COLLEGE of AMERICAN PATHOLOGISTS

# Protocol for the Examination of Specimens From Patients With Primary Carcinoma of the Vagina

**Version:** Vagina 4.1.0.0 **Protocol Posting Date:** August 2018
Includes pTNM requirements from the 8th Edition, AJCC Staging Manual, and 2015 FIGO Cancer Report

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

| Procedure | Description |
|---|---|
| Resection | Includes vaginectomy |
| **Tumor Type** | **Description** |
| Carcinoma | Includes squamous cell carcinoma, adenocarcinoma and variants, carcinosarcoma, neuroendocrine carcinoma, and mixed epithelial – neuroendocrine tumors |

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

| Procedure |
|---|
| Biopsy |
| Primary resection specimen with no residual cancer (eg, following neoadjuvant therapy) |
| Cytologic specimens |

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

| Tumor Type |
|---|
| Lymphoma (consider the Hodgkin or non-Hodgkin Lymphoma protocols) |
| Sarcoma (consider the Soft Tissue protocol) |

**Authors**
Saeid Movahedi-Lankarani, MD*; Uma Krishnamurti, MD, PhD*; Debra A. Bell, MD; George G. Birdsong, MD; Charles V. Biscotti, MD; Christopher N. Chapman Jr, MD; Dina H. Kandil, MD; Veronica Klepeis, MD, PhD; Anthony G. Montag, MD; Christopher N. Otis, MD

With guidance from the CAP Cancer and CAP Pathology Electronic Reporting Committees.

** Denotes primary authors. All other contributing authors are listed alphabetically.*

**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.

**CAP Laboratory Accreditation Program Protocol Required Use Date: April 2019**

## CAP Vagina Protocol Summary of Changes

**Version 4.1.0.0**
**The following data elements were modified:**
**Regional Lymph Nodes** - Revised the format to clarify reporting involved and uninvolved nodes

# Surgical Pathology Cancer Case Summary

Protocol posting date: August 2018

**VAGINA: Biopsy**

**Note: This case summary is recommended for reporting biopsy specimens, but is not required for accreditation purposes.**

**Select a single response unless otherwise indicated.**

**+ Procedure (Notes A through C)**
+ ___ Incisional biopsy
+ ___ Other (specify): _____
+ ___ Not specified

**+ Tumor Site**
+ ___ Vagina, upper third
+ ___ Vagina, middle third
+ ___ Vagina, lower third
+ ___ Not specified

**+ Histologic Type (Note D)**
+ ___ Squamous cell carcinoma, NOS
+ ___ Squamous cell carcinoma, keratinizing
+ ___ Squamous cell carcinoma, nonkeratinizing
+ ___ Squamous cell carcinoma, basaloid
+ ___ Squamous cell carcinoma, verrucous
+ ___ Squamous cell carcinoma, warty
+ ___ Squamous cell carcinoma, papillary
+ ___ Adenocarcinoma, NOS
+ ___ Mucinous carcinoma, NOS
+ ___ Endometrioid carcinoma
+ ___ Clear cell carcinoma
+ ___ Mesonephric carcinoma
+ ___ Adenosquamous carcinoma
+ ___ Adenoid basal carcinoma
+ ___ Small cell neuroendocrine carcinoma
+ ___ Large cell neuroendocrine carcinoma
+ ___ Undifferentiated carcinoma
+ ___ Carcinosarcoma
+ ___ Other histologic type not listed (specify): _____
+ ___ Carcinoma, type cannot be determined

*Note: Microinvasive/superficial invasive carcinoma is not currently a recognized entity in the vagina, and thus the term is not used.*

**+ Histologic Grade (Note E)**
+ ___ G1: Well differentiated
+ ___ G2: Moderately differentiated
+ ___ G3: Poorly differentiated
+ ___ G4: Undifferentiated
+ ___ Other (specify): _____
+ ___ GX: Cannot be assessed
+ ___ Not applicable

+ Data elements preceded by this symbol are not required for accreditation purposes. These optional elements may be clinically important but are not yet validated or regularly used in patient management.

**+ Tumor Extension**
+ ___ Stromal invasion
+ ___ Muscle invasion
+ ___ Cannot be assessed

**+ Margins**
+ ___ Not applicable
+ ___ Cannot be assessed
+ ___ Uninvolved by tumor
+ ___ Involved by tumor
    + Specify site: _____

**+ Additional Pathologic Findings (select all that apply) (Note G)**
+ ___ None identified
+ ___ High-grade squamous intraepithelial neoplasia (VAIN 2-3)
+ ___ Low-grade squamous intraepithelial neoplasia (VAIN 1)
+ ___ Condyloma accuminatum
+ ___ Adenocarcinoma in situ (AIS)
+ ___ Atypical adenosis
+ ___ Other (specify): _____

**+ Comment(s)**

# Surgical Pathology Cancer Case Summary

Protocol posting date: August 2018

**VAGINA: Resection**

**Select a single response unless otherwise indicated.**

**Procedure (Notes A through C)**
___ Excision
___ Partial vaginectomy
___ Radical vaginectomy
___ Other (specify): _____
___ Not specified

**Tumor Site (select all that apply)**
___ Vagina, upper third
___ Vagina, middle third
___ Vagina, lower third
___ Vagina, further delineation not specified

**Tumor Size**
Greatest dimension (centimeters): ___ cm
+ Additional dimensions (centimeters): ___ x ___ cm
___ Cannot be determined (explain): _____

**Histologic Type (Note D)**
___ Squamous cell carcinoma, NOS
___ Squamous cell carcinoma, keratinizing
___ Squamous cell carcinoma, nonkeratinizing
___ Squamous cell carcinoma, basaloid
___ Squamous cell carcinoma, verrucous
___ Squamous cell carcinoma, warty
___ Squamous cell carcinoma, papillary
___ Adenocarcinoma, NOS
___ Mucinous carcinoma, NOS
___ Endometrioid carcinoma
___ Clear cell carcinoma
___ Mesonephric carcinoma
___ Adenosquamous carcinoma
___ Adenoid basal carcinoma
___ Small cell neuroendocrine carcinoma
___ Large cell neuroendocrine carcinoma
___ Undifferentiated carcinoma
___ Carcinosarcoma
___ Other histologic type not listed (specify): _____
___ Carcinoma, type cannot be determined

*Note: Microinvasive/superficial invasive carcinoma is not currently a recognized entity in the vagina, and thus the term is not used.*

**Histologic Grade (Note E)**
___ G1: Well differentiated
___ G2: Moderately differentiated
___ G3: Poorly differentiated
___ G4: Undifferentiated

+ Data elements preceded by this symbol are not required for accreditation purposes. These optional elements may be clinically important but are not yet validated or regularly used in patient management.

___ Other (specify): _____
___ GX: Cannot be assessed
___ Not applicable

**Other Tissue/ Organ Involvement (select all that apply)**
*Note: Any organ not selected is either not involved or was not submitted.*
___ Not applicable
___ Not identified
___ Paravaginal tissues
___ Pelvic sidewall
___ Vagina, lower third
___ Bladder mucosa
___ Rectal mucosa
___ Other organs/tissue (specify): _____
___ Cannot be determined (explain):_____

**Margins**[#]

Peripheral Margin (select all that apply)
___ Cannot be assessed (explain): _____
___ Uninvolved by invasive carcinoma
+ Distance of invasive carcinoma from margin (millimeters): ___ mm
+ Specify location: _____
___ Involved by invasive carcinoma
Specify location(s), if possible: _____
___ Uninvolved by intraepithelial neoplasia
___ Involved by high-grade squamous intraepithelial lesion (VAIN 2-3)
+ Specify location(s): _____

Deep Margin (select all that apply)
___ Cannot be assessed (explain): _____
___ Uninvolved by invasive carcinoma
+ Distance of invasive carcinoma from margin (millimeters): ___ mm
+ Specify location: _____
___ Involved by invasive carcinoma
Specify location(s), if possible: _____
___ Uninvolved by intraepithelial neoplasia
___ Involved by high-grade squamous intraepithelial lesion (VAIN 2-3)
+ Specify location(s): _____

[#] *Reporting high-grade squamous intraepithelial lesion (VAIN 2-3) is not required if margin is involved by invasive carcinoma.*

**Lymphovascular Invasion**
___ Not identified
___ Present
___ Cannot be determined (explain): _____

**Regional Lymph Nodes**
*Note: For upper two-thirds of the vagina, the following are considered regional lymph nodes: pelvic, parametrial, obturator, internal iliac (hypogastric), external iliac, common iliac, sacral, presacral, and para-aortic. For lower third of the vagina, the following are considered regional lymph nodes: inguinal and femoral. Any involved nonregional 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+).*

___ No lymph nodes submitted or found

*Lymph Node Examination (required only if lymph nodes are present in the specimen)*

___ All lymph nodes negative for tumor cells

___ Positive for tumor cells (select all that apply)
Number of Nodes with Metastasis (excludes isolated tumor cells): _____
Number of Nodes with Isolated Tumor Cells (0.2 mm or less) (if applicable): _____
Number cannot be determined (explain): _____

*Note: Reporting the number of lymph nodes with isolated tumor cells is required only in the absence of metastasis greater than 0.2 mm in other lymph nodes.*

+ Nodal Site(s) with Tumor Cells (specify): _____

+ Additional Lymph Node Findings (select all that apply)
+ ___ None identified
+ ___ Extranodal extension
+ ___ Fixed/ulcerated nodes
+ ___ Other (specify): _____
+ ___ Cannot be determined

Number of Lymph Nodes Examined: _____
___ Number cannot be determined (explain): _____
+ Specify Site(s): _____

**Pathologic Stage Classification (pTNM, AJCC 8th Edition) (Note F)**

*Note: Reporting of pT, pN, and (when applicable) pM categories is based on information available to the pathologist at the time the report is issued. Only the applicable T, N, or M category is required for reporting; their definitions need not be included in the report. The categories (with modifiers when applicable) can be listed on 1 line or more than 1 line.*

TNM Descriptors (required only if applicable) (select all that apply)
___ m (multiple primary tumors)
___ r (recurrent)
___ y (posttreatment)

Primary Tumor (pT)
___ pTX: Primary tumor cannot be assessed
___ pT0: No evidence of primary tumor
___ pT1: Tumor confined to the vagina
___ pT1a: Tumor confined to the vagina, measuring ≤2.0 cm
___ pT1b: Tumor confined to the vagina, measuring >2.0 cm
___ pT2: Tumor invading paravaginal tissues but not to pelvic sidewall
___ pT2a: Tumor invading paravaginal tissues but not to pelvic wall, measuring ≤2.0 cm
___ pT2b: Tumor invading paravaginal tissues but not to pelvic wall, measuring >2.0 cm
___ pT3: Tumor extending to the pelvic sidewall[#] and/or causing hydronephrosis or nonfunctioning kidney
___ pT4: Tumor invading the mucosa of the bladder or rectum and/or extending beyond the true pelvis (bullous edema is not sufficient evidence to classify a tumor as T4)

[#] *Pelvic sidewall is defined as the muscle, fascia, neurovascular structures, or skeletal portions of the bony pelvis. On rectal examination, there should be no cancer-free space between the tumor and pelvic sidewall. Tumor causing hydronephrosis or nonfunctioning kidney is an indirect indication of pelvic sidewall involvement.*

Regional Lymph Nodes (pN)
___ pNX: Regional lymph nodes 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: Pelvic or inguinal lymph node metastasis

Distant Metastasis (pM) (required only if confirmed pathologically in this case)
___ pM1: Distant metastasis
Specify site(s), if known: _____

+ FIGO Stage (2015 FIGO Cancer Report)
+ ___ I: Carcinoma is limited to the vaginal wall
+ ___ II: Carcinoma has involved the para-vaginal tissue but has not extended to the pelvic wall
+ ___ III: Carcinoma has extended to the pelvic wall and/or involving the lower third of the vagina and/or causing hydronephrosis or nonfunctioning kidney
+ ___ IV: Carcinoma has extended beyond the true pelvis or has involved the mucosa of the bladder or rectum (bullous edema as such does not permit a case to be allotted to stage IV)
+ ___ IVA: Tumor invades bladder and/or rectal mucosa and/or direct extension beyond the true pelvis
+ ___ IVB: Spread to distant organs

**+ Additional Pathologic Findings (select all that apply) (Note G)**
+ ___ None identified
+ ___ Low-grade squamous intraepithelial lesion (VAIN 1)
+ ___ High-grade squamous intraepithelial lesion (VAIN 2-3)
+ ___ Condyloma acuminatum
+ ___ Adenocarcinoma in situ (AIS)
+ ___ Atypical adenosis
+ ___ Other (specify): _____

**+ Comment(s)**

## Explanatory Notes

### A. Prenatal DES Exposure

Prenatal exposure to diethylstilbestrol (DES) or related synthetic drugs was relatively common in the United States and other countries until 1971, when its relation to clear cell adenocarcinomas of the vagina and cervix led to proscription of these drugs by the Food and Drug Administration. From the 1970s to the turn of the 21st century, most patients with clear cell adenocarcinoma of the vagina had a history of DES exposure.[1] As this cohort ages, the diagnosis has been less common, and most women with this diagnosis currently have no DES exposure history. Furthermore, it has been reported that these patients have significantly worse outcomes than do patients with history of DES exposure and patients with squamous cell carcinoma.[2] A bimodal age peak for DES-related carcinoma has, however, been recently reported, and therefore a history of this type of prenatal drug exposure should alert the pathologist to the possible presence of those tumors and associated lesions.[3,4]

Ectropion (erosion, eversion) of the cervix, which is characterized by the appearance of glandular (columnar) epithelium outside the external os of the cervix, is seen in approximately 90% of women exposed to DES in utero (but is often seen in nonexposed women as well). Approximately one-third of patients exposed to DES have 1 or more gross structural abnormalities of the cervix.[1,4]

The fallopian tubes are abnormal in some women exposed to DES in the form of hypoplasia or defects demonstrated on hysterosalpingographic examination.[4]

### B. Prior Tumors and Operations

A history of dysplasia, carcinoma in situ, or invasive carcinoma of the cervix, as well as knowledge of the tumor's microscopic features, may be essential in the determination whether a subsequent vaginal tumor is a recurrent or new tumor. Also, a history of a carcinoma higher in the female genital tract may influence the interpretation of a neoplasm that is detected in a specimen from the vagina. Prior pathology slides and reports should be obtained and reviewed if a review is deemed essential by the clinician or pathologist for optimal pathologic evaluation of the present specimen.

### C. Clinical Findings and DES Exposure

Naked-eye examination, colposcopy, and iodine staining of the cervix and vagina may disclose a variety of changes highly suspicious of prenatal DES exposure, such as cervical hypoplasia, pseudopolyp, or coxcomb deformity, and vaginal adenosis or ridge, any of which should alert the pathologist to look carefully for DES changes.[4]

### D. Histologic Type

The World Health Organization (WHO) classification and nomenclature of vaginal tumors is recommended because of its wide acceptance.[5] The most common subtype is squamous cell carcinoma. However, when such tumor simultaneously involves the cervix or the vulva and the vagina, the tumor is considered to originate from the cervix or vulva, with secondary extension to the vagina. Also, when an adenocarcinoma is present in the vagina, it is important to keep in mind that many of those tumors represent secondary involvement either by direct extension or metastases, more commonly from the endometrium, colorectal, ovary, vulva, urethra, and urinary bladder. Although not included in the current WHO classification, primary intestinal type adenocarcinoma has recently been described in the vagina.[6] These tumors usually arise in a background of benign adenomatous lesion. Awareness of this new subtype is necessary to avoid misdiagnosis of a metastatic colorectal adenocarcinoma.[6-8]

**WHO Classification[5]**
**Precancerous Lesions and Carcinomas of the Vagina (Modified)**

Epithelial Tumors
Squamous tumors and precursors

| | |
|---|---|
| Squamous intraepithelial lesions (SIL) | Vaginal intraepithelial neoplasia (VAIN) |
| Low-grade SIL (LSIL) | VAIN 1 |
| High-grade SIL (HSIL) | VAIN 2-3 |

Squamous cell carcinoma, not otherwise specified
- Keratinizing
- Nonkeratinizing
- Papillary
- Basaloid
- Verrucous
- Warty

Glandular tumors
- Clear cell carcinoma
- Endometrioid adenocarcinoma
- Mucinous adenocarcinoma
- Mesonephric adenocarcinoma

High-grade neuroendocrine carcinoma
- Small cell neuroendocrine carcinoma
- Large cell neuroendocrine carcinoma

Other epithelial tumors
- Adenosquamous carcinoma
- Adenoid basal carcinoma
- Undifferentiated carcinoma

**E. Histologic Grade**

No specific grading system for vaginal cancers is recommended. For the sake of uniformity, however, it is suggested that 3 grades be used, as shown below, with grades 1 to 3 assigned to carcinomas showing squamous or glandular differentiation.

| | |
|---|---|
| Grade X | Cannot be assessed |
| Grade 1 | Well differentiated |
| Grade 2 | Moderately differentiated |
| Grade 3 | Poorly differentiated |
| Grade 4 | Undifferentiated |

**F. Pathologic Stage Classification**

The TNM staging system for vaginal cancer endorsed by the American Joint Committee on Cancer (AJCC) and the International Union against Cancer (UICC),[12,13] and the parallel system formulated by the International Federation of Gynecology and Obstetrics (FIGO)[14] are recommended.

By AJCC/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, 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.

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 unfeasible) 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, the “m” suffix and “y,” “r,” and “a” prefixes are used. Although they do not affect the stage grouping, they indicate cases needing separate analysis.

The "m" suffix indicates the presence of multiple primary tumors in a single site and is recorded in parentheses: pT(m)NM.

The "y" prefix indicates those cases in which classification is performed during or following 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 prior to 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
Lymphovascular Invasion (LVI)
LVI indicates whether microscopic lymphovascular invasion is identified. LVI includes lymphatic invasion, vascular invasion, or lymphovascular invasion. By AJCC/UICC convention, LVI does not affect the T category indicating local extent of tumor unless specifically included in the definition of a T category.

N Category Considerations
Isolated tumor cells (ITCs) are single cells or small clusters of cells not more than 0.2 mm in greatest dimension. Lymph nodes or distant sites with ITCs found by either histologic examination (eg, immunohistochemical evaluation for cytokeratin) or nonmorphological techniques (eg, flow cytometry, DNA analysis, polymerase chain reaction [PCR] amplification of a specific tumor marker) should be so identified. There is currently no guidance in the literature as to how these patients should be coded; until more data are available, they should be coded as "N0(i+)" with a comment noting how the cells were identified.

**TNM and FIGO Staging Systems for Vaginal Carcinoma**

**Primary Tumor (T)**

| TNM Category | FIGO Stage | Definition |
|---|---|---|
| TX | (--) | Primary tumor cannot be assessed |
| T0 | (--) | No evidence of primary tumor |
| Tis | 0 | Carcinoma in situ |
| T1 | I | Tumor confined to vaginal wall |
| T2 | II | Tumor invades paravaginal tissues but not the pelvic sidewall[#] |

| | | |
|---|---|---|
| T3 | III | Tumor extends to pelvic sidewall# and/or causing hydronephrosis or nonfunctioning kidney |
| T4 | IVA | Tumor invades mucosa of bladder or rectum and/or extends beyond the true pelvis (bullous edema is not sufficient to classify a tumor as T4) |
| (M1) | IVB | Distant metastasis (excludes peritoneal metastasis) |

# Pelvic sidewall is defined as muscle, fascia, neurovascular structures, or skeletal portions of the bony pelvis. Tumor causing hydronephrosis or nonfunctioning kidney is an indirect indication of pelvic sidewall involvement.

**Regional Lymph Nodes (N): TNM**

NX Regional lymph nodes cannot be assessed
N0 No regional lymph node metastasis
N1 Pelvic or inguinal lymph node metastasis

**Distant Metastasis (M): TNM**

M0 No distant metastasis
M1 Distant metastasis

**G. Other Lesions**

Squamous dysplasia or carcinoma in situ, adenocarcinoma in situ, or atypical adenosis, particularly if such changes are at the resection margin, may increase the frequency of recurrent tumor. Also, few cases of primary invasive carcinoma of vagina have been reported to occur in association with severe vaginal prolapse.[9-11]

**References**


1. Herbst AL, Ulfelder H, Poskanzer DC. Adenocarcinoma of the vagina: association of maternal stilbestrol therapy with tumor appearance in young women. *N Engl J Med.* 1971;284:878-881.
2. Frank SJ, Deavers MT, Jhingran A, et al. Primary adenocarcinoma of the vagina not associated with diethylstilbestrol (DES) exposure. *Gynecol Oncol*. 2007;105:470-474.
3. Hanselaar A, van Loosbroek M, Schuurbiers O, et al. Clear cell adenocarcinoma of the vagina and cervix: an update of the central Netherlands registry showing twin age incidence peaks. *Cancer*. 1997;79:2229-2236.
4. Kaufman RH, Noller K, Adam E, et al. Upper genital tract abnormalities and pregnancy outcome in diethylstilbestrol-exposed progeny. *Am J Obstet Gynecol*. 1984;148:973-984.
5. Kurman RJ, Carcangiu ML, Harrington CS, Young RH, eds. *WHO Classification of Tumors of the Female Reproductive Organs.* Geneva, Switzerland: WHO Press; 2014. *World Health Organization Classification of Tumors.* 4th edition
6. Tjalma WA, Colpaert CG. Primary vaginal adenocarcinoma of intestinal type arising from a tubulovillous adenoma. *Int J Gynecol Cancer*. 2006;16:1461-1465.
7. Mudhar HS, Smith JH, Tidy J. Primary vaginal adenocarcinoma of intestinal type arising from an adenoma: case report and review of the literature*. Int J Gynecol Pathol.* 2001;20:204-209.
8. Ditto A, Martinelli F, Carcangiu ML, et al. Incidental diagnosis of primary vaginal adenocarcinoma of intestinal type: a case report and review of the literature. *Int J Gynecol Pathol.* 2007;26:490-493.
9. Iavazzo C, Vorgias G, Vecchini G, et al. Vaginal carcinoma in a completely prolapsed uterus: a case report. *Arch Gynecol Obstet*. 2007;275:503-505.
10. Batista TP, Morais JA, Reis TJ, et al. A rare case of invasive vaginal carcinoma associated with vaginal prolapse. *Arch Gynecol Obstet.* 2009;280(5):845-848.
11. Gupta N, Mittal S, Dalmia S, et al. A rare case of primary invasive carcinoma of vagina associated with irreducible third degree uterovaginal prolapse. *Arch Gynecol Obstet.* 2007; 276:563-4.
12. Amin MB, Edge SB, Greene FL, et al, eds. *AJCC Cancer Staging Manual.* 8th ed. New York, NY: Springer; 2017.
13. Brierley JD, Gospodarowicz M, Wittekind Ch, eds. *TNM Classification of Malignant Tumors.* 8th ed. Oxford, UK: Wiley; 2016.
14. Oncology FCoG. Current FIGO staging for cancer of the vagina, fallopian tube, ovary, and gestational trophoblastic neoplasia. *Int J Gynaecol Obstet.* 2009;105(1):3-4.