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Research Letter

Successful surgical treatment of recurrent choriocarcinoma with laparoscopic resection of intraperitoneal pelvic tumor

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Choriocarcinoma is a rare malignant spectrum of gestational trophoblastic disease (GTD) and may arise after miscarriage, molar pregnancy, or term delivery. The incidence of choriocarcinoma after miscarriage or term delivery is estimated to be 1 in 50,000 pregnancies [1]. The ultrasound findings for choriocarcinoma can be normal, with an elevated beta-human chorionic gonadotrophin (β-hCG) level. Persistent disease is responsive to chemotherapy in more than 90% of cases; based on World Health Organization (WHO) risk scoring criteria, either single-agent or multiagent chemotherapy will be used [2]. However, 25% of those with a high-risk WHO score and 5% with a low-risk WHO score have an incomplete response to chemotherapy or experience relapse following a period of remission [3]. Among these selected patients, surgical resection of localized disease may be considered as an alternative approach.

In this paper, we present a case of focal recurrent choriocarcinoma successfully treated with laparoscopic surgical resection without adjuvant chemotherapy.

A 32-year-old woman who had four previous pregnancies presented to the emergency department during her early gestational weeks with lower abdominal pain and a positive urine pregnancy test. Physical examination revealed tenderness at the lower quadrant. Pelvic ultrasonographic examination showed a hyperechoic endometrial lining without evidence of intrauterine pregnancy. A right solid hyperechoic adnexal mass measuring 4 cm × 3 cm was seen outside the uterine cavity, along with fluid at the cul-de-sac. No fetal activity was detected and findings were consistent with an ectopic pregnancy. The β-hCG level was elevated at 7400 m IU/L. The patient underwent emergency laparoscopic right salphingectomy and endometrial curettage. The intraoperative finding was right tubal gestational tissue with hemoperitoneum of 800 mL.

The histology of endometrial curettage and adnexa mass were complete hydatidiform mole of the uterus and hemorrhagic trophoblastic cell of the right fallopian tube, respectively. Postoperative follow-up revealed persistently elevated levels of β-hCG (17,094 m IU/L). A diagnosis of GTD was made. According to WHO scoring criteria, the patient was in the low-risk group and received six cycles of single-agent methotrexate (50 mg/m^2).

Despite administration of single-agent chemotherapy, the patient's β-hCG levels remained high; therefore, a second-line multiagent chemotherapy regimen, EMACO (etoposide 100 mg/m^2, methotrexate 300 mg/m^2, actinomycin 0.5 mg, cyclophosphamide, and vincristine 1 mg/m^2), was started. Her β-hCG levels returned to a normal level after completion of the second-line chemotherapy. The patient remained in remission for 7 months.

However, after the period of remission, an incremental increase of β-hCG level was noted. The patient was counseled regarding the need for multiagent chemotherapy but she refused this treatment. Computed tomography (CT) and transvaginal ultrasonography were normal, fludeoxyglucose-positron emission tomography (FDG-PET) scan showed a focal F18 FDG uptake lesion in the right lower pelvic area with maximum standardized uptake value of 4.7 (Fig. 1). CT

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performed 1 hour after the first scan did not reveal significant change. The patient was counseled regarding treatment options and she decided on the surgical resection of the focal lesion via a laparoscopic approach. A diagnostic laparoscopy revealed a focal right tumor at the anterior pelvic peritoneal wall with a normal uterus. The focal pelvic tumor was excised and histology confirmed recurrent choriocarcinoma (Figs. 2 and 3). Hysterectomy was not performed because a PET scan showed negative biochemical intrauterine findings and supported the intraoperative findings of a normal uterus. The patient's β-hCG level dramatically decreased from 364 m IU/L to a normal level (<2 m IU/L) and her clinical condition remained good after surgical resection of the focal tumor without any evidence of port-site metastasis. There was no evidence of recurrence 30 months after the treatment was completed (Fig. 4).

Gestational trophoblastic neoplasm (GTN) is a rare malignancy that consists of a spectrum of interrelated tumors that can be cured even in the presence of widespread metastases. The spectrum of GTN includes invasive mole, choriocarcinoma, placenta site trophoblastic tumor (PSTT), and epithelioid trophoblastic tumor (ETT), which have several propensities of invasion [4]. Hydatidiform moles, which act as benign lesions, are mostly regarded as a precancerous lesion because 16% of complete moles and 0.5% of partial moles can be transformed into a malignant form of gestational trophoblastic neoplasm [5]. The incidence of GTD varies geographically. The incidence of complete hydatidiform mole is approximately 0.5–1 in 1000 pregnancies and partial hydatidiform mole is three in 1000 pregnancies in Europe and is highest in southeast Asia (up to 8 in 1000 pregnancies in Thailand) [6,7]. Genetic, social, economic, and environmental factors may play a role in these differences in geographical incidence.

After evacuation of a complete mole, locally invasive GTN occurs in 15% of patients and metastasis of GTN develops in 5% of patients [8]. In our patient, persistent elevation of serum β-hCG levels after evacuation of a complete mole was the clinical evidence for a diagnosis of choriocarcinoma. Choriocarcinoma is often characterized by an early vascular invasion with widespread blood-borne dissemination. The most common sites of choriocarcinoma metastases are the lung (80%), the vagina (30%), the pelvis (20%), the liver (10%), and the brain (10%) [4,9]. Patients in whom GTN has been diagnosed should undergo a thorough pretreatment assessment to determine the extent of the disease. The WHO

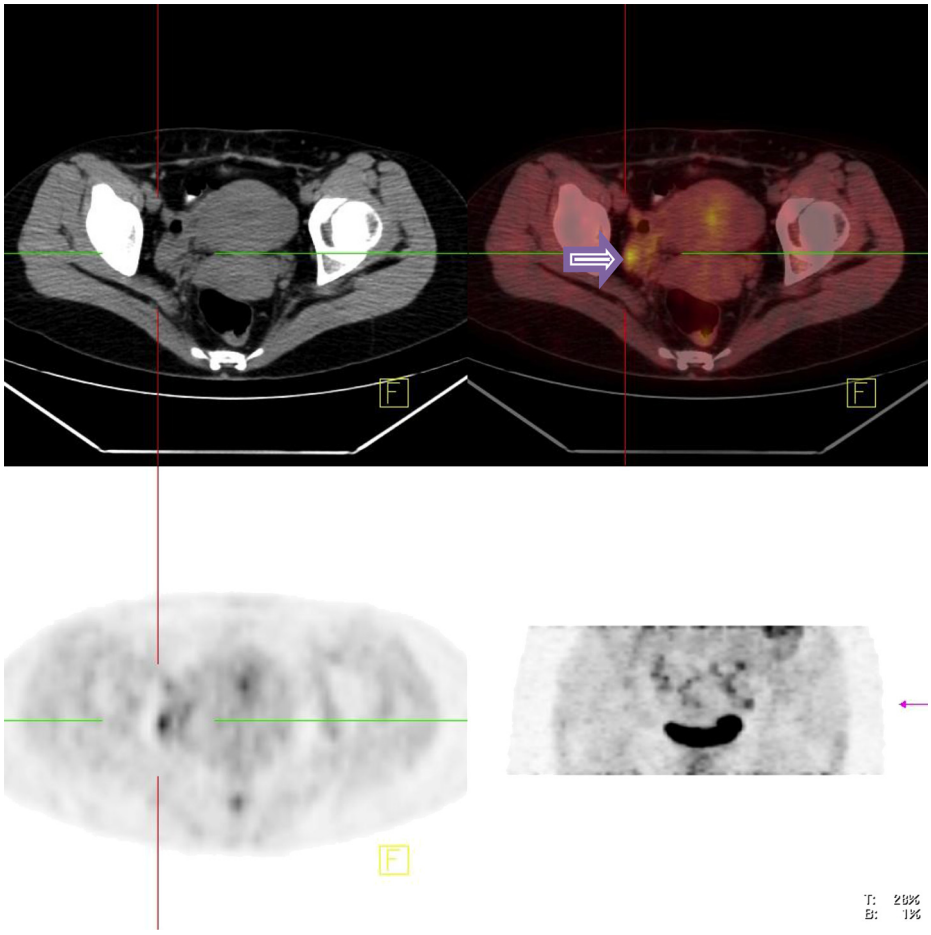

Fig. 1. Fludeoxyglucose-positron emission tomography computed tomography (FDG PET CT) scan shows suspicious uptake and an F18 FDG avid lesion in the right lower pelvic area with evidence of suspicious recurrent choriocarcinoma.

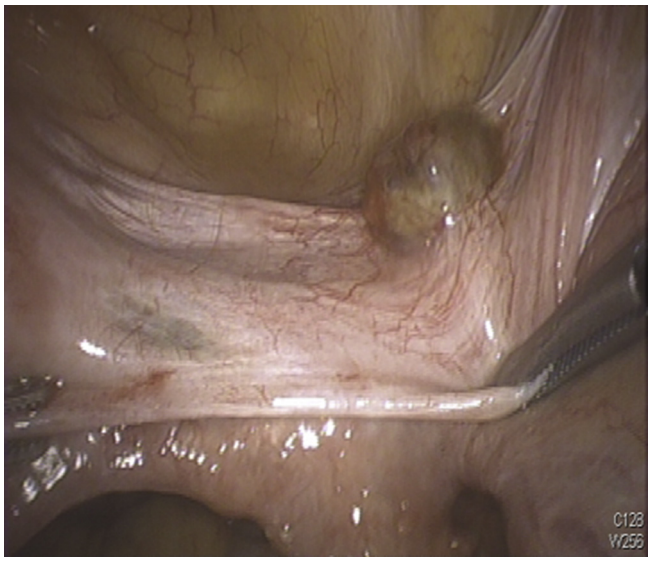

Fig. 2. Laparoscopic view of a focal anterior intraperitoneal tumor lesion.

prognostic scoring system categorizes these patients into low-risk and high-risk groups.

GTN is a chemosensitive tumor with a cure rate that is steadily increasing and may exceed 90% [2]. Patients in the low-risk group required single-agent methotrexate, whereas those in the high-risk group should receive multiagent chemotherapy because tumor resistance to single-agent therapy is likely to develop. The most common regimen used as a first-line multiagent chemotherapy is the EMACO regimen; it was highly effective and well tolerated, with a 91% response rate and 5-year survival rate of 75–90% [10]. Other regimens that can be used as second-line treatment in those patients who experience resistance to primary chemotherapy are CHAMOCA (methotrexate, dactinomycin, cyclophosphamide, doxorubicin, melphalan, hydroxycarbamide, and vincristine), MAC (methotrexate, dactinomycin, cyclophosphamide), PVB (cisplatin, vinblastine, bleomycin), and BEP (bleomycin, etoposide, and cisplatin) with a response rate of 71%, 95%, 62%, and 74%, respectively [8,10,11].

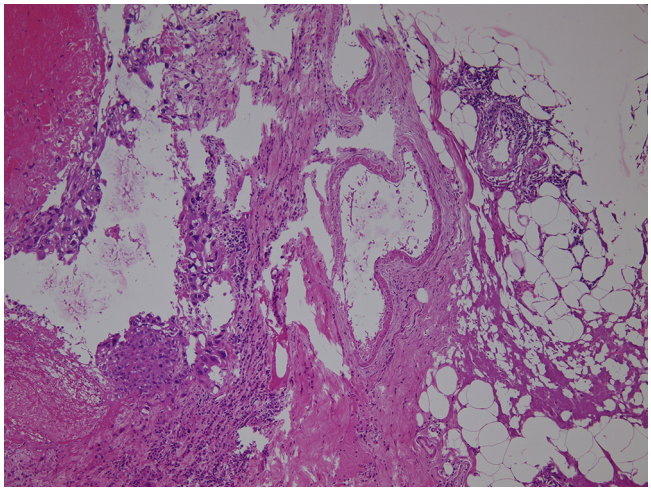

Fig. 3. Peritoneal tumor resection showing features of choriocarcinoma. Hemorrhagic nodules adhered to the peritoneal fibroadipose tissue. A few viable aggregates of syncytiotrophoblasts were seen in the blood clots (hematoxylin and eosin, 100×).

Despite the success of chemotherapy in inducing a complete response in GTN, approximately 5% of those in the low-risk group and 25% of the high-risk group will have an incomplete response to single-agent or multiagent chemotherapy or will relapse after a period of remission [3]. Our patient relapsed with an isolated focal tumor after a short remission.

In patients with drug resistance disease in whom the active site of the tumor can be circumscribed to allow curative surgical resection, an accurate localization of the lesion is crucial for a successful remission. Various imaging studies are able to identify a viable, active lesion in recurrent GTN. Sironi et al, in their series of studies on recurrent GTN, reported FDG-PET is superior in detecting lesions that are otherwise missed or misinterpreted by conventional CT [12]. PET provides functional information that is useful in differentiating viable neoplastic tissue and necrotic lesion. The exact location of a metastatic lesion is crucial because surgical resection may be an important aspect of additional treatment. In our patients, surgical resection of the tumor guided by PET scan has proved to be successful in inducing remission.

Although the emergence of effective chemotherapy lessened the importance of surgical intervention in patients with malignant GTN, in certain situations surgical resection is still a viable option in the management of recurrent GTN. This tumor tends to bleed profusely because of the great vascularity of the trophoblastic tumor. Therefore, the surgeon should proceed with caution during resection of local metastases. In cases such as PSTT or ETT, hysterectomy plays an important role as primary intervention because of the risk of uterine perforation, which can lead to massive hemoperitoneum and disseminated intraperitoneal disease, or severe vaginal bleeding.

In our patients, laparoscopy is more beneficial compared with laparatomy. In addition to shorter hospitalization, less pain, earlier recovery, less morbidity, and better quality of life, the laparoscopic approach provides a complete intraperitoneal inspection and magnified visualization of any intraperitoneal lesion missed by imaging. We are fully aware that the risk of port-site metastasis is between 0–1.2% in laparoscopic oncology cases. The exact etiology of port metastases is unknown, but multiple factors have been implicated, such as direct wound implantation, contamination of the instrument, excessive manipulation of the tumor, and local and systemic effects of pneumoperitoneum [13]. Our patients did not have port-site metastasis and remained in remission after laparoscopic resection.

In summary, the options for management of recurrent choriocarcinoma depend on various factors. With a focal lesion, surgical resection should be considered to encourage remission and avoid the need for adjuvant chemotherapy. However, it is important to monitor levels of β-hCG so that further recurrence can be detected.

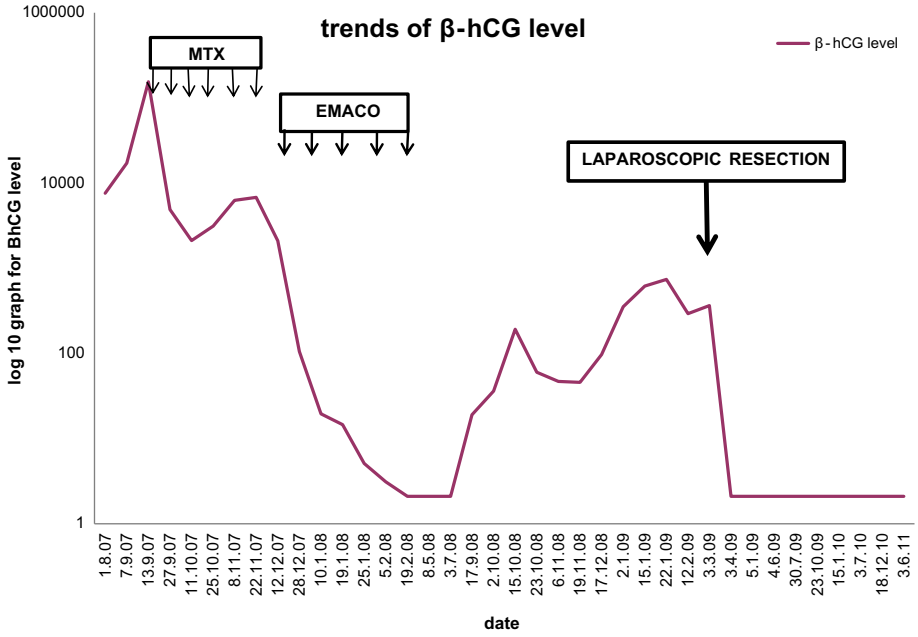

Fig. 4. A logarithm graphical representation of beta-human chorionic gonadotropin (β-hCG) levels. The *x* axis represents the date of β-hCG level taken throughout surveillance and during treatment. The *y* axis represents the serum concentration of serial β-hCG.

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