

RESEARCH COMMUNICATION

Hysterectomy in Gestational Trophoblastic Neoplasia: Chiang Mai University Hospital's Experience

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Abstract

Indications and outcomes of hysterectomy in women with gestational trophoblastic neoplasia (GTN) were reviewed at Chiang Mai University Hospital, Chiang Mai, Thailand. From January 1998 through December 2008, 18 women underwent simple transabdominal hysterectomy (TAH). Indications for TAH included suspicious lesions confined to the uterus (5), chemoresistant lesions confined to the uterus (7), hemoperitonium (4), and other diagnoses of gynecologic diseases (2). The final histology reports included choriocarcinoma (9), invasive mole (6), placental site trophoblastic tumor or PSTT (1), uterine fibroid without residual GTN (1), and unknown (1). Two women experienced massive blood loss (4700 ml and 7500 ml, respectively). Postoperatively, only one woman with diagnosis of PSTT did not receive other adjuvant treatment. One woman failed to survive. In conclusion, hysterectomy continues to be an important treatment strategy for selected women with GTN. The common indications include drug-insensitive disease, PSTT, and hemorrhagic complications.

Key Words: Gestational trophoblastic neoplasia - hysterectomy - indication - outcomes

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Introduction

Gestational trophoblastic neoplasia (GTN) is malignant disease arising from placental trophoblastic tissue. Approximately 50% of GTNs occur after molar pregnancies; the remaining cases are the consequence of normal pregnancies (25%) and ectopic pregnancies or abortions (25%). GTNs are classified histologically into 3 distinct subgroups: choriocarcinoma destruens (invasive mole), choriocarcinoma and, placental site trophoblastic tumors (PSTT) (Ngan et al., 2003).

Decades ago when hysterectomy was the principle treatment, the prognosis of women diagnosed with GTN was poor particularly in cases of choriocarcinoma. However, after the introduction of the highly effective chemotherapeutic agents and sensitive assays of human chorionic gonadotrophins (HCG) used as tumor marker, the outcomes of women with GTN are dramatically improved, making GTN a disease that can be treated with chemotherapy alone in the majority of cases and rendering routine histological diagnosis before chemotherapy unnecessary. Consequently, in the 2000 International Federation of Obstetrics and Gynecology (FIGO) consensus guideline, the diagnosis of GTN could be made for women whose serum HCG level failed to normally regress (Ngan et al., 2003).

Although hysterectomy has a limited role in the modern treatment of GTN, the procedure may be required in certain patients. Accordingly, this study was undertaken

to review indications and outcomes of hysterectomy in women with GTN at Chiang Mai University Hospital, Chiang Mai, Thailand.

Materials and Methods

After approval of the Research Ethics Committee, Faculty of Medicine, Chiang Mai University, the medical records of women with GTNs who had undergone hysterectomy between January 1998 and December 2008 were reviewed. Abstracted data included the patient's demographic characteristics, the international Federation of Gynecology and Obstetrics (FIGO) stage and modified World Health Organization (WHO) score, surgical complications, detailed histopathology, and remission outcome after hysterectomy.

Data were analyzed using the statistical package SPSS for Windows (Chicago, IL) to describe median and range for continuous data and to describe number, percentage, and range for categorical data.

Results

Between January 1998 and December 2008, 162 women with GTN were treated at Chiang Mai University Hospital. Eighteen (11.1%) women underwent hysterectomy. All were simple and were transabdominal hysterectomy (TAH). Median age was 39 years (range 28-51 years). Eleven TAHs were performed at Chiang

Mai University Hospital while the remaining 7 underwent the same procedure at another hospital before patient referral for further treatment at our institute.

The women's FIGO anatomical stages were as follows; 9 (50.0%) women were at stage I, 8 (44.4%) were stage III, and 1 (5.6%) was stage IV. According to the WHO modified scoring system, 16 (88.9%) were considered to be high risk (a modified WHO prognostic score of 7 or greater). The median serum β -hCG level before TAH was 2716 iu/l (range 18-500000 iu/l). Only 4 women had a level before TAH of below 500 iu/l.

Indications for TAHs including suspicious lesion confined to uterus with complete family (5), chemoresistant lesion confined to uterus (7), hemoperitonium (4), and TAH for other diagnoses of gynecologic diseases (2).

Among 11 TAHs which were performed at our institute, 2 women experienced massive blood loss (4700 ml and 7500 ml, respectively). No other major peri-operative complications were noted. The final histology reports included choriocarcinoma (9), invasive mole (6), placental site trophoblastic tumor or PSTT (1), uterine fibroid without residual GTN (1), and unknown (1).

In this series, one 31-year-old woman was diagnosed with GTN. Her antecedent pregnancy was partial mole at 11 months prior. She presented with missed period, localized lesion in uterine cavity, and an increase of serum β -hCG level. Due to her wish to preserve future fertility, multiple chemotherapeutic regimens including either single or combination chemotherapy were given. However, no favorable response could be achieved. TAH was then performed after distant disease surveys turned out negative. The final pathological report was PSTT invading the inner half of her myometrium. Complete remission could be obtained without any additional postoperative chemotherapy.

Postoperatively, only one woman with a diagnosis of PSTT did not receive other adjuvant treatment as mentioned previously. At the time of this study, one woman had failed to survive after multiple regimens of salvage combination chemotherapy. One woman had disease recurrence in both sides of lungs after TAH; she was lost to follow-up after receiving 2 courses of salvage combination chemotherapy.

For one woman whose hysterectomy specimen contained only uterine fibroid without residual GTN, intrauterine mass with high vascular flow was noted preoperatively by pelvic ultrasonography. Given her increased of serum β -hCG level, this intrauterine mass was suspicious for residual GTN, so TAH was performed. Unfortunately, the lesion was uterine fibroid only. After the procedure, the serum β -hCG remained elevated without any suspicious lesions detected by metastatic surveys. She is now receiving salvage chemotherapy with a favorable treatment response.

Discussion

The majority of women with GTN are young and wish to preserve their fertility. Additionally, most of them can be completely treated with chemotherapy alone. Thus,

hysterectomy should be reserved for only women with lesions which are considered as chemotherapy insensitive, particularly for lesions confined to the uterus. In this study, approximately 39% of TAHs were performed because of this indication. However, in cases with metastatic disease, hysterectomy may be performed as a salvage treatment, but the benefits are not consistently reported because the outcomes of these women greatly depend on the efficacy of the control of extrauterine disease (Soper 2003).

Hysterectomy, although nowadays uncommon, can be a primary treatment for women with non-metastatic GTN if there is no longer a requirement for future pregnancy. In this study, 5 women (27.8%) underwent primary hysterectomy. The major advantage of primary hysterectomy followed by chemotherapy compared to chemotherapy alone is the reduction of the total doses of chemotherapeutic drugs (Suzuka et al., 2001). This benefit is of utmost relevance, particularly in cases receiving etoposide, not only because of acute toxicities, but also etoposide's potential risk of future secondary malignancy development (Rustin et al., 1996). This long-term consequence is recognized as a cumulative dose dependent pattern, undoubtedly; a lesser cumulative dose of etoposide confers a lesser risk for such malignancies.

PSTT is a very rare but important histological type of GTN. This tumor originates from abnormal proliferation of intermediate trophoblastic cells at the placental implantation site. In contrast to other GTNs, PSTT is relatively resistant to chemotherapy. However, a high cure rate could be achieved by hysterectomy alone if the lesion is localized in the uterus, making hysterectomy the first choice treatment for uterine-confined PSTT (Kim 2003). In this study, one woman who failed with multiple chemotherapy regimens was eventually noted as having PSTT in hysterectomy specimen. As reported in the literature (Papadopoulos et al., 2002; Kim, 2003), this case could be cured with TAH alone.

Intraabdominal hemorrhage and severe vaginal bleeding from GTN are serious life-threatening complications requiring emergency hysterectomy in the majority of cases. In this study, 22.2% of women underwent emergency hysterectomy due to uterine perforation causing massive hemoperitonium. With the advancement of radio-intervention techniques particularly selective arterial embolization, the authors recently reported successfully uterine conservation management in women with large cervical choriocarcinoma with life-threatening vaginal bleeding using selective uterine arterial embolization (Chandacham et al., 2009). So, there is a possibility of avoiding hysterectomy in select patients by using this technique, especially in hemodynamically stable cases.

Hysterectomy for GTN may occasionally be a difficult procedure. The high pelvic vascularity and extensive tumor necrosis which are the nature of disease can complicate the procedure particularly in cases with extrauterine diseases. So, significant perioperative complications i.e. massive blood loss, postoperative febrile morbidity, and injury to adjacent organs, can be expected (Pisal et al., 2002; Doumplis et al., 2007; Alazzam et al., 2008). In this series, 2 women experienced massive

intraoperative blood loss (4700 ml and 7500 ml, respectively). So, some authors proposed that hysterectomy should be performed by an experienced surgeon in a setting with ready availability of an anesthetist, blood component therapy, and intensive postoperative care (Pisal et al., 2002; Doumplis et al., 2007).

As mentioned earlier, hysterectomy would be highly beneficial in women with uterine-confined disease. Therefore, the comprehensive survey for metastatic disease before treatment decision making is crucial. The accuracy of metastatic work up generally depends on the type of imaging technique. For example, 40% of women with negative chest x-ray will eventually be found to have pulmonary micrometastasis on subsequent chest CT scan (Gamer et al., 2004). Recently, 18-fluorodeoxyglucose positron emission tomography (FDG-PET) has proven to be the most accurate imaging for metastatic work up in various malignancies including GTN (Nieves et al., 2008). Because of differences in available resources in each setting, the accuracy of metastatic surveys may vary because of different imaging used. However, information regarding the accuracy of imaging used would be provided to the patient at the time of management counseling and planning for hysterectomy.

In conclusion, hysterectomy continues to be an important treatment strategy in select women with GTN. The common indications include primary hysterectomy, hysterectomy for drug-insensitive disease, and PSTT. Hysterectomy either as primary treatment or after a diagnosis of drug resistance is clearly beneficial in women whose lesions are still confined to the uterus. Therefore, comprehensive metastatic surveys are of the utmost relevant. In addition, hysterectomy may be necessary in women with severe tumor bleeding.

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