Protocol for the Examination of Specimens From Patients With Primary Sarcoma of the Uterus

Version: 4.3.0.0
Protocol Posting Date: November 2021
CAP Laboratory Accreditation Program Protocol Required Use Date: August 2022
The changes included in this current protocol version affect accreditation requirements. The new deadline for implementing this protocol version is reflected in the above accreditation date.

For accreditation purposes, this protocol should be used for the following procedures AND tumor types:

Procedure	Description
Resection	Includes total hysterectomy and supracervical hysterectomy
Tumor Type	**Description**
Sarcoma	Includes leiomyosarcoma, adenosarcoma, endometrial stromal sarcoma, and undifferentiated uterine/endometrial sarcoma

This protocol is NOT required for accreditation purposes for the following:

Procedure
Biopsy, myomectomy, or removal of tumor in fragments
Primary resection specimen with no residual cancer (eg, prior myomectomy)
Cytologic specimens

The following tumor types should NOT be reported using this protocol:

Tumor Type
Carcinoma (consider the Endometrium or Cervix protocols)
Lymphoma (consider the Hodgkin or non-Hodgkin Lymphoma protocols)

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With guidance from the CAP Cancer and CAP Pathology Electronic Reporting Committees.
* Denotes primary author.

Accreditation Requirements

This protocol can be utilized for a variety of procedures and tumor types for clinical care purposes. For accreditation purposes, only the definitive primary cancer resection specimen is required to have the core and conditional data elements reported in a synoptic format.

- Core data elements are required in reports to adequately describe appropriate malignancies. For accreditation purposes, essential data elements must be reported in all instances, even if the response is "not applicable" or "cannot be determined."
- Conditional data elements are only required to be reported if applicable as delineated in the protocol. For instance, the total number of lymph nodes examined must be reported, but only if nodes are present in the specimen.
- Optional data elements are identified with "+" and although not required for CAP accreditation purposes, may be considered for reporting as determined by local practice standards.

The use of this protocol is not required for recurrent tumors or for metastatic tumors that are resected at a different time than the primary tumor. Use of this protocol is also not required for pathology reviews performed at a second institution (ie, secondary consultation, second opinion, or review of outside case at second institution).

Synoptic Reporting

All core and conditionally required data elements outlined on the surgical case summary from this cancer protocol must be displayed in synoptic report format. Synoptic format is defined as:

- Data element: followed by its answer (response), outline format without the paired Data element: Response format is NOT considered synoptic.
- The data element should be represented in the report as it is listed in the case summary. The response for any data element may be modified from those listed in the case summary, including "Cannot be determined" if appropriate.
- Each diagnostic parameter pair (Data element: Response) is listed on a separate line or in a tabular format to achieve visual separation. The following exceptions are allowed to be listed on one line:
    - Anatomic site or specimen, laterality, and procedure
    - Pathologic Stage Classification (pTNM) elements
    - Negative margins, as long as all negative margins are specifically enumerated where applicable
- The synoptic portion of the report can appear in the diagnosis section of the pathology report, at the end of the report or in a separate section, but all Data element: Responses must be listed together in one location

Organizations and pathologists may choose to list the required elements in any order, use additional methods in order to enhance or achieve visual separation, or add optional items within the synoptic report. The report may have required elements in a summary format elsewhere in the report IN ADDITION TO but not as replacement for the synoptic report ie, all required elements must be in the synoptic portion of the report in the format defined above.

Summary of Changes

v 4.3.0.0

- Added ITC into Regional Lymph Nodes

Reporting Template

Protocol Posting Date: November 2021
Select a single response unless otherwise indicated.

CASE SUMMARY: (UTERUS (SARCOMA))
Standard(s): AJCC-UICC 8, FIGO Cancer Report 2018

SPECIMEN

Procedure (select all that apply)
For information about lymph node sampling, please refer to the Regional Lymph Node section.
___ Total hysterectomy and bilateral salpingo-oophorectomy
___ Radical hysterectomy
___ Simple hysterectomy
___ Supracervical hysterectomy
___ Bilateral salpingo-oophorectomy
___ Right salpingo-oophorectomy
___ Left salpingo-oophorectomy
___ Salpingo-oophorectomy, side not specified
___ Right oophorectomy
___ Left oophorectomy
___ Oophorectomy, side not specified
___ Bilateral salpingectomy
___ Right salpingectomy
___ Left salpingectomy
___ Salpingectomy, side not specified
___ Omentectomy
___ Peritoneal biopsy(ies)
___ Peritoneal washing
___ Other (specify): _____

+Hysterectomy Type
___ Abdominal
___ Vaginal
___ Vaginal, laparoscopic-assisted
___ Laparoscopic
___ Laparoscopic, robotic-assisted
___ Other (specify): _____
___ Not specified

Specimen Integrity
___ Intact
___ Opened
___ Morcellated
___ Other (specify): _____

TUMOR

Tumor Site
___ Uterine corpus: _____
___ Uterine cervix: _____
___ Uterus, not otherwise specified: _____

Tumor Size
___ Greatest dimension in Centimeters (cm): _____ cm
+Additional Dimension in Centimeters (cm): ____ x ____ cm
___ Cannot be determined (explain): _____

Histologic Type (Note A)
___ Leiomyosarcoma NOS
___ Spindle (conventional) leiomyosarcoma
___ Epithelioid leiomyosarcoma
___ Myxoid leiomyosarcoma
[#] Low-grade endometrial stromal sarcoma is distinguished from benign endometrial stromal nodule by depth of myometrial invasion greater than or equal to 3 mm, lymphovascular invasion, or greater than or equal to 3 foci of myometrial invasion of any depth. Minor marginal irregularity in the form of tongues less than 3 mm is allowable for an endometrial stromal nodule. This checklist does not apply to endometrial stromal nodules.
___ Endometrial stromal sarcoma, low-grade[#]
___ Endometrial stromal sarcoma, high-grade
___ Undifferentiated sarcoma
___ Adenosarcoma
___ Adenosarcoma, NOS
___ Adenosarcoma with sarcomatous overgrowth
___ Rhabdomyosarcoma
___ Malignant perivascular epithelioid cell tumor
___ Other histologic type not listed (specify): _____
+Histologic Type Comment: _____

Histologic Grade (Note A)
Required only for adenosarcoma. Adenosarcoma with sarcomatous overgrowth is usually high grade and should be considered high grade because of a poorer prognosis.
___ Not applicable
___ Low grade
___ High grade
___ Cannot be assessed: _____

Myometrial Invasion (Note A)
Required only for adenosarcoma
___ Not applicable
___ Not identified
___ Present
Depth of Myometrial Invasion
___ Specify in Millimeters (mm): _____ mm
___ Other (specify): _____
___ Cannot be determined (explain): _____

Myometrial Thickness
___ Specify in Millimeters (mm): _____ mm
___ Other (specify): _____
___ Cannot be determined (explain): _____

Percentage of Myometrial Invasion
___ Specify Percentage: _____ %
___ Estimated to be less than 50%
___ Estimated to be 50% or greater
___ Cannot be determined (explain): _____
___ Cannot be determined (explain): _____

Other Tissue / Organ Involvement[#] (select all that apply)
[#] Any organ not selected is either not involved or was not submitted.
___ Not identified
___ Adnexa: _____
___ Other pelvic tissue (specify): _____
___ Abdominal tissue in one site (specify): _____
___ Abdominal tissue in multiple sites (specify): _____
___ Bladder mucosa
___ Rectal mucosa
___ Other organs / tissue (specify): _____
___ Cannot be determined (explain): _____
___ Not applicable

Lymphovascular Invasion (Note B)
___ Not identified
___ Present
___ Equivocal (explain): _____
___ Cannot be determined: _____

+Peritoneal / Ascitic Fluid Involvement
___ Not submitted / unknown
___ Not identified
___ Atypical (explain): _____
___ Suspicious (explain): _____
___ Present
___ Cannot be determined: _____
___ Results pending

+Tumor Comment: _____

MARGINS

Margins Status
___ All margins negative for sarcoma
+Distance from Sarcoma to Closest Margin
Specify in Millimeters (mm)
___ Exact distance: _____ mm
___ Greater than: _____ mm
___ At least: _____ mm
___ Less than: _____ mm
___ Less than 1 mm
___ Other (specify): _____
___ Cannot be determined: _____
+Closest Margin(s) to Sarcoma
___ Specify closest margin(s): _____
___ Cannot be determined: _____
___ Sarcoma present at margin
Margin(s) Involved by Sarcoma
___ Specify involved margin(s): _____
___ Cannot be determined: _____
___ Other (specify): _____
___ Cannot be determined (explain): _____
___ Not applicable

+Margin Comment: _____

REGIONAL LYMPH NODES

Regional Lymph Node Status
 # Lymph nodes designated as pelvic, parametrial, obturator, internal iliac (hypogastric), external iliac, common iliac, sacral, presacral, and para-aortic are considered regional lymph nodes. Any other involved nodes should be categorized as metastases (pM1) and commented on in the distant metastasis section. Presence of isolated tumor cells no greater than 0.2 mm in regional lymph node(s) is considered N0 (i+).
___ Not applicable (no regional lymph nodes submitted or found)
___ Regional lymph nodes present
___ All regional lymph nodes negative for tumor
___ Tumor present in regional lymph node(s)
Number of Lymph Nodes with Tumor
___ Exact number (specify): _____
___ At least (specify): _____
___ Other (specify): _____
___ Cannot be determined (explain): _____
Total Number of Lymph Nodes with Isolated Tumor Cells# (0.2 mm or less)
 # Reporting the number of lymph nodes with isolated tumor cells is required only in the absence of macrometastasis or micrometastasis in other lymph nodes.
___ Not applicable
___ Exact number : _____
___ At least : _____
___ Other (specify) : _____
___ Cannot be determined (explain) : _____

+Nodal Site(s) with Tumor (select all that apply)
___ Right pelvic: _____
___ Left pelvic: _____
___ Pelvic, NOS: _____
___ Right para-aortic: _____
___ Left para-aortic: _____
___ Para-aortic, NOS: _____
___ Other (specify): _____
___ Cannot be determined: _____
___ Other (specify): _____
___ Cannot be determined (explain): _____

Number of Lymph Nodes Examined
___ Exact number (specify): _____
___ At least (specify): _____
___ Other (specify): _____
___ Cannot be determined (explain): _____

+Nodal Site(s) Examined (select all that apply)
___ Right pelvic: _____
___ Left pelvic: _____
___ Pelvic, NOS: _____
___ Right para-aortic: _____
___ Left para-aortic: _____
___ Para-aortic, NOS: _____
___ Other (specify): _____
___ Cannot be determined: _____

+Regional Lymph Node Comment: _____

DISTANT METASTASIS

Distant Site(s) Involved, if applicable (select all that apply)
___ Not applicable
___ Lung: _____
___ Liver: _____
___ Bone: _____
___ Other (specify): _____
___ Cannot be determined

PATHOLOGIC STAGE CLASSIFICATION (pTNM, AJCC 8th ed.) (Note C)
Reporting of pT, pN, and (when applicable) pM categories is based on information available to the pathologist at the time the report is issued. As per the AJCC (Chapter 1, 8th Ed.) it is the managing physician's responsibility to establish the final pathologic stage based upon all pertinent information, including but potentially not limited to this pathology report.

TNM Descriptors (select all that apply)
___ Not applicable: _____
___ r (recurrent)
___ y (post-treatment)

pT Category

___ For All Sarcomas Excluding Adenosarcoma (including Leiomyosarcoma, Endometrial Stromal Sarcoma, and Undifferentiated Endometrial Sarcoma / Uterine Sarcoma).

pT Category

___ pT not assigned (cannot be determined based on available pathological information)
___ pT0: No evidence of primary tumor
pT1: Tumor limited to the uterus
___ pT1a: Tumor 5 cm or less in greatest dimension
___ pT1b: Tumor more than 5 cm
___ pT1 (subcategory cannot be determined)
pT2: Tumor extends beyond the uterus, within the pelvis
___ pT2a: Tumor involves adnexa
___ pT2b: Tumor involves other pelvic tissues
___ pT2 (subcategory cannot be determined)
pT3: Tumor infiltrates abdominal tissues
___ pT3a: Tumor infiltrates abdominal tissues in one site
___ pT3b: Tumor infiltrates abdominal tissues in more than one site
___ pT3 (subcategory cannot be determined)
___ pT4: Tumor invades bladder or rectum

___ For Adenosarcoma

pT Category

___ pT not assigned (cannot be determined based on available pathological information)
___ pT0: No evidence of primary tumor
pT1: Tumor limited to the uterus
___ pT1a: Tumor limited to the endometrium / endocervix
___ pT1b: Tumor invades to less than half of the myometrium
___ pT1c: Tumor invades one half or more of the myometrium
___ pT1 (subcategory cannot be determined)
pT2: Tumor extends beyond the uterus, within the pelvis
___ pT2a: Tumor involves adnexa
___ pT2b: Tumor involves other pelvic tissues
___ pT2 (subcategory cannot be determined)
pT3: Tumor infiltrates abdominal tissues
___ pT3a: Tumor infiltrates abdominal tissues in one site
___ pT3b: Tumor infiltrates abdominal tissues in more than one site
___ pT3 (subcategory cannot be determined)
___ pT4: Tumor invades bladder or rectum

pN Category

___ pN not assigned (no nodes submitted or found)
___ pN not assigned (cannot be determined based on available pathological information)
___ pN0: No regional lymph node metastasis
___ pN0(i+): Isolated tumor cells in regional lymph node(s) no greater than 0.2 mm
___ pN1: Regional lymph node metastasis

pM Category (required only if confirmed pathologically)

___ Not applicable - pM cannot be determined from the submitted specimen(s)
___ pM1: Distant metastasis (excluding adnexa, pelvic, abdominal tissues, and regional lymph nodes)

FIGO STAGE

+FIGO Stage (2018 FIGO Cancer Report) for All Sarcomas Except Adenosarcoma[#]

[#] Including leiomyosarcoma, endometrial stromal sarcoma, and undifferentiated endometrial sarcoma / uterine sarcoma

___ I: Tumor limited to uterus
___ IA: Less than or equal to 5 cm
___ IB: More than 5 cm
___ II: Tumor extends beyond the uterus, within the pelvis
___ IIA: Adnexal involvement
___ IIB: Involvement of other pelvic tissues
___ III: Tumor invades abdominal tissues (not just protruding into the abdomen)
___ IIIA: One site
___ IIIB: More than one site
___ IIIC: Metastasis to pelvic and / or para-aortic lymph nodes
___ IV: Tumor invades bladder and / or rectum and / or distant metastasis
___ IVA: Tumor invades bladder and / or rectal mucosa
___ IVB: Distant metastasis

+FIGO Stage (2018 FIGO Cancer Report) for Adenosarcoma

___ I: Tumor limited to uterus
___ IA: Tumor limited to endometrium / endocervix with no myometrial invasion
___ IB: Less than or equal to half myometrial invasion
___ IC: More than half myometrial invasion
___ II: Tumor extends beyond the uterus, within the pelvis
___ IIA: Adnexal involvement
___ IIB: Tumor extends to extrauterine pelvic tissue
___ III: Tumor invades abdominal tissues (not just protruding into the abdomen)
___ IIIA: One site
___ IIIB: More than one site
___ IIIC: Metastasis to pelvic and / or para-aortic lymph nodes
___ IV: Tumor invades bladder and / or rectum and / or distant metastasis
___ IVA: Tumor invades bladder and / or rectal mucosa
___ IVB: Distant metastasis

SPECIAL STUDIES

+Ancillary Studies

___ Specify: _____
___ Not performed

COMMENTS

Comment(s): _____

Explanatory Notes

A. Histologic Type

Carcinosarcoma
Carcinosarcoma (malignant mixed Müllerian tumor) is excluded from the uterine sarcoma diagnostic category as it is considered in tumors of the endometrial epithelium.

Adenosarcoma[1,2,3,4,5,6]
Adenosarcoma is a biphasic neoplasm composed of a benign epithelial component and a malignant stromal component. Classically, the tumor has phyllodes (leaf like) architecture, cleft-like or dilated glands that are lined by benign endometrial or ciliated epithelium and surrounded by a proliferative stroma, which is typically hypercellular relative to nearby benign tissue. Stromal proliferation and atypia are present but may be minimal. Stromal mitotic activity can be minimal or even absent. The epithelial component may show some cytological atypia and often displays metaplastic changes. The sarcomatous component is often of the homologous type, but rhabdomyosarcomatous differentiation is possible and rarely there is sex cord differentiation. There may be transformation to high-grade sarcoma. There may be sarcomatous overgrowth, defined as the presence of pure sarcoma, usually high grade and without an epithelial component, occupying at least 25% of the tumor. Immunohistochemically, the tumors are often positive for CD10, ER, and PR, although these are often negative in sarcomatous overgrowth. The stroma in conventional adenosarcoma is p53 “wild-type” and exhibits a low MIB1 proliferation index. Thus, the immunophenotype resembles that of low-grade endometrial stromal sarcoma. Smooth muscle actin and desmin may also be positive. In areas of high-grade sarcoma and of sarcomatous overgrowth, the mesenchymal component exhibits a higher MIB1 proliferation index and may be p53 positive/aberrant.

Endometrial Stromal Sarcoma
Low-grade endometrial stromal sarcoma (LG-ESS)[7,8,9,10] shows proliferative-phase endometrial stromal-type tumor cells infiltrating the myometrium with or without lymphovascular invasion. About 60% of LG-ESS have genetic fusions with JAZF1-SUZ12 being most common, followed by JAZF1-PHF1, EPC1-PHF1, and MEAF6-PHF1. Tumors usually show diffuse strong expression of CD10, IFITM1, ER, and PR, with focal cyclin D1 positivity.

High-grade ESS (HG-ESS)[8,9,10] is malignant endometrial stromal tumor with uniform high-grade round and/or spindle morphology. A low-grade component may be present. They usually show lymphovascular invasion, brisk mitotic activity, and necrosis. Invasion may be expansile, permeative, or infiltrative in pattern. Tumors harbor YWHAE-NUTM2A/B fusions, ZC3H7B-BCOR fusions, or BCOR ITD (internal tandem duplications). For a diagnosis of HG-ESS it is essential to see a tumor with monomorphic high-grade round and/or spindle cells, brisk mitotic activity, cyclin D1 and BCOR immunohistochemical positivity if associated withYWHAE-NUTM2A/B, ZC3H7B-BCOR fusion, BCOR ITD or a low-grade endometrial stromal component (if HG-ESS is NOS). The ZC3H7B-BCOR variant often mimics myxoid leiomyosarcoma but usually has more uniform nuclei and contains more collagen bands; BCOR molecular analysis will usually identify this variant.

Leiomyosarcoma[11,12,13,14,15,16]
Leiomyosarcoma is the most common uterine sarcoma (~40–50%) and patients are generally > 50 years of age. Conventional uterine LMS is a cellular tumor composed of fascicles of spindle-shaped cells exhibiting smooth muscle differentiation with moderate to severe pleomorphism. Two of the following three features: tumor cell necrosis, marked cytological atypia, and ≥ 4 mitoses/mm^2 (equal to or greater than 10 mitoses/10 HPF of 0.55 mm in diameter and 0.24 mm2 in area) are required to make a diagnosis of spindle

leiomyosarcoma. Tumor cell necrosis is characterized by an abrupt transition from viable to non-viable tumor cells. Epithelioid leiomyosarcoma (E-LMS) is composed predominantly (> 50%) of round or polygonal cells with eosinophilic to clear cytoplasm exhibiting nested, plexiform, corded, nodular, or diffuse growth patterns. Focally, cells with rhabdoid morphology or cells mimicking signet-ring cells may be present. Pseudo-glandular spaces may be seen. Tumors may occasionally be extensively hyalinized. Diagnostic criteria include moderate to severe cytological atypia and/or tumor cell necrosis or ≥ 1.6 mitoses/mm^2 (equal to or greater than 4 mitoses/10 HPF of 0.55 mm in diameter and 0.24 mm^2 in area). Myxoid tumors contain abundant myxoid stroma and are often paucicellular with fewer mitoses. They may display vague fascicular or nodular growth. Extensive sampling may be required to identify regions diagnostic of malignancy. The presence of any degree of cytological atypia, tumor cell necrosis, or > 0.4 mitoses/mm^2 (equating to > 1 mitosis/10 HPF of 0.55 mm in diameter and 0.24 mm^2 in area) is considered sufficient for a diagnosis of myxoid leiomyosarcoma. In LMS, tumor cells express h-caldesmon (more specific), desmin, and SMA, but expression may be weak and/or patchy if the tumor is poorly differentiated or myxoid. It is common for tumors to be positive for CD10, EMA, and cytokeratin. EMA and cytokeratin positivity is more frequent in epithelioid tumors. Spindle cell leiomyosarcomas often express ER and PR; p16 and/or p53 overexpression is also common.

Undifferentiated Uterine/Endometrial Sarcoma[17]

Undifferentiated uterine/endometrial sarcoma is a high-grade sarcoma that lacks specific differentiation and due to molecular analysis, is a shrinking category. Adequate sampling is important to exclude poorly differentiated carcinoma, carcinosarcoma, HGESS, and sarcomatous overgrowth in adenosarcoma before rendering this diagnosis. Histopathologically, these tumors show marked cellular pleomorphism and abundant mitotic activity with atypical forms. They lack the typical infiltrative growth pattern and vascularity of low-grade ESS and displace the myometrium. They often resemble the sarcomatous component of a carcinosarcoma. These sarcomas are most often aneuploid and are negative for ER and PgR. Immunohistochemistry for diagnosis of ZC3H7B-BCOR, YWHAE-NUTM2 (FAM22), and BCOR ITD high-grade endometrial stromal sarcomas and NTRK sarcomas is required and employment of molecular tests to exclude fusion genes associated with other sarcoma types are desirable before making a diagnosis of undifferentiated sarcoma.[17]

Other Histologic Types

Other differential diagnostic considerations included in spindle/sarcomatous lesions primary to the uterus include perivascular epithelioid cell tumor (PEComa) and rhabdomyosarcoma. PEComa belongs to a group of tumors characterized by both melanocytic and smooth muscle differentiation, and should be recognized separately from smooth muscle tumors. Conventional PEComas are composed of epithelioid and/or spindled cells with clear to eosinophilic granular cytoplasm. Conventional PEComas variably express HMB45, melan-A, and smooth muscle markers (SMA, desmin, and h-caldesmon). HMB45 is most sensitive, being positive in nearly all tumors, whereas melan-A is more specific, being positive (sometimes only focally) in at least half of the tumors. Cathepsin K is positive in essentially all tumors. TFE3 translocation–associated PEComas are diffusely positive for TFE3. It has been proposed that the benign category of PEComa be eliminated and that the tumor be classified as malignant PEComa if there are three or more of the following features: ≥ 5 cm, high nuclear grade, mitotic count of > 1 mitosis/50 mm^2, necrosis, vascular invasion. If there are less than 3 features it is considered to be of uncertain malignant potential[18,19,20] Rhabdomyosarcoma is rare but is the most common uterine heterologous sarcoma. Pleomorphic and embryonal subtypes are most frequent, while the alveolar and spindled variants are extremely rare. Rhabdomyosarcomas are usually positive for desmin, muscle-specific actin, myogenin, Myo D1, and myoglobin, and negative for smooth muscle actin. Pleomorphic and alveolar subtypes have a worse prognosis than the embryonal subtype.[21,22]

Uterine inflammatory myofibroblastic tumors (IMT) are rare and while the majority are benign, a minority may have an aggressive course. Necrosis, tumour size > 7 cm, moderate to severe atypia, high mitotic activity, and lymphovascular invasion have been associated with aggressive course. ~95% of IMTs are positive for ALK by immunohistochemistry typically correlating with alterations of the ALK gene rearrangements with IGFBP5, THBS1, and TIMP3 being common fusion partners.[23]

SMARCA4 deficient uterine sarcoma (SDUS) is a recently described entity that may mimic adenosarcoma by protruding from the cervix, forming leaf-like architecture and entrapping benign glands in an expanded, malignant stroma that may exhibit hyalinization.[24] These occur in a younger age group (median 42 years), present at advanced stage, are aggressive and uniformly fatal. The tumor cells have a monotonous uniformity without marked size or shape variation and are loosely cohesive with frequent rhabdoid morphology. They are negative for pankeratin, CAM5.2, PAX8, S100, EMA (rare cells may be positive), CD10, ER, PR, claudin-4, SOX10, S100, SMA and desmin. They are positive for cyclin D1 (though often patchy), show intact mismatch repair proteins, are microsatellite stable, and have a loss of SMARCA4. These tumors have inactivated SWI/SNF genes (SMARCA4 or SMARCB1) and rare patients may harbor germline mutations for loss of function mutations of SMARCA4.

NTRK-rearranged spindle cell neoplasm is a low-grade spindle cell sarcoma with NTRK gene rearrangements. These are predominantly located in the cervix or lower uterine segment. The spindle cells express S100, CD34, TRK, and cyclin D1, and are negative for CD10, SMA, desmin, BCOR, ER, or PR. NTRK rearrangement is diagnostic. Some are associated with metastasis and an aggressive clinical course.[25]

Uterine tumor resembling ovarian sex cord tumor should be staged as a uterine sarcoma. Other malignant sarcomas that may also occur in the uterine corpus include angiosarcoma, liposarcoma, and alveolar soft part sarcoma.[26]

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B. Lymphovascular Invasion

LVI is of prognostic value in uterine sarcomas.[1,2] At times, it may be difficult to evaluate a specimen for vascular/lymphatic vessel invasion, as in cases with crush artifact or suboptimal fixation. In these cases, it can be categorized as “cannot be determined'. At other times, it may be difficult to be definitive whether vascular/lymphatic vessel invasion is present. This can include cases where retraction artifact or artifactual transfer of tumor cells is a consideration. In other cases, foci may be suspicious but not definitive for invasion. All of these situations can be categorized as “equivocal for invasion”. A study shows that LVI in LGESS are fundamentally different from LVI seen in HG sarcomas. LGESS had cohesive intravascular tumor foci with direct communication from the main tumor and attached to the vessel wall. In contrast, intravascular tumor foci in HGS were composed of discohesive cells clusters, lacking the features seen in LGESS. They propose that in most LGESSs, LVI represents vascular intrusion, and does not have an adverse outcome as is seen in typical LVI as seen in HG sarcomas. In cases where one cannot be definitive, a qualifying note explaining the interpretive difficulty and the extent of possible involvement is recommended, since it may help to direct medical management.

References

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2. Roma AA, Barbuto DA, Samimi SA, Stolnicu S, Alvarado-Cabrero I, Chanona-Vilchis J, Aguilera-Barrantes I et al. Hum Pathol. 2015; 46(11):1712-21.

C. Pathologic Stage Classification

The TNM staging system for uterine sarcoma endorsed by the American Joint Committee on Cancer (AJCC) and the parallel system formulated by the International Federation of Gynecology and Obstetrics (FIGO) are recommended, as shown below.[1,2]

According to AJCC/International Union Against Cancer (UICC) convention, the designation "T" refers to a primary tumor that has not been previously treated. The symbol "p" refers to the pathologic classification of the TNM, as opposed to the clinical classification, and is based on gross and microscopic examination. 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. Single tumor cells or small clusters of cells not more than 0.2 mm in greatest diameter are classified as isolated tumor cells. These may be detected by routine histology or by immunohistochemical methods and are designated N0(i+). 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.

Pathologic staging is usually performed after surgical resection of the primary tumor. Pathologic staging depends on pathologic documentation of the anatomic extent of disease, whether or not the primary tumor has been completely removed. If a biopsied tumor is not resected for any reason (eg, when technically infeasible) and if the highest T and N categories or the M1 category of the tumor can be confirmed microscopically, the criteria for pathologic classification and staging have been satisfied without total removal of the primary cancer.

TNM Descriptors

For identification of special cases of TNM or pTNM classifications, "y," "r," and "a" prefixes are used. Although they do not affect the stage grouping, they indicate cases needing separate analysis.

The "y" prefix indicates those cases in which classification is performed during or after initial multimodality therapy (ie, neoadjuvant chemotherapy, radiation therapy, or both chemotherapy and radiation therapy). The cTNM or pTNM category is identified by a "y" prefix. The ycTNM or ypTNM categorizes the extent of tumor actually present at the time of that examination. The "y" categorization is not an estimate of tumor before multimodality therapy (ie, before initiation of neoadjuvant therapy).

The "r" prefix indicates a recurrent tumor when staged after a documented disease-free interval and is identified by the "r" prefix: rTNM.

The "a" prefix designates the stage determined at autopsy: aTNM.

Additional Descriptors

Residual Tumor (R)

Tumor remaining in a patient after therapy with curative intent (eg, surgical resection for cure) is categorized by a system known as R classification, shown below.

RX	Presence of residual tumor cannot be assessed
R0	No residual tumor
R1	Microscopic residual tumor

R2	Macroscopic residual tumor

For the surgeon, the R classification may be useful to indicate the known or assumed status of the completeness of a surgical excision. For the pathologist, the R classification is relevant to the status of the margins of a surgical resection specimen. That is, tumor involving the resection margin on pathologic examination may be assumed to correspond to residual tumor in the patient and may be classified as macroscopic or microscopic according to the findings at the specimen margin(s).

T Category Considerations

It is important to note that in uterine sarcoma, as in cancer of other organs, the validity of T stage depends upon the adequacy and completeness of the surgical staging.

TNM Classification and FIGO Staging System for Leiomyosarcoma, Endometrial Stromal Sarcoma, and Undifferentiated Uterine Sarcoma

TNM Category	FIGO Stage	Definition
Primary Tumor		
pTX	[--]:	Primary tumor cannot be assessed
pT0	[--]:	No evidence of primary tumor
pT1	[I]:	Tumor is limited to the uterus
pT1a	[IA]:	Tumor is 5 cm or less (≤5 cm) in greatest dimension
pT1b	[IB]:	Tumor is greater than 5 cm (>5 cm) in greatest dimension
pT2	[II]:	Tumor extends beyond the uterus, but is within the pelvis (tumor extends to extrauterine pelvic tissue)
pT2a	[IIA]:	Tumor involves the adnexa
pT2b	[IIB]:	Tumor involves other pelvic tissue
pT3	[III]:	Tumor invades abdominal tissues (not just protruding into the abdomen)
pT3a	[IIIA]:	Tumor invades abdominal tissues at 1site
pT3b	[IIIB]:	Tumor invades abdominal tissues at more than 1 site
pT4	[IVA]:	Tumor invades bladder mucosa and/or rectum

Regional Lymph Nodes (pN)#

pNX:		Cannot be assessed
pN0:		No regional lymph node metastasis
pN0(i+):		Isolated tumor cells in regional lymph node(s) no greater than 0.2 mm
pN1	[IIIC]:	Regional lymph node metastasis to pelvic lymph nodes

#Regional lymph nodes include the pelvic, obturator, internal iliac (hypogastric), external iliac, common iliac, para-aortic, presacral, and parametrial lymph nodes.

Distant Metastasis (pM)

pM0		No distant metastasis (no pathologic M0; use clinical M to complete stage group)
pM1	[IVB]:	Distant metastasis (excluding adnexa, pelvic and abdominal tissues)

Adenosarcoma

TNM Category	FIGO Stage	Definition
Primary Tumor		
pTX	[--]:	Primary tumor cannot be assessed
pT0	[--]:	No evidence of primary tumor
pT1	[I]:	Tumor is limited to the uterus
pT1a	[IA]:	Tumor is limited to the endometrium/endocervix without myometrial invasion
pT1b	[IB]:	Tumor invades less than or equal to 50% (≤50%) total myometrial thickness
pT1c	[IC]:	Tumor invades greater than 50% (>50%) total myometrial thickness
pT2	[II]:	Tumor extends beyond the uterus, but is within the pelvis (tumor extends to extrauterine pelvic tissue)
pT2a	[IIA]:	Tumor involves the adnexa
pT2b	[IIB]:	Tumor involves other pelvic tissue
pT3	[III]:	Tumor invades abdominal tissues (not just protruding into the abdomen)
pT3a	[IIIA]:	Tumor invades abdominal tissues at one site
pT3b	[IIIB]:	Tumor invades abdominal tissues at more than one site
pT4	[IVA]:	Tumor invades bladder mucosa and/or rectum

Regional Lymph Nodes (pN)[#]

pNX:		Cannot be assessed
pN0:		No regional lymph node metastasis
pN1	[IIIC]:	Regional lymph node metastasis to pelvic lymph nodes

[#]Regional lymph nodes include the pelvic, obturator, internal iliac (hypogastric), external iliac, common iliac, para-aortic, presacral, and parametrial lymph nodes.

Distant Metastasis (pM)

pM0:		No distant metastasis (no pathologic M0; use clinical M to complete stage group)
pM1	[IVB]:	Distant metastasis (excluding adnexa, pelvic and abdominal tissues)

References

1. Amin MB, Edge SB, Greene FL, et al., eds. AJCC Cancer Staging Manual. 8th ed. New York, NY: Springer; 2017.
2. Mbatani N, Olawaiye AB, Prat J: Uterine sarcomas FIGO cancer report 2018. Int J Gynecol Obstet 2018; 143 (Suppl. 2): 51–58