MEDDOCS Open Access Publisher

Journal of Gynecology Case Reports

Open Access | Case Series

Local Myometrial Resection for Chemo-Resistant Gestational Trophoblastic Neoplasia: Case Series and a Surgical Video

Reda Hemida[1]*; Emad Fyala[1]; Ahmed Ragab[1]; Hesham Abu-Taleb[2]

[1]Gynecologic Oncology Unit, Department of Obstetrics and Gynecology, Mansoura University, Egypt.

[2]Gynecologic Oncology Unit, Department of Obstetrics and Gynecology, Assiut University, Egypt.

***Corresponding Author(s): Reda Hemida**

Gynecologic Oncology Unit, Department of Obstetrics and Gynecology, Faculty of Medicine, Mansoura University, Mansoura, Egypt.

Email: redaelshouky@hotmail.com

Received: Mar 20, 2023

Accepted: Apr 06, 2023

Published Online: Apr 13, 2023

Journal: Journal of Gynecology Case Reports

Publisher: MedDocs Publishers LLC

Online edition: http://meddocsonline.org/

Keywords: Chemo-resistant GTN; Surgery; Local myometrial resection.

Abstract

Objective: To present 4 case of chemo-resistant Gestational Trophoblastic Neoplasms (GTN) who were treated with local myometrial resection with uterine reconstruction as a fertility-preserving surgery.

Design: A retrospective report of four cases who were managed from January, 2018 to July, 2022 and description of the surgical technique with a video presentation.

Materials and Methods: The data of four cases were collected from computer and paper files of Gestational Trophoblastic clinic, Department of Obstetrics and Gynecology, Mansoura University, Egypt (3 cases) and one case treated at Gynecologic Oncology Unit, Assiut University. All cases were diagnosed initially as low-risk non metastatic GTN who developed resistance to chemotherapy. After re-assessment and counselling; she had been performed local myometrial resection as fertility-preserving surgery. The surgical steps and operative video were presented.

Results: The mean age of the cases was 24.5 years. Three patients were nullipara and one case was primipara. The median operative time was 57.5 minutes and no blood transfusion were needed in all cases. Also; the postoperative course was smooth in all. The post-operative histopathology revealed choriocarcinoma in two cases, invasive mole in one, and Placental Site Trophoblastic Tumor (PSTT) in another one. Serum β-hCG was measured weekly and reached a non-pregnant level after mean 3.0 weeks of surgery. The follow up data were uneventful after surgery.

Conclusion: Chemo-resistant, non-metastatic GTN at young age can be managed with local myometrial resection with uterine reconstruction instead of hysterectomy. A multicenter-prospective study is recommended.

Cite this article: Hemida R, Fyala E, Ragab A, Abu-Taleb H. Local Myometrial Resection for Chemo-resistant Gestational Trophoblastic Neoplasia: Case Series and a Surgical Video. J Gynecol Case Rep. 2023; 2(1): 1005.

Background

Gestational Trophoblastic Neoplasia (GTN) is the malignant form of Gestational Trophoblastic Disease (GTD). GTN is a highly chemo-sensitive disease with a high-ranking cure rate [1]. Low risk GTN cases were found to be resistant to methotrxate monotherapy in 15.15% [2] and it was reported that 25 % of high-risk GTN patients developed chemotherapy resistance or relapsed after the initial therapy [3]. Zhou et al, [4] classified refractory GTN into: chemo-resistant; who had never a normal serum β-hCG level during their previous treatment, relapsed; who had elevated serum β-hCG levels 3 months or more after treatment, and undetermined GTN; who had elevated serum β-hCG levels less than 3 months after completed treatment in the absence of the pregnancy. The predictors of resistance to single-agent treatment in low-risk GTN were reported to be non-molar antecedent pregnancy, higher pre-treatment β-hCG level, and higher WHO risk scores, and histological diagnosis of choriocarcinoma [3].

As most of patients with GTN are within the reproductive age; Local Myometrial Resection (LMR) combined with uterine reconstruction might be considered in highly selected patients with non-metastatic GTN who wish to preserve their fertility. The lesions should be localized in the myometrium, defined by pelvic angiography, ultrasound, and CT scan [5]. Kanazawa et al [6] reported after his series that the reproductive outcome of patients who had undergone LMR was comparable to patients treated with chemotherapy only. In absence of international guidelines about indications of LMR; the decision and patient selection is based on expert opinions and wish of the patient. Due to the rarity of the disease and strict selection criteria; the publications and reported cases of LMR are few; so, we aimed to share our experience in the management and outcome of these four cases.

Materials and Methods

The data of the four cases were collected from computer and paper files of Gestational Trophoblastic Clinic, Department of Obstetrics and Gynecology, Mansoura University (3 cases) and one case treated at Gynecologic Oncology Unit, Assiut University. All cases were diagnosed initially as low-risk, non-metastatic GTN who developed resistance to chemotherapy. After re-assessment and counselling; she had been performed local myometrial resection as fertility-preserving surgery. All the cases were advised to receive Combined Oral Contraceptive Pills (COCs) and to attend bi-weekly follow up for one year.

The surgical steps of LMR with uterine reconstruction and operative video are presented.

Ethical consideration

A formal consent was obtained from all cases to publish their data. All procedures performed in this case series study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

The study was approved by the Institutional Research Board of Faculty of Medicine, Mansoura University (IRB approval number R.22.07.1756).

The video abstract was accepted for presentation during the ESGO 2022, Berlin, Germany on 27-30 October 2022.

Statistical Analysis

The details of the four cases were recorded on an Excel sheet. We used mean (±SD) and median (minimum-maximum) to describe the socio-demographic data of the cases

Case I

A 31 years old lady, P1A1. Her first pregnancy was diagnosed as complete mole that was treated by suction evacuation. She developed low-risk GTN Six months after normalization of β-hCG and treated by 3 courses of MTX/FA, followed by 2 consolidation courses.

After one year of combined oral contraceptive pills (COCs), she got pregnant delivered at term by caesarean section. However, she developed non-cyclic uterine bleeding four months after delivery, Doppler ultrasound detected a heterogeneous mass within the myometrium 5X4 cm with increased vascularity.

Serum β-hCG was 3400 mIu/ml and no metastases detected after workup. The case was diagnosed as relapsed low-risk GTN. Methotrexate monotherapy was started but β-hCG was stationary. The tumor board recommended to give a second line etoposide, methotrexate, actinomycin-D/ cyclophosphamide, vincristine (EMA/CO) but a slow decline of β-hCG after 3 courses occurred. The patient was referred to Gynecology department for hysterectomy that was refused by the patient for fertility issues.

Subsequently, a third line etoposide, methotrexate, actinomycin-D/etoposide, cisplatin (EMA/EP) was started for 3 courses, without reaching non pregnant level. Furthermore, the patient experienced severe adverse effects of chemotherapy side effects as febrile neutropenia, vomiting, hair loss, and deep venous thrombosis. The patient was referred once more for hysterectomy, and she refused one again. The metastatic work up was investigated again, distant metastases were excluded, Serum β-hCG 3270 was mIu/ml, and the updated risk scoring after failure of combination chemotherapy was "9". After counseling of the patient and family, Local Myometrial Resection (LMR) with uterine construction was done. A well-defined single necrotic mass (5X4 cm) was resected from the myometrium with a safety margin of 1 cm confirmed by frozen section, followed by uterine reconstruction. The operative time was 65 minutes. Post-operative course was uneventful. Serum β-hCG was normalized three weeks after resection. The lady was followed up in our GTD clinic by checking hCG every 2 weeks and chest-abdomen-pelvis CT every 3 months during the first year and follow up was extended till pregnancy occur. The lady had received one year of COCs then she tried to conceive for 3 years. Hysterosalpingography (HSG) was performed one year after LMR and showed normal uterine cavity and patent tubes **(Figure 1)**.

Case II

The patient aged 25 years at time of diagnosis of post-molar low risk GTN. Chemotherapy was started but resistance to 5 courses of methotrexate monotherapy and 4 courses of second-line EMA/CO was encountered. After workup; distant metastases were excluded and a solitary myometrial mass 4X4 cm was found. Serum β-hCG was 2760 mIu/ml. The metastatic follow up was investigated again and the updated risk scoring was 3. After tumor board discussion and counselling of the patient; LMR with uterine reconstruction was performed without complications. The operative time was 55 minutes. The post-

operative histopathology revealed invasive mole. Serum β-hCG was normalized after 2 weeks without further chemotherapy. The patient received COCs for one year with regular follow up by bi-weekly β-hCG and chest-abdomen-pelvis CT scan every 3 months for one year after which, the lady got spontaneous pregnancy and delivered a healthy female fetus by caesarean section. After 2 years of contraception; the lady experienced a second normal pregnancy ended by caesarean section at term.

Case III

A 21 years old lady, P0 A1, married for 1.5 years, medically free and irrelevant family history. She developed a Complete Mole (CM) one year ago, followed by low- risk GTN (FIGO risk score of 4). After referral to GTD clinic of MUH; remission occurred after 4 (+2) courses of methotrexate/folinic acid. Then, she used combined oral pills for contraception. But during the fourth month after remission; relapse of GTN occurred. We repeated pelvic ultrasound and CT of chest-abdomen that showed the disease is limited to myometrium 4X4 cm (figures 2A&2B). Methotrexate/folinic acid regimen was given but β-hCG titer was rising instead. Serum β-hCG has reached 17,000 mIu/ml. The tumor board decision was to start EMA/CO combination. However, after counseling and explanation of treatment plan; the patient refused to receive this combination chemotherapy for fear of its toxic side effects and asked for possibility of conservative surgery. Metastatic workup was repeated to confirm the strict criteria of LMR. The patient gave a consent for the operation and use of her data in future researches.

The operative time was 50 minutes. A well-defined hemorrhagic mass (5X4 cm) was resected from the myometrium with a safety margin of 1 cm proved by intraoperative frozen section **(Figure 2)**. No blood transfusion was needed. The postoperative course was smooth, and the patient was discharged second day of surgery. Serum β-hCG was measured weekly and reached a non-pregnant level after 3 weeks of surgery. The postoperative histopathology revealed choriocarcinoma invading myometrium with free safety margins. The post operative MDT recommended to start EMA/CO; however, considering the possible toxic effect on the gonads; the lady had undergone an Intra-Cytoplasic Sperm Injection (ICSI) cycle and 8 grade A embryos were cryopreserved. Then the patient received 3 courses of EMA/CO. Serum β-hCG was normalized and 2 consolidation courses were received. The patient received combined oral contraceptive pills for one year and attending a regular follow up visit. Chest-abdomen-pelvis CT scans were repeated every 6 months. Nowadays the lady is being prepared for embryo transfer.

Case IV

The patient aged 23 years, G1P0A1. She developed abnormal uterine bleeding after two weeks of spontaneous miscarriage without any evident histopathology. Hysteroscopy was performed and biopsy from a lesion extended to the cavity revealed Placental Site Trophoblastic Tumor (PSTT). The uterine bleeding continued and serum β-hCG was 410 mIu/ml. Metastatic workup revealed no distant metastases whereas a solitary myometrial mass 3X3 cm that was in contact with endometrial line was found. A combination regimen of EMA/CO was started with no decline of β-hCG after 3 courses which is expected in this chemoresistant histologic type. A second line EMA/EP for 3 more courses resulted in plateau β-hCG levels. After tumor board discussion and counselling of the patient and her husband; LMR was performed. The operative time was 60 minutes. The postoperative histopathology revealed (PSTT). The serum β-hCG declined to non-pregnant level after 4 weeks without chemotherapy. The patient is now under follow up every 2 weeks and imaging was repeated every 3 months. She is using COCs and follow up is uneventful.

Surgical technique **(Supplementary video)**.

General or spinal anesthesia, supine position, abdominal wall sterilization, and draping.

Laparotomy via Pfannenstiel incision, and exploration of abdominal organs.

Exposure of uterus, a rubber tourniquet was applied around the cervix to reduce uterine blood supply.

4. Identification of boundaries of the mass by its distinguished color, enucleating the mass from the surrounding healthy myometrium **(Figure 3)**.

5. Further excision of 1-2 cm of the surrounding myometrium and sent with the mass for frozen section, to ensure free safety margin.

6. Two milliliters of methotrexate (25 mg/ml ampoule) were injected locally in the wall of the lesion.

7. The uterine wall was reconstructed in two layers using 2/0 vicryl sutures. Finally, abdominal wall was closed in layers with a tube intraperitoneal drain.

Figure 1: Hysterosalpingography picture of case 1 one year after LMR, showing normal uterine cavity and patent both tubes.

Discussion

Most patients with GTN are young where the fertility is keened especially in the developing countries. Local myometrial resection with uterine reconstruction was reported to be a successful fertility-preserving therapy for chemo-resistant cases [5,6]. However; the procedure is suitable for a minority of cases as strict selection criteria should be fulfilled [5].

The current report describes management and outcome of four cases of chemo-resistant GTN who had underwent LMR

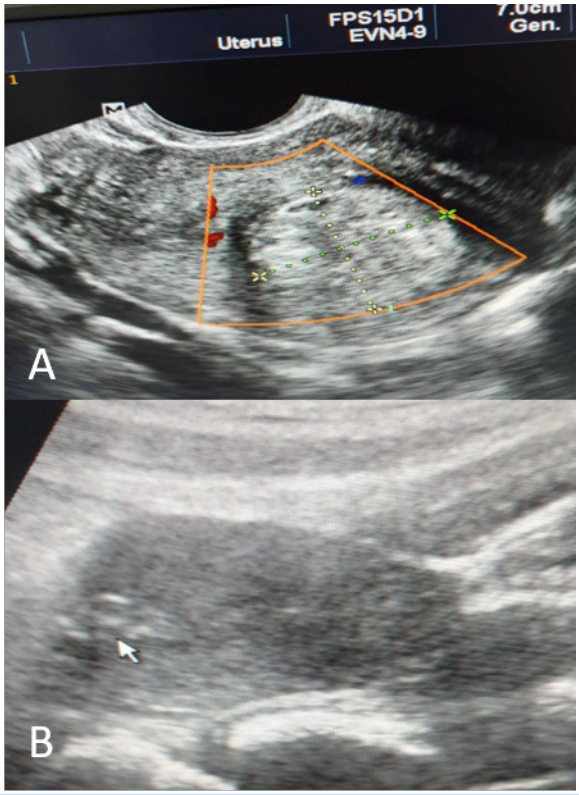

Figure 2: (A): A transvaginal ultrasound photo of "case 3" showing a solitary well-defined fundal myometrial mass about 4x4cm. Figure 2 (B): A transabdominal ultrasound photo two weeks after excision of the mass showing no residual at the site of the lesion (white arrow).

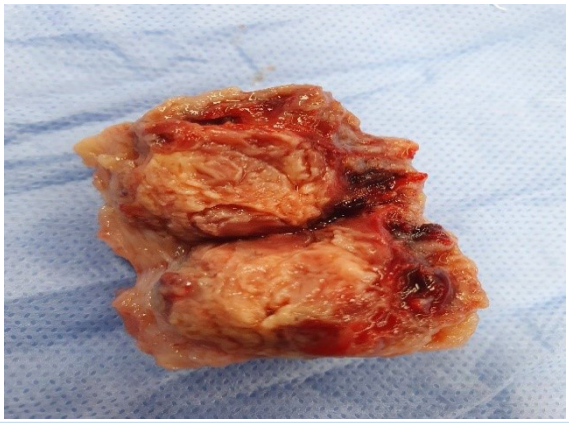

Figure 3: The specimen after excision showing 4X4 cm hemorrhagic lesion surrounded by a safety margin of the myometrium (case 3).

with uterine reconstruction. The mean age of the cases was 24.5 years. Three patients were nullipara and one case was primipara. The median operative time recorded 57.5 minutes with no blood transfusion needed in all cases. The postoperative course was uneventful. The post-operative histopathology revealed choriocarcinoma in two cases, invasive mole in one, and Placental Site Trophoblastic Tumor (PSTT) in another one. Serum β-hCG has reached a non-pregnant level after a mean of 3.0 weeks of surgery. The follow up data were uneventful except "case 3" who developed recurrence one month after surgery.

When a young lady with GTN resistant to chemotherapy; the next step could be hysterectomy. However, for fertility issues; she can be treated with LMR with uterine reconstruction. After enucleation of the mass with a safety margin; 2 milliliters of methotrexate (25 mg/ml ampoule) were injected in the wall of the cavity following the same concept of use in tubal ectopic [7] and caesarean scar pregnancy [8]. The operation was simple, technically easy, and safe. However, the procedure does not preclude post-treatment follow up.

Unfortunately; the postoperative histopathology revealed choriocarcinoma in two cases and our tumor board advised the ladies to receive 3 courses of EMA/CO after Charing Cross Gestational Trophoblast Disease Hospital (London, UK) recommendations [9]. Serum β-hCG was normalized within 3 weeks after surgery. The rapid decline of serum β-hCG after surgery denotes local removal of majority of the malignant trophoblast that was resistant to chemotherapy.

The authors recommend that LMR with uterine construction may be discussed in a trophoblastic disease management consensus to produce a clear international guideline for inclusion of this line of management. A large multicenter prospective study may be needed too. LMR may be a hope for young patients with GTN who are resistant, cannot tolerate, or refuse chemotherapy.

Conclusion

Chemo-resistant, non-metastatic GTN at young age can be managed with local myometrial resection with uterine reconstruction instead of hysterectomy. Routine post-treatment follow up and contraception for one year is mandatory. A multicenter-prospective study is recommended.

Abbreviations: GTD: Gestational Trophoblastic Diseases; **GTN:** Gestational Trophoblastic Neoplasia; **PSTT:** Placental Site Trophoblastic Tumors; **β-hCG:** Beta- Human Chorionic Gonadotrophin; **LMR:** Local Myometrial Resection; **MTX/FA:** Methotrexate, Folic Acid; **EMA/CO:** Etoposide, Methotrexate, Actinomycin D, Cyclophosphamide, Oncovin [Vincristin]; **EMA/EP:** Etoposide, Methotrexate, Actinomycin D, Etoposide, Cisplatin; **CT:** Computerized Tomography.

Acknowledgements

Not applicable.

Authors' contributions

Ahmed Ragab: data collection and analysis, manuscript writing and editing. Reda Hemida: protocol/project development, data collection and management. Hesham Abu-Taleb and Emad Fyala: data collection and management, and manuscript writing. The authors read and approved the final manuscript

Funding

Self-funded

Availability of data and materials: available on reasonable request.

References

1. Ngan HY, Kohorn EI, Cole LA, Kurman RJ, Kim SJ, et al. Trophoblastic disease. Int J Gynaecol Obstet. 2012; 119: S130-S136.

2. Hemida RA, Toson E, Shalaby H, Refaie E, Sharaf-Eldin D. Chemoresistant gestational trophoblastic neoplasia, 5-years' experience of Mansoura University Hospital, Egypt. Open Journal of Obstetrics and Gynecology. 2011; 1: 153-157.

3. Alazzam M, Tidy J, Hancock BW, Osborne R, Lawrie TA. First-line chemotherapy in low-risk gestational trophoblastic neoplasia. Cochrane Database Syst Rev. 2012; 7: CD007102.

4. Zhou Y, Feng F, Xiang Y, Wan X. Clinical analysis of patients with relapsed and chemo-resistant gestational trophoblastic neoplasia .Chinese Journal of Obstetrics and Gynecology. 2010; 12: 804-807.

5. Leiserowitz GS, Webb MJ. Treatment of placental site trophoblastic tumor with hysterotomy and uterine reconstruction. Obstet Gynecol. 1996; 88: 696-699.

6. Kanazawa K, Sasagawa M, Suzuki T, Takeuchi S. Clinical evaluation of focal excision of myometrial lesion for treatment of invasive hydatidiform mole. Acta Obstet Gynecol Scand. 1988; 67: 487-492.

7. Pansky M, Bukovsky I, Golan A, Herman A, Hertziano I, et al. Methotrexate local injection for unruptured tubal pregnancy: an alternative to laparotomy? Int J Gynaecol Obstet. 1992; 37: 265-270.

8. Tam LM, Kotani T, Linh TM. Outcome of cesarean scar pregnancy treated with local methotrexate injection. Nagoya J Med Sci. 2020; 82: 15-23.

9. Diagnosis and Treatment of Choriocarcinoma. Charing Cross Gestational Trophoblast Disease Service.