je opisana žena od 50 godina, P2G4, upućena na Kliniku zbog sumnje na molarnu trudnoću, postavljenu na osnovu ultrazvučnog nalaza. Žalila se na nelagodnost u maloj karlici i često mokrenje. Inicijalna vrednost β-hCG-a iznosila je 128 359 mIU/mL. Urađena joj je instrumentalna revizija materične duplje, a histopatološki je dijagnostikovana parcijalna HM. Zbog rastućih vrednosti

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β-hCG-a, sumnje na perzistirajuću GTN, postavljene na osnovu ultrazvučnog nalaza, a shodno godinama bolesnice i činjenici da je imala redovne cikluse, urađena joj je totalna laparoskopska histerektomija, sa konzervacijom jajnika. Histopatološkom analizom dijagnostikovan je trofoblastni tumor placentnog ležišta. **Zaključak.** Laparoskopska histerektomija bi mogla biti tretman izbora u lečenju bolesnica sa GTN rezistentnih na hemioterapiju, kao i bolesnica sa horiokarcinomom koje su završile svoju reproduktivnu aktivnost i koje odbijaju lečenje hemioterapijom.

Ključne reči:
horiokarcinom; trofoblastne bolesti, gestacijske; histerektomija; laparoskopija; neoplazme, trofoblastne; trofoblastni tumor, posteljičnog ležišta.

Introduction

Gestational trophoblastic diseases (GTD) represent a spectrum of abnormal proliferation of trophoblast cells. They include complete and partial hydatidiform mole (HM), sometimes marked as "premalignant GTD", and gestational trophoblastic neoplasia (GTN), which include the following: choriocarcinoma, placental site trophoblastic tumor, epithelioid trophoblastic tumor, and invasive mole [1].

Measuring the serum levels of human chorionic gonadotropin's beta isoform (β-hCG) remains a crucial marker for diagnosing the GTN, but also a valuable indicator of (un)successful therapy [1, 2]. The diagnosis of postmolar GTN is usually made by observing the persistent or increasing levels of β-hCG following the evacuation of the HM. Choriocarcinoma is commonly diagnosed due to extremely high levels of β-hCG, but the presence of distant metastasis is not uncommon [1–3]. At the same time, choriocarcinoma is highly chemotherapy-sensitive; therefore, nowadays, a complete recovery is possible in 90% of cases [3]. On the other hand, placental site trophoblastic tumors and epithelioid trophoblastic tumors remain an enigma because the levels of β-hCG are usually low or even normal, and these tumors are resistant to chemotherapy in most cases [1–3].

Even though modern chemotherapy protocols provide almost complete remission of the disease, cases of chemotherapy-resistant GTNs require surgical treatment [4]. A particular challenge in surgical treatment represents patients who wish to preserve their fertility and those whose ovarian function must be conserved [4]. On the other hand, another challenge represents the group of patients who refuse the chemotherapy treatment method.

We present two patients with GTN with unusual clinical features in which total laparoscopic hysterectomy provided a complete recovery for the patients.

Case report

Case I

A 44-year-old patient, P2G3, was admitted to the Clinic under the suspicion of molar pregnancy. Vaginal bleeding of variable intensity was the only symptom she was complaining about. Levels of β-hCG were 1,837,787 mIU/mL (Figure 1). On the first and the fourth hospital day, explorative curettages were performed. From the obtained samples, a histopathological diagnosis of partial HM was made. After the procedures, the levels of β–hCG were in decline (Figure 1). After one month, she was once again admitted to the Clinic. The levels of β-hCG were increasing (from 630 to 1,263 mIU/mL). A suspicious mass in the right uterine cornu, intimately beside the uterine cavity, was seen on the ultrasonographic exam (Figure 2A). A diagnostic hysteroscopy was performed. Hysteroscopically, no residual tissue nor trophoblastic protrusion was seen, and the histopathological exam of the tissue obtained from the endometrial biopsy revealed a secretory endometrium. After diagnostic hysteroscopy and one chemotherapy cycle, the serum levels of β-hCG dropped

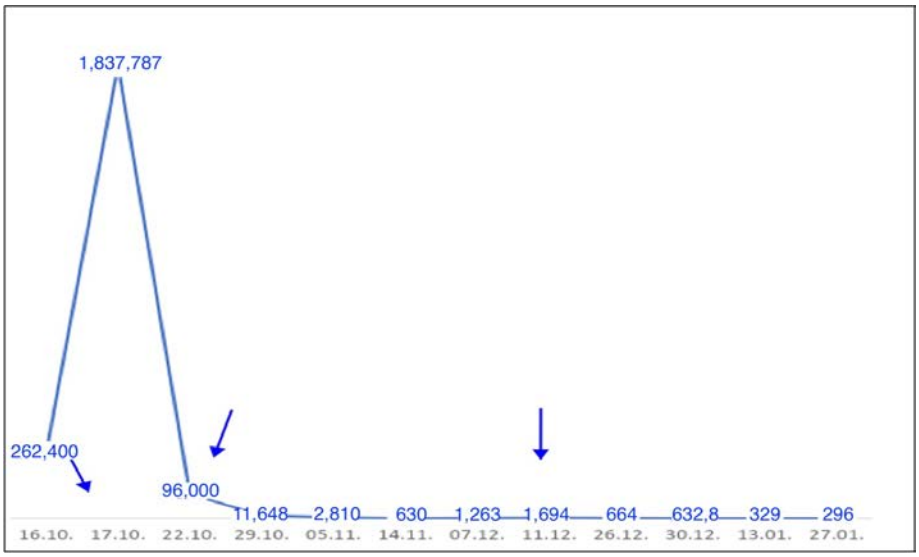


Fig. 1 – Levels of serum β-hCG (mIU/mL) in the first patient; interventions are marked with an arrow.

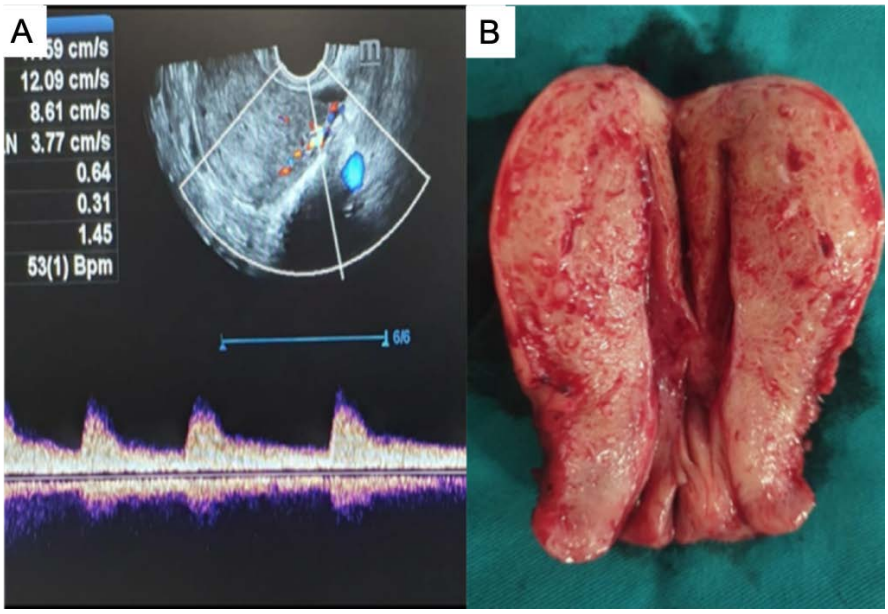


Fig. 2 – A) Gynecologic ultrasonographic image of the first patient reveals a suspicious mass in the right uterine cornu, intimately beside the uterine cavity; B) Uterus after the hysterectomy.

(from 1,694 to 664 mIU/mL) (Figure 1). After more than one month, she was admitted again to the Clinic, given that β–hCG levels were persisting (329 and 296 mIU/mL) (Figure 1). The patient refused further chemotherapy treatment, and it was decided to perform a total laparoscopic hysterectomy with preservation of the ovaries (Figure 2B). A histopathological exam of the obtained tissue revealed choriocarcinoma. The levels of β-hCG significantly dropped, and the patient was discharged.

Case 2

A 50-year-old woman, P2G4, was admitted to the Clinic under the ultrasonographic suspicion of molar pregnancy. She was complaining of pelvic discomfort and frequent urination. Serum levels of β–hCG were 128,359 mIU/mL (Figure 3). Since the ultrasonographic exam confirmed the suspicion of molar pregnancy, explorative curettage of the uterine cavity was performed. Histopathological diagnosis from the obtained sample of the partial HM was made. Levels of serum β–hCG were in decline after the intervention (31,661 mIU/mL) (Figure 3). Since the concentration of β–hCG saw a trend of increase (from 430 to 598 mIU/mL) (Figure 3), the patient was once again admitted to the Clinic. When the patient's age, the fact that she had regular menstrual cycles, and her serum levels of β–hCG were taken into account, along with the suspicion of the development of GTN in the uterine corpus (Figure 4A), it was decided to perform a total laparoscopic hysterectomy with the conservation of the one ovary (Figure 4B). Histopathologically, the decidual remains and

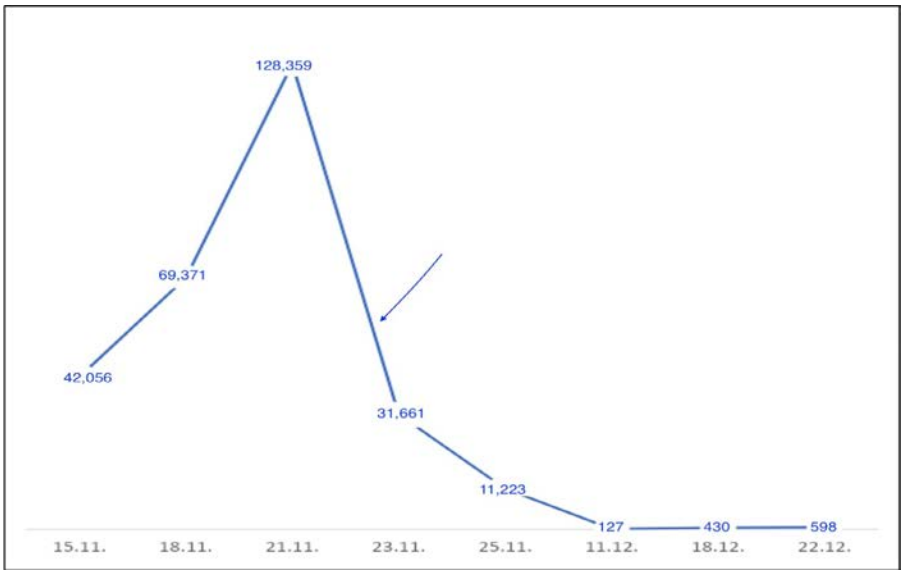


Fig. 3 – Levels of serum β–hCG (mIU/mL) in the second patient; intervention is marked with an arrow.

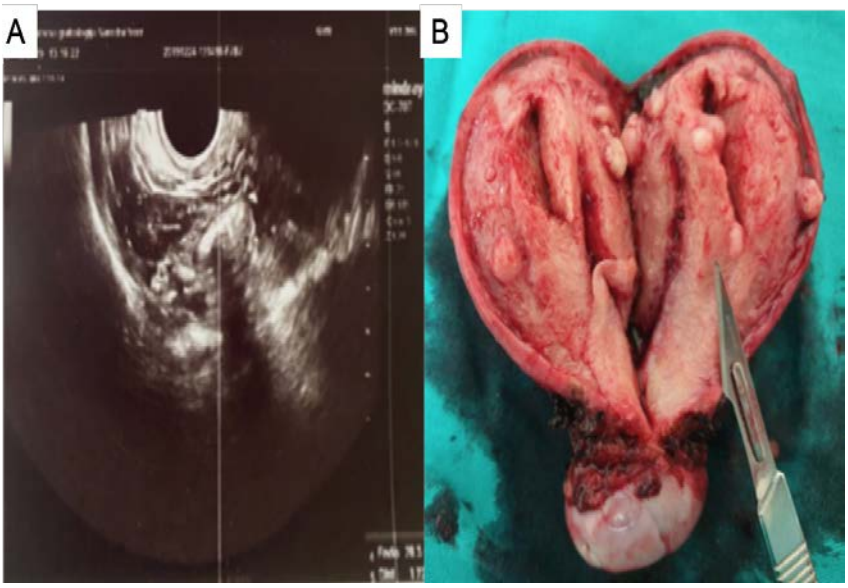


Fig. 4 – A) Ultrasonographic image in the second patient before the operation: the suspect development of a gestational trophoblastic neoplasm (GTN) in the uterine corpus; B) Uterus after the hysterectomy.

the several intermediate trophoblastic cells of the placental site in the endometrium were seen. Chorionic villi were not present. The diagnosis of the placental site trophoblastic tumor was made. A few days after the surgery, serum β-hCG was negative, and the patient was discharged.

Discussion

Complete HMs usually present with high levels of serum β-hCG [5]. It was shown that in more than 50% of patients with complete HM, the levels of β-hCG before evacuation exceeded 100,000 mIU/mL [5]. On the other hand, only 10% of the patients with partial HM had such high serum β-hCG levels [5]. Our patient, whose final diagnosis was choriocarcinoma, was initially diagnosed with partial HM, along with β-hCG levels of 1,837,787 mIU/mL, a concentration unusually high for this type of GTD. Moreover, it has been reported that 15–20% of complete HMs progress into an invasive mole or other forms of GTN [5]. However, only 0.5–2.0% of partial HMs transform into some form of GTN [2, 5]. In both of our patients with GTN, the initial diagnosis was partial HM.

About 50% of choriocarcinomas arise based on complete HM, 25% after a normal pregnancy, and about 25% after a miscarriage or ectopic pregnancy [6]. Only a few reports in the literature regarding choriocarcinomas occurred based on partial HMs [6, 7]. One of the main features of choriocarcinoma is extremely high β-hCG levels [1, 6]. In our first case, the levels of β–hCG persisted in the range from 329 to 1,694 mIU/mL, which is unusual for this type of GTN. Choriocarcinomas are chemotherapy-sensitive [6], which can explain the significant drop in β-hCG levels after one chemotherapy cycle. When there is no distant metastasis, an individualized chemotherapy protocol for each patient is made, and the chemotherapy itself is usually the treatment of choice [5, 6].

Placental site trophoblastic tumor is extremely rare, and the epithelioid trophoblastic tumor accounts for about 0.2–3.0% of GTNs [8]. A special challenge for the correct diagnosis and proper treatment of these tumors is relatively low levels of β-hCG, often nonspecific clinical features, and chemotherapy resistance [8]. Even though the data is limited, it has been reported that placental site trophoblastic tumor occurs in 61% after a normal pregnancy, in 12% after a molar pregnancy, in 9% after a spontaneous miscarriage, in 8% after induced abortions, and in 3% after ectopic pregnancy [8, 9]. The remaining 7% does not have a clear etiology [8, 9]. This tumor arises exclusively from the proliferation of the intermediate trophoblasts [8–10]. The absence of syncytiotrophoblasts is exactly the reason why the levels of β-hCG in these tumors are usually low or even normal. Therefore, the measurement of human placental lactogen (hPL) is a good marker for diagnosing these tumors [8, 9]. These tumors usually present with irregular bleeding and an invasion of the myometrium and endometrium [9]. In our case, the invasion of the tumor into the uterine walls was not present. In almost all cases of this tumor, the treatment of choice was total hysterectomy with the preservation of the adnexa, except in those cases with a family history of ovarian cancer and postmenopausal women [10]. To the best of our knowledge, there are no reports of laparoscopic hysterectomy as a treatment method for the placental site trophoblastic tumor.

Conclusion

Even though gestational trophoblastic diseases have been known for a long time, they can still be a mystery for modern gynecological practice. Owing to everyday progress in chemotherapy, they are often marked as completely curable diseases. Although chemotherapy is usually the treatment of choice, there are types of GTN that are resistant to chemo-

therapy and require surgical treatment. Laparoscopy, on the other hand, brings many advantages for the patients, from less intraoperative bleeding to shorter postoperative recovery. With these two cases, we have shown that laparoscopic hysterectomy could become a treatment of choice for chemotherapy-resistant GTNs, but also for the treatment of choriocarcinomas in patients who have finished their reproductive activity and refuse the treatment with chemotherapeutics.

Conflict of interest

The authors declare no conflict of interest.

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