

# Role of Minimal Access Surgery in Gestational Trophoblastic Disease

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## ABSTRACT

Gestational trophoblastic diseases (GTD) comprise a spectrum of tumor and tumor-like conditions that originate from the fetal chorion. Trophoblastic tumors are fetal allograft in maternal tissues and present unique biological, immunological and pathological problems. Suction and evacuation followed by serial estimation of serum hCG and chemotherapy are the mainstay of treatment. Hysterectomy is the treatment of choice for patients with placental site trophoblastic tumors and also for persistent chemotherapy resistant uterine disease. This treatment may be unacceptable to the woman who wishes to retain her fertility. With quality of life issues becoming more important in medicine, therapies which preserve fertility, without compromising adequate treatment of the disease, should receive serious consideration. Laparoscopic hysterectomy and robotic hysterectomy are good options for women who are considered for surgery. Hysteroscopy also has a role in localizing and obtaining uterine (endometrial/myometrial) tissues for histopathological studies. It also helps in differentiating the diagnosis of gestational trophoblastic neoplasia from other conditions of raised serum hCG like ectopic pregnancy (cornual), incomplete abortion and nongestational trophoblastic tumors.

*Aim of study:* The aim of this study is to evaluate the role of minimal access surgical procedures like laparoscopy, hysteroscopy and robotic surgery in the management of gestational trophoblastic tumors.

*Methodology:* (1) Materials: The study was carried out through a literature search using the information technology installations of the World Laparoscopy Hospital, Gurgaon, NCR, Delhi. (2) Time: The study was carried out during a period of 2 weeks between July 12th, 2011 and July 26th, 2011.

*Data collection:* All the publications used in the current study was accessed from the electronic (virtual) library using the following search engines: Google, SpringerLink, PubMed, Highwire press, Medline.

*Abbreviations:* (1) GTD: Gestational trophoblastic disease, (2) GTT: Gestational trophoblastic tumor, (3) GTN: Gestational trophoblastic neoplasia, (4) PSTT: Placental site trophoblastic tumor.

**Keywords:** Gestational trophoblastic tumors, Laparoscopy, Hysteroscopy, Laparoscopic hysterectomy, Robotic hysterectomy.

## INTRODUCTION

Gestational trophoblastic diseases comprise of a spectrum of disorders characterized by abnormal and excessive proliferation of the chorionic villi. The spectrum of cellular proliferation includes as follows:

- Hydatidiform mole (complete or partial)
- Invasive mole
- Choriocarcinoma
- Placental site trophoblastic tumor.

If there is any evidence of persistence of gestational trophoblastic disease (GTD), usually defined as persistent elevation of serum beta hCG (human chorionic gonadotrophin), the condition is referred to as gestational trophoblastic neoplasia (GTN). GTN includes invasive mole, choriocarcinoma and placental site trophoblastic tumor (PSTT). GTN are very curable. They arise from the products of conception in the uterus. The most common preceding pregnancy is a hydatidiform mole. Choriocarcinoma most often follows a molar pregnancy, but can follow a normal pregnancy, ectopic pregnancy, or abortion and should always be considered when a patient has continued vaginal bleeding after the end of a pregnancy. The risk of malignancy after a complete mole is 10 to 15% and after a partial mole is 0.5%.

## INVESTIGATIONS

A urine pregnancy test should be performed in all cases of persistent or irregular vaginal bleeding after a pregnancy event. Definitive diagnosis is made by histological examination of the products of conception.

The important investigative modalities are as follows:

- Ultrasound
- Serum beta-hCG levels
- CT scanning for liver or other intra-abdominal metastases
- MRI or CT scanning for brain metastases
- Histology.

## DIAGNOSIS OF POSTMOLAR GTN

The diagnosis of GTN is made on the basis of elevated hCG levels, supported, but not necessarily by histologic or radiologic evidence. The criteria for the diagnosis of postmolar GTN are as follows:

- When there is plateau of hCG for > 4 weeks
- When there is rise in hCG on three consecutive measurements
- If hCG > 20,000 IU/l weeks after evacuation
- If hCG remains positive even after 16 weeks of evacuation
- When there is histological evidence of choriocarcinoma.

## MANAGEMENT

- *Suction curettage*: Suction and evacuation followed by gentle curettage is the first line of management for hydatidiform mole. Patient follow-up is very important and essential in these cases. Serum beta-hCG is estimated one day prior to and one day after suction and evacuation to detect the initial level. Then serum hCG serial estimation is done every two weeks till the levels are undetectable. Then serum hCG is done once a month for 6 months if the levels are negative and without any clinical symptoms.
- Chemotherapy for evidence of malignant disease.
- Hysterectomy is the treatment of choice for patients with:
  - Placental site trophoblastic tumor (they are relatively resistant to chemotherapy)
  - Persistent chemotherapy resistant tumor
  - Women who has completed her childbearing
  - Uncontrolled vaginal or intra-abdominal bleeding due to the tumor
- Radiotherapy (for some cases of distant metastases like brain metastases).

## REVIEW OF LITERATURE

Kanazawa et al<sup>1</sup> evaluated 22 patients with local myometrial resection of invasive moles. All patients had lesions localized in the myometrium, defined by pelvic angiography, ultrasound and CT scans. Any patient considered for this procedure should be carefully evaluated for systemic metastases and the uterine lesions should be localized by imaging and hysteroscopy. A normal laparoscopy can reasonably rule out an ectopic pregnancy (tubal, ovarian or abdominal). Nongestational trophoblastic neoplasia associated with raised serum hCG includes ovarian or extragonadal germ cell tumors containing trophoblastic components and many nongynecological tumors, like lung, bladder, liver, pancreas and stomach. These tumors are associated with low serum hCG, although concentrations up to 750,000 IU/l have been reported. A normal laparoscopic finding can reasonably exclude these diagnoses as well.<sup>2</sup>

Lang J et al<sup>3</sup> reported a case of performing laparoscopic hysterectomy in a woman with persistent GTN.

A retrospective descriptive analysis of data was done using charts of diagnosed cases of GTN from 1996 to 2006 by Cagayan MS et al<sup>5</sup> The patients were classified according to FIGO staging and WHO prognostic scoring. A total of 129 patients out of 420 cases of GTN underwent adjuvant hysterectomy. The overall survival was 98.4% with 2 of the 11 patients who had hysterectomy for chemotherapy-resistant disease dying. So, they concluded that with the increasing use of early surgical intervention combined with chemotherapy, the benefits of the patients were being maximized.

Lurain et al<sup>6,12</sup> from the Brewer Trophoblastic Disease Centre reported that 24 (48%) of 50 patients with high-risk GTN treated with EMA-CO as primary or secondary chemotherapy

underwent surgical procedures and 21(87.5%) were cured. Much et al<sup>13</sup> reported curing 10 (71%) of 14 patients who underwent hysterectomy as part of treatment for recurrent GTN at the South-Eastern Regional Trophoblastic Disease Centre, The Sheffield, UK. Trophoblastic Disease Centre reported that 9(75%) of 12 patients who underwent hysterectomy because of chemotherapy resistant uterine disease had a complete clinical response to surgery. Deumplis et al<sup>14</sup> evaluated the role of hysterectomy in the management of 25 patients with GTN at the Charing Cross Trophoblastic Disease Centre over a 13-year period. Histology was choriocarcinoma in 9, PSTT in 6 and hydatidiform mole in 10. The two main reasons for surgery were chemoresistance during initial treatment and relapse after treatment. Postoperative chemotherapy was given to 21 of the 25 patients although the hysterectomy appeared to be therapeutic as demonstrated by a rapid return of the hCG levels to normal in 22 of the 25 patients. Survival rate was 88% (22/25). Of the three who died, all had high-risk metastatic disease, one of whom had a PSTT. Intensive multimodality therapy of patients with high-risk GTN using EMA-CO chemotherapy (or some variations of it) along with adjuvant radiotherapy for brain metastasis results in primary remission rates of 65 to 80%. Approximately, 20 to 35% of high-risk patients will therefore fail first-line therapy or relapse from remission. Most of these patients will have a clinicopathologic diagnosis of choriocarcinoma, a large tumor burden reflected by a high serum hCG level and multiple metastases to sites other than lungs and pelvis, resulting in very high FIGO scores. Salvage chemotherapy with platinum/etoposide-containing drug regimens often combined with surgical resection of sites of persistent tumor (usually in the uterus and lungs) will result in high cure rates in these patients (approaching 90%).

Feng et al<sup>15</sup> reported a study of 27 patients with suspected diagnosis of GTN at Peking Union Medical College Hospital from Sep 2003 to Mar 2006. Clinical data of these patients were reviewed. Most patients had abnormal vaginal bleeding and persistently elevated serum hCG levels. Ultrasound revealed lesions with affluent blood flow in the intrauterine aspect, unilateral horn of the uterus or myometrium. No negative findings were revealed by CT scan or X-ray chest in all these patients. A total of 11 patients underwent evacuation under hysteroscope, 10 patients were diagnosed and treated by laparoscopy and six by hysteroscopy and laparoscopy. Choriocarcinoma was diagnosed in four patients, who achieved complete remission by chemotherapy later. The diagnosis of GTN was ruled out in the other 23 patients including cornual pregnancy in 12, pregnancy in the rudimentary horn in one and incomplete abortion in 10, who were cured by hysteroscopic and laparoscopic surgery and postoperative adjuvant single dose methotrexate. The major causes of pregnancy-related abnormal bleeding and elevated serum hCG levels include incomplete abortion, ectopic pregnancy and GTN. This study shows that hysteroscopy and laparoscopy are effective

alternative for diagnosis in the differentiation of GTN from nonGTN and can also offer therapeutic benefits.

L Savelli et al<sup>7</sup> reported a case of a 34-year-old woman admitted for persistent vaginal bleeding and slightly raised serum hCG on five different occasions, 6 months after second cesarean section. Transvaginal sonography showed a slightly enlarged uterus and the presence of an inhomogenous lesion, measuring 3 cm in mean diameter in the myometrium of the posterior uterine wall, displacing the endometrium. Pelvic MRI confirmed the presence of the lesion. The patient underwent a diagnostic hysteroscopy which disclosed the presence of irregularly shedding friable endometrium. Endometrial biopsy revealed only necrotic inactive endometrium and fibrin deposits. An operative hysteroscopy was done and with a monopolar hook the lesion was resected out. The histological diagnosis was PSTT. The patient then underwent total laparoscopic hysterectomy.

Devin et al<sup>8</sup> reported a case of a patient with elevated serum hCG despite therapy with methotrexate. A dilatation and curettage could not provide pathological diagnosis. A mass was found in the uterus by ultrasound and CT scan but there was no evidence of extrauterine disease. GTD was suspected. The patient underwent robotic hysterectomy for both therapy and diagnosis of suspected GTD. The final pathological diagnosis was PSTT. The robotic approach<sup>16,17</sup> allows for a minimally invasive surgical procedure with thorough examination of the pelvic cavity and adnexa. There is better visualization of the operative field with increased dexterity allowing more precise and controlled movements of the surgical instrument maneuvers. This minimizes the pain and risk associated with large incisions. It increases the likelihood of a fast recovery and excellent clinical outcome. It does not require an uterine manipulator which may be contraindicated in the setting of uterine GTD.

A Corusic et al<sup>9</sup> reported a case of a patient where after four cycles of methotrexate chemotherapy, a vascular tangle was noted that emerged from the right uterine horn, invading the broad ligament adjacent to the uterine artery. Doppler ultrasound along with magnetic resonance arteriography confirmed the diagnosis. The location, size and relation of this arteriovenous malformation to the uterine vasculature demanded urgent intervention. Laparoscopy was performed and bipolar coagulation of the ovarian and uterine artery feeding branches was achieved after surgical resection of the tumor.

Lindholm et al<sup>10</sup> reported a study where three cases with elevated serum hCG had negative ultrasound and color Doppler studies. In these cases, myometrial biopsies containing tumors were obtained by means of hysteroscopy. Michael R et al<sup>11</sup> reported a case where a patient after methotrexate injection for ectopic pregnancy reached a plateau level of serum hCG 3 weeks later and then the level started to increase. She underwent dilatation and curettage that did not reveal any trophoblastic tissue. A diagnostic hysteroscopy that followed revealed

occlude ostia of the left tube. The patient then had diagnostic laparoscopy that confirmed a mass in the left cornua, which was removed with wide wedge resection and histopathological examination revealed choriocarcinoma.

## DISCUSSION

Despite advances in chemotherapy regimens for treating malignant GTN, hysterectomy and other extirpative procedures continue to play a role in the management of patients with both low-risk and high-risk GTN. Primary hysterectomy can reduce the amount of chemotherapy required to treat low-risk disease,<sup>4</sup> whereas surgical resection including hysterectomy, pulmonary resection and other extirpative procedures can be invaluable for treating highly selected patients with persistent drug-resistant disease. Conservative myometrial resection combined with uterine reconstruction might be considered in highly selected patients with nonmetastatic GTN who wish to avoid hysterectomy. In a postpartum woman with urine pregnancy test positive but transvaginal sonography showing no intrauterine or extrauterine pregnancy, laparoscopy has an important role.<sup>2</sup> A normal laparoscopy can reasonably rule out an ectopic pregnancy and many nongestational trophoblastic neoplasia associated with raised serum hCG. Majority of women undergoing hysterectomy for malignant GTD are treated with abdominal hysterectomy. Laparoscopic-assisted vaginal hysterectomy and total laparoscopic hysterectomy has been used in few patients with GTN. This technique allows surveillance of the upper abdomen combined with shorter convalescence than abdominal hysterectomy. This procedure offers advantage that proper intra-abdominal inspection is possible, morcellation can be avoided (in laparoscopic-assisted vaginal hysterectomy) and the uterine arteries were transected at their origin before uterine manipulation to avoid potential tumor embolization. In addition, an abdominal incision is not required and so the patient has shorter hospitalization, less pain, shorter convalescence and faster recovery for an earlier start of chemotherapy if required. With robotic hysterectomy, there is better visualization of the operative field with increased dexterity allowing more precise and controlled movements of the surgical instrument maneuvers. It does not require an uterine manipulator which may be contraindicated in the setting of GTD. It has faster recovery and excellent clinical outcome. Hysteroscopy can also play a role in some selective and peculiar situations of GTD both for diagnosis and therapeutic purpose.

## CONCLUSION

GTN are very chemosensitive. Despite success of chemotherapy in inducing remission in most patients with GTN, surgical procedures play an important role in the management. Hysterectomy has a definitive role in PSTT, persistent chemoresistant GTN, in cases with uncontrolled vaginal bleeding, high-risk patients with disease confined to the uterus,

also in high-risk patients with uterine disease with metastases to reduce the tumor load prior to chemotherapy and in patients who do not wish to retain their fertility. Approximately, one-half of patients with high-risk GTN (FIGO stage 2-4, WHO risk score  $\geq 7$ ) will require some form of surgical procedure during the course of therapy to either remove disease or treat complications. These results in cure rates approaching 90% in the high-risk patients. Hysteroscopy and laparoscopy though not the mainstay of diagnosis and management are effective aids in certain selective and peculiar situations of GTN both diagnostically and therapeutically. For patients who are candidates for surgery, a minimal invasive procedure like laparoscopic-assisted vaginal hysterectomy, laparoscopic hysterectomy or robotic hysterectomy offers advantage when compared to the traditional abdominal hysterectomy. Minimal access surgical procedures have various benefits like better and thorough visualization of the abdominal and pelvic cavity, cost-effectiveness (including indirect costs), shorter convalescence time, faster return to work, earlier initiation of postoperative chemotherapy (if required), improved cosmetic effects and better patient satisfaction.

## REFERENCES

1. Kanazawa K, Sasawaga M, Suzuki T, et al. Clinical evaluation of focal excision of myometrial lesion for treatment of invasive hydatidiform mole. *Acta Obstet Gynecol Scand* 1988;67:487-92.
2. Rozenholc Alexandre, Petignat Patrick. Normal pregnancy or neoplasia. *BMJ* 2008;337:a2107.
3. Lang J, Childers J, Survit E. Laparoscopic hysterectomy for persistent gestational trophoblastic neoplasia. *The Journal of the American Association of Gynecologic Laparoscopists* 1995;2(4):475-77.
4. Sergent F, Verspyck E, Lemoine JP, Marpeau L. Place of surgery in the management of gestational trophoblastic tumours. *Gynecologic Obstetrique Fertilite* 2006;34(3):233-38.
5. Cagayan MS, Magallanes MS. The role of adjuvant surgery in the management of gestational trophoblastic neoplasia. *The Journal of Reproductive Medicine* 2008;53(7):513-18.
6. Lurain John R, Singh Diljeet K, Schink Julian C. Role of surgery in the management of high risk gestational trophoblastic neoplasia. *The Journal of Reproductive Medicine* 2006;51(10):773-76.
7. Savelli L, Pollastri P, Mabrouk M, Serracchioli R, Venturoli S. Placental site trophoblastic tumour diagnosed on transvaginal sonography. *Ultrasound Obstet Gynecol* 2009;34:234-36.
8. Namaky Devin, Basil Jack, Pavelka James. Placental site trophoblastic tumour presenting as an intramural mass with negative markers: An opportunity for novel diagnosis and treatment with robotic hysterectomy. *J Robotic Surg* 2010;4(1):57-59.
9. Ante Corusic, Dubrevko Barisic, Helena Lovrik, Albert. Successful laparoscopic bipolar coagulation of a large arteriovenous malformation due to invasive trophoblastic disease: A case report. *The Journal of Minimally Invasive Gynecology* May 2009;16(3):368-71.
10. Lindholm H, Radestad A, Flam F. Hysteroscopy provides proof of trophoblastic tumours in three cases with negative color Doppler images. *Ultrasound Obstet Gynecol* Jan 1997;9(1):59-61.
11. Michael Rotas, Neekinaund Khulpateea, David Binder. Gestational choriocarcinoma arising from a cornual ectopic pregnancy: A case report. *Archives of Gynecology and Obstetrics* 276(6):645-47.
12. Lurain JR. Advances in management of high-risk gestational trophoblastic tumors. *J Reprod Med* 2002;47:451-59.
13. Mutch DG, Soper JT, Babcock CJ, et al. Recurrent gestational trophoblastic disease. Experience of the South-Eastern Regional Trophoblastic Disease Center. *Cancer* 1990;66:978-82.
14. Doumplis D, Al Khatib K, Sieunarine K, et al. A review of the management of hysterectomy of 25 cases of gestational trophoblastic tumours from March 1993 to January 2006. *Br J Obstet Gynecol* 2007;114:1168-71.
15. Feng FZ, Xiang Y, He HJ, Wan XR, Yang XY. Value of hysteroscopy and laparoscopy in differential diagnosis of gestational trophoblastic neoplasia. *Zonghua Fu Chan Ke Za Zhi* July 2007;42(7):464-67.
16. Chen, Grace Chi Chiung, Falcone, Tommaso. Robotic gynecologic surgery: Past, present and future. *Clinical Obstetrics and Gynecology* Sep 2009;52(3):335-43.
17. Bandera, Christina Aa, Magrina, Javier Fb. Robotic surgery in gynecologic oncology. *Current Opinion in Obstetrics and Gynecology* Feb 2009;21(1):25-30.