Protocol for the Examination of Specimens From Patients With Gestational Trophoblastic Malignancies

A Basis for Checklists

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This protocol is intended to assist pathologists in providing clinically useful and relevant information as a result of the examination of surgical specimens. Use of this protocol is intended to be entirely voluntary. If equally valid protocols or similar documents are applicable, the pathologist is, of course, free to follow these authorities. Indeed, the ultimate judgment regarding the propriety of any specific procedure must be made by the physician in light of the individual circumstances presented by a specific patient or specimen.

It should be understood that adherence to this protocol will not guarantee a successful result. Nevertheless, pathologists are urged to familiarize themselves with this document. Should a physician choose to deviate from this protocol owing to the circumstances of a particular patient or specimen, the physician is advised to make a contemporaneous written notation of the reason for the procedure followed.

The College recognizes that this document may be used by hospitals, attorneys, managed care organizations, insurance carriers, and other payers. However, the document was developed solely as a tool to assist pathologists in the diagnostic process by providing information that reflects the state of relevant medical knowledge at the time the protocol was first published. It was not developed for credentialing, litigation, or reimbursement purposes. The College cautions that any uses of the protocol for these purposes involve considerations that are beyond the scope of this document.

PROTOCOL FOR THE EXAMINATION OF SPECIMENS FROM PATIENTS WITH GESTATIONAL TROPHOBLASTIC MALIGNANCIES

I. Dilation and Curettage

A. Clinical information

1. Patient identification
   a. Name
   b. Identification number
   c. Age (birth date)

2. Responsible physician(s)

3. Date of procedure

4. Other clinical information
   a. Relevant history (note A)
      (1) Menstrual history
      (2) Week of pregnancy
      (3) Passage of tissue
   b. Relevant findings (eg, size of uterus, ultrasound, human chorionic gonadotropin [hCG] level)
   c. Clinical diagnosis
   d. Procedure (eg, endometrial biopsy, dilation and curettage, spontaneous passage of tissue)
   e. Anatomic site(s) of specimen(s) (eg, uterine corpus, cervix)

B. Macroscopic examination

1. Specimen
   a. Unfixed/fixed (specify fixative)
   b. Size (aggregate dimensions if multiple, after separating tissue from blood)
   c. Lesion/tumor
      (1) Dimensions
      (2) Descriptive features
      (3) Vesicles, with size of largest
      (4) Fetal tissue and anomaly
      (5) Firmness
      (6) Necrosis
   d. Results of intraprocedural consultation

2. Tissue submitted for microscopic evaluation
   a. Villous tissue
      (1) Representative samples, if abundant
      (2) All, if sparse
   b. Fetal tissue
   c. Uterine tissue

3. Special studies (specify) (eg, immunohistochemistry, DNA, analysis [specify type], oncogene analysis, karyotype analysis)

C. Microscopic evaluation

1. Adequacy of specimen (if inadequate for evaluation, specify reason)

2. Lesion/tumor
a. Histologic type (note B)
b. Presence in sharp curettage specimen
c. Presence in suction curettage specimen

3. Additional tissues or pathologic findings, if present
   a. Implantation site
   b. Endometrium
   c. Myometrium
d. Cervix
e. Fetal tissues (cord, amnion, chorion, yolk sac)
f. Fetal anomalies, if present

4. Results/status of special studies

5. Comments
   a. Correlation with intraprocedural consultation, as appropriate
   b. Correlation with other specimens, as appropriate
c. Correlation with clinical information, including hCG level, as appropriate

**II. Resection**

**A. Clinical information**

1. Patient identification
   a. Name
   b. Identification number
   c. Age (birth date)
2. Responsible physician(s)
3. Date of procedure
4. Other clinical information
   a. Relevant history (note A)
      (1) Menstrual history
      (2) Week of pregnancy
      (3) Passage of tissue
      (4) History of hydatidiform mole
   b. Relevant findings (eg, size of uterus, ultrasound, hCG level)
c. Clinical diagnosis
d. Procedure (eg, abdominal hysterectomy, radical hysterectomy with bilateral salpingo-oophorectomy, staging laparotomy, pelvic exenteration)
e. Anatomic site(s) of specimen(s) (eg, uterine corpus, cervix)

**B. Macroscopic examination**

1. Specimen
   a. Organ(s)/tissue(s) included
   b. Unfixed/fixed (specify fixative)
c. Number of pieces
d. Dimensions
e. Orientation, if indicated by surgeon
f. Areas indicated by surgeon for specific microscopic evaluation
g. Results of intraoperative consultation
2. Lesion/tumor
   a. Location (eg, corpus/fundus/cornu/isthmus/cervix)
b. Size (3 dimensions)
c. Descriptive characteristics (eg, villous tissue/exophytic/color)
d. Extent of invasion (note C)
   (1) Into myometrium/serosa/parametrium/cervix
   (2) To other organ(s)/tissue(s)
e. Distance from margins
3. Additional pathologic findings, if present (evidence of prior sampling or treatment at apparent site of lesion)
4. Uterine corpus
   a. Dimensions
   b. Descriptive features of endometrium, myometrium, and serosa
c. Lesion/tumor
   (1) Descriptive features, including size, location, and extent
   (2) Relation to main lesion/tumor
d. Resection margins, if appropriate
e. Additional findings, if present
5. Uterine cervix
   a. Descriptive features, including appearance of ectocervix and endocervix
   b. Lesion/tumor
   (1) Descriptive features, including size, location, and extent
   (2) Relation to main lesion/tumor
c. Resection margins, if appropriate
d. Additional findings, if present
6. Vagina
   a. Size (length, circumference, thickness)
b. Descriptive features, including inner and outer surfaces, wall
c. Lesion/tumor
d. Descriptive features, including size, location, and relation to main lesion/tumor
e. Resection margins, if appropriate
f. Additional findings, if present
7. Fallopian tube(s)
   a. Dimensions
   b. Descriptive features, including dimensions
   c. Lesion/tumor
   (1) Descriptive features, including size, location, and extent
   (2) Relation to main lesion/tumor
d. Resection margins, if appropriate
e. Additional findings
8. Ovary(ies)
   a. Descriptive features, including measurements, outer surface, and sectioned surface
   b. Lesion/tumor
   (1) Descriptive features, including size, location, and extent
   (2) Relation to main lesion/tumor
c. Resection margins, if appropriate
d. Additional findings (eg, multiple luteinized follicle cysts)
9. Organ in which lesion/tumor primary (uninvolved component)
   a. Dimensions
   b. Descriptive features
   c. Resection margins, if appropriate
d. Additional findings, if present
10. Regional lymph nodes
   a. Lesion/tumor
   (1) Size
   (2) Descriptive features
   b. Additional findings, if present
11. Other organ(s) or tissue(s) removed (eg, omentum, staging biopsy specimens)
   a. Type(s) or site(s)
   b. Dimensions and other descriptive features
c. Lesion/tumor
   (1) Descriptive features, including size, location, and extent
   (2) Relation to main lesion/tumor
   d. Resection margins, if appropriate

12. Tissues submitted for microscopic evaluation
   a. Primary lesion/tumor of uterus or other organ, adequate number to demonstrate
      the following:
      (1) Deepest myometrial invasion or extent of involvement
      (2) Distance from serosa or resection margin
      (3) Cornual/isthmic/cervical/parametrial involvement, if present
   b. Other lesions
   c. Grossly uninvolved tissue, as appropriate
   d. Staging and lymph node specimens (at least 1 section of each)
      e. Omentum (multiple sections whether or not grossly involved)
   f. Vaginal cuff
   g. Frozen section tissue fragment(s) (unless saved for special studies)
   h. Other organs/tissues, as appropriate for gross clinical indications

13. Special studies (eg, DNA flow cytometry, genetic studies such as karyotype analysis, image analysis, DNA polymorphism analysis)

C. Microscopic evaluation
1. Organ primarily involved
   a. Lesion/tumor
      (1) Histologic type (note B)
      (2) Site
      (3) Extent of invasion (note C)
      (4) Depth of invasion from endometrial junction/thickness of myometrium; or extent of primary tumor in other organs
      (5) Closest distance to serosa
      (6) Blood/lymphatic vessel invasion
   b. Resection margins
   c. Status of inked areas or areas designated by surgeon

2. Additional pathologic findings, if present
   a. Implantation site, if present (endometrium, myometrium, cervix)
   b. Fetal tissues (chorion, amnion, yolk sac)
   c. Fetal anomalies, if present

3. Regional lymph nodes
   a. Total number
   b. Number involved by tumor
   c. Other findings (eg, decidua)

4. Other organ(s) and tissue(s)
   a. Lesion/tumor
      (1) Location
      (2) Extent
      (3) Relation to primary lesion/tumor
   b. Resection margins, if appropriate
   c. Additional findings (eg, decidua, hyperreactio luteinalis of ovaries)

5. Results/status of special studies (specify)
6. Comments
   a. Correlation with intraoperative consultation, as appropriate
b. Correlation with other specimens, as appropriate
   c. Correlation with clinical information, as appropriate

EXPLANATORY NOTES

A: Previous History.—Previous slides should be reviewed by the pathologist if it is deemed necessary by the gynecologist or pathologist for optimal evaluation of the specimen.

B: Histologic Type.—The World Health Organization Histologic Classification of Gestational Trophoblastic Lesions1 is as follows.

World Health Organization Classification

- Hydatidiform mole
  - Complete*
  - Partial²
- Invasive hydatidiform mole
- Choriocarcinoma
- Placental site trophoblastic tumor³
- Trophoblastic lesions, miscellaneous
  - Exaggerated placental site
  - Placental site nodule and plaque§
- Unclassified trophoblastic lesions
  * Usually diploid, 46 chromosomes; no fetal tissues unless with a twin gestation; villi markedly enlarged, hydropic, central cistern; prominent trophoblastic hyperplasia.
  ‡ Usually triploid, 69 chromosomes; fetal tissues present; villi scalloped, have stromal trophoblastic inclusions; focal trophoblastic hyperplasia, usually of syncytiotrophoblast.
  ‡§ Malignant tumor of intermediate trophoblast.
  § Retention of a nodule or plaque of benign intermediate trophoblast.

C: TNM and International Federation of Gynecology and Obstetrics Staging of Gestational Trophoblastic Tumors.—The TNM staging system of the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC)² and the corresponding staging system of the International Federation of Gynecology and Obstetrics (FIGO) are recommended, as follows. Both are based not only on the anatomic extent of the tumor but on additional factors, including clinical and laboratory findings.

FIGO Staging for Gestational Trophoblastic Tumors (GTTs) (1991)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>Disease confined to the uterus</td>
</tr>
<tr>
<td>IB</td>
<td>Disease confined to the uterus with no risk factors</td>
</tr>
<tr>
<td>IC</td>
<td>Disease confined to the uterus with 1 risk factor</td>
</tr>
<tr>
<td>IIA</td>
<td>GTT involving genital structures without risk factors</td>
</tr>
<tr>
<td>IIB</td>
<td>GTT extends outside of the uterus but limited to genital structures with 1 risk factor</td>
</tr>
<tr>
<td>Stage II</td>
<td>GTT extends outside of the uterus but limited to genital structures (adnexa, vagina, broad ligament)</td>
</tr>
</tbody>
</table>

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AJCC/UICC TNM Staging for Trophoblastic Tumors

**Primary Tumor (T)**

- TX: Primary tumor cannot be assessed
- T0: No evidence of primary tumor
- T1: Tumor confined to uterus
- T2: Tumor extends to other genital structures: vagina, ovary, broad ligament, fallopian tube by metastasis or direct extension

* By AJCC/UICC convention, the designation “T” of the TNM classification refers exclusively to the first resection of a primary tumor. The prefix symbol “p” refers to the pathologic classification of the TNM (pTNM), as opposed to the clinical classification. Pathologic classification is based on gross and microscopic examination. Therefore, pT entails a resection of the primary tumor or biopsy adequate to evaluate the highest pT category; pN entails removal of nodes adequate to validate lymph node metastasis; and pM implies microscopic examination of distant lesions. Clinical classification (cTNM) is usually carried out by the referring physician before treatment during initial evaluation of the patient or when pathologic classification is not possible.

The absence or presence of residual tumor following preoperative nonsurgical therapy (eg, chemotherapy or radiation treatment) may be described by the symbol “R” and is classified as follows:

- RX: Presence of residual tumor cannot be assessed
- R0: No residual tumor
- R1: Microscopic residual tumor
- R2: Macroscopic residual tumor

If residual tumor is present, its extent may be documented by the TNM classification preceded by the symbol “y” (eg, ypT1). Local recurrence following a previous resection should be classified with the prefix “r” (eg, rpT1).

**Distant Metastasis (M)**

- MX: Distant metastasis cannot be assessed
- M0: No distant metastasis
- M1: Distant metastasis
- M1a: Metastasis to lungs(s)*
- M1b: Other distant metastasis (eg, brain) with or without lung metastasis*

* Genital metastasis (vagina, broad ligament, ovary, fallopian tube) is classified as T2.

**TNM Stage Groupings**

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>M</th>
<th>Risk Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>T1</td>
<td>M0</td>
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</tr>
<tr>
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</tr>
<tr>
<td>IVC</td>
<td>Any T</td>
<td>M1b</td>
<td>2</td>
</tr>
</tbody>
</table>

The following factors should be considered and noted in reporting:

1. Prior chemotherapy for known GTT
2. Placental site tumors should be reported separately
3. Histological verification of disease is not required

**References**


**Bibliography**


Silva E, Tornos C, Lage J, Ordonez M, Kavanagh J. Multiple nodules of interme-


