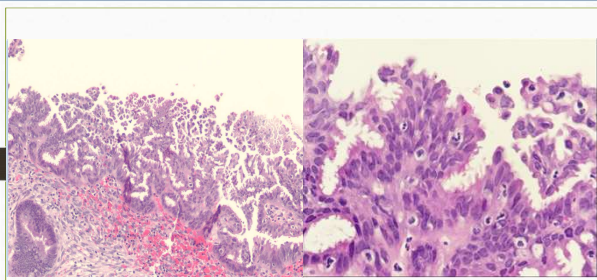
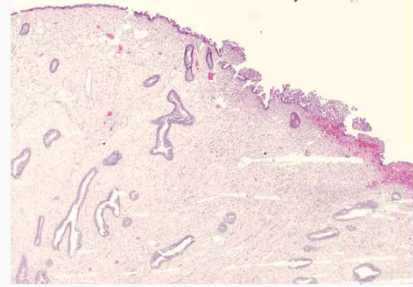


Case 2

- 56 y old women with vaginal bleeding,
- US endometrial thickness 4 mm.



What is your diagnosis

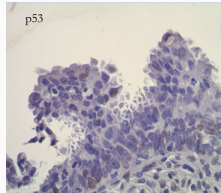
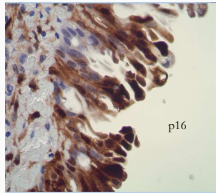
Papillary proliferation
of endometrium

EIN

EIC

Need immunos

Would you order immunos?



Papillary proliferation of endometrium

- Simple and complex papillary branching of endometrium without significant atypia
- Frequently involves polyp
- Epithelium involved with metaplasia
 - Mucinous
 - Ciliated
 - Tubal
 - Eosinophilic
 - Squamous

Papillary proliferation

Simple papillary proliferations

- Postmenopausal women
- Associated with polyp
- Non branching papillae lined by bland epithelium

Complex papillary proliferations

- Complex papillae with second and third-degree branching lined by bland epithelium

Immunohistochemistry

- Not always necessary (not always very helpful)
- MIB-1 **low**
- p53 **wild type**
- PTEN, ARIDA and PAX 2 **usually intact**
- P16 **positive and not helpful**
- ER **expressed**, PR **decreased expression**

Papillary Proliferation of the Endometrium
A Clinicopathologic Study of 59 Cases of Simple and Complex Papillae Without Cytologic Atypia

Pap at al. Am J Surg Pathol 2013;37:167-177

Papillary lesion with well-developed fibrovascular cores and with no cytologic atypia

Papillary proliferation of endometrium (PPE)

- Simple, non-branching or with occasional 2nd degree branching
- Frequent 2nd and 3rd degree branching, or extensive non-branching papillae involving a polyp
- With striking mucinous metaplasia

Simple PPE

If simple PPE is the only abnormal finding in hysterectomy, with no hyperplasia or carcinoma, it may be considered benign.

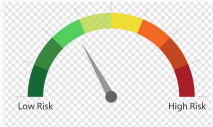
Complex PPE*

Small sample, lack clinical information, or clinical suspicion

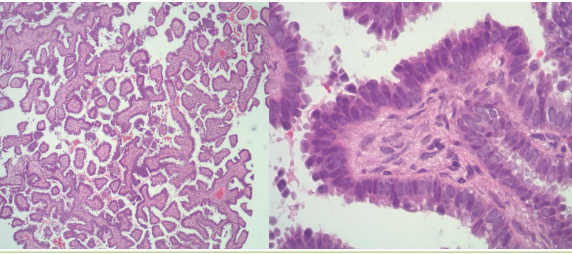
Papillary mucinous metaplasia or atypical mucinous glandular proliferations if papillae are architecturally complex.

Clinical assessment of endometrial thickness or polyps, consider uterine curettage.

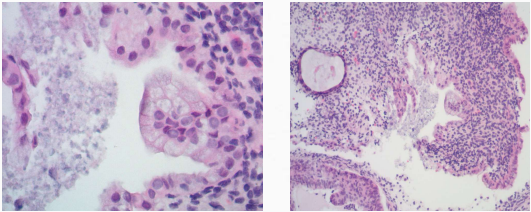
- MULTIFOCAL, EXTENSIVE OR MUCINOUS CHANGE**
- higher association with concurrent or subsequent atypical hyperplasia or low grade endometrioid carcinoma.

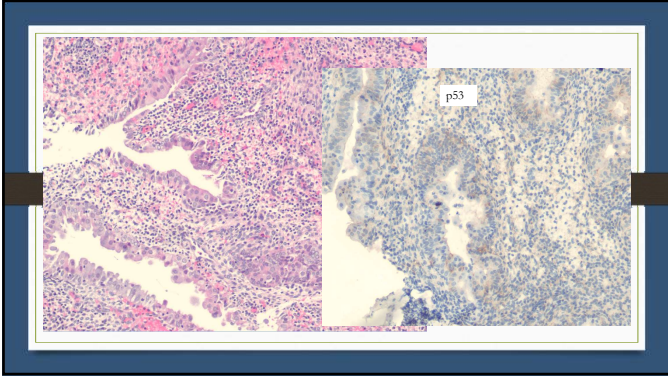


Focal distribution with complex branching



Focal distribution, no complex branching but with mucinous metaplasia





DDx

- Endometrial intraepithelial neoplasm (EIN)
- Endometrial intraepithelial carcinoma (EIC)
- Artefacts
- Reactive papillary changes with menstrual breakdown
- Reactive papillary and atypical changes due to progesterone treatment
- Benign endocervical tissue and microglandular hyperplasia

Case 1. Polyp with focal papillary surface change

Two histological images showing endometrial polypoid tissue. The left image shows a low-power view of the polypoid structure, and the right image shows a high-power view of the surface epithelium with focal papillary changes.

Your diagnosis

Papillary proliferation with mucinous metaplasia, follow up and clinical correlation

EIN

EIC

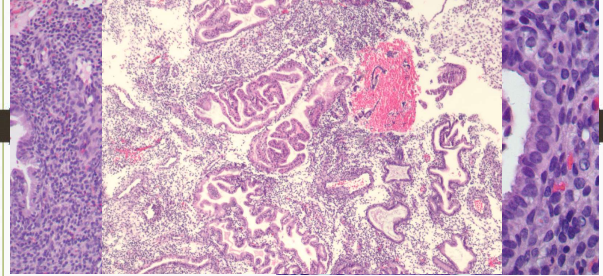
This is endocervix

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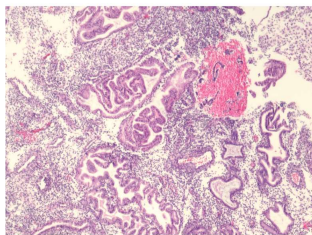
Papillary proliferation with mucinous metaplasia, follow up and clinical correlation

- What goes against EIC
 - No significant atypia
 - No prominent nucleoli,
 - No mitoses or apoptotic bodies
 - Mucinous metaplasia
 - P53 wild type

Case 2.



Your diagnosis



Benign simple papillary proliferation

EIN

EIC

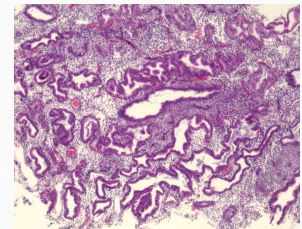
Pseudopapillary artefact, secretory endometrium

None of the above

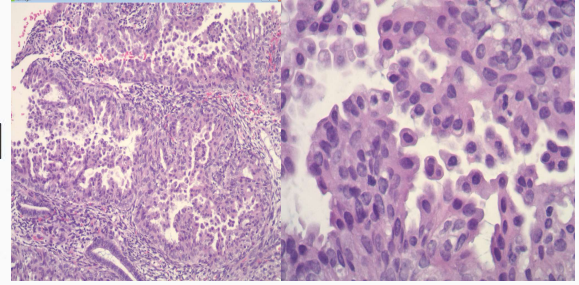
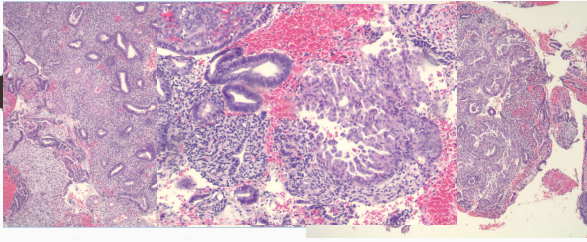
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Secretory endometrium with artefactual telescoping and pseudo-papillary artifact

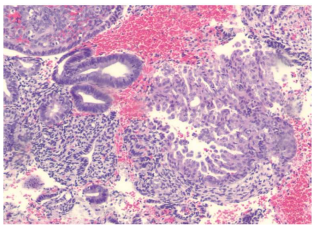
Do not forget to look at the background endometrium !



Case 3. Multiple foci



Your diagnosis



EIN
EIC

Multifocal papillary proliferation, follow up and clinical correlation

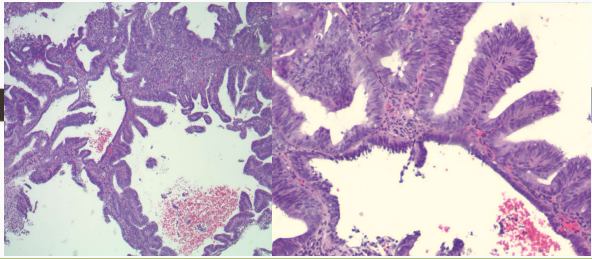
Non-atypical hyperplasia

Atypical papillary proliferation of crowded gland c/w treated EIN

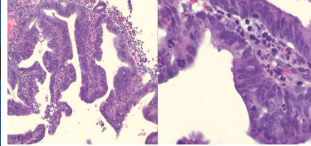
Atypical papillary proliferation consistent with (progesterone) treated EIN

- What goes against EIN
 - Crowded glands but bland morphology
 - No mitoses
 - No pseudostratification
- What goes against EIC
 - No significant atypia
 - No prominent nucleoli,
 - No mitoses or apoptotic bodies
 - p53 wild type
- What would help is history and prior biopsy!

Case 4. Multifocal papillary process



Your diagnosis

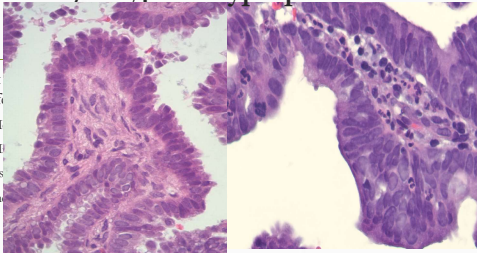


- EIC **A**
- EIN **B**
- Complex papillary proliferation **C**
- This is not fair, terrible photo **D**

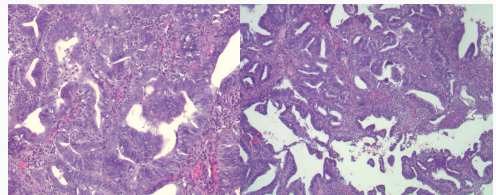
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EIN/ Atypical hyperplasia

- What proliferation
- M
- M
- Ps
- en



Do not forget to look at the background



Case 5. Papillary proliferation on the surface of polyp

What is your diagnosis

Papillary proliferation, complex, follow up

EIC

EIN

I need to see p53

Start the presentation to see live content. For screen share software, share the entire screen. Get help at pollen.com/app

EIC arising in a polyp

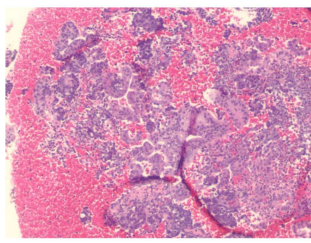
p53

What goes against papillary proliferation

- Marked atypia
- Red cherry nucleoli
- Apoptosis
- Mitoses
- p53

Case 6. Multiple foci like this

Your diagnosis



papillary syncycial metaplasia associated with menstruation

EIC

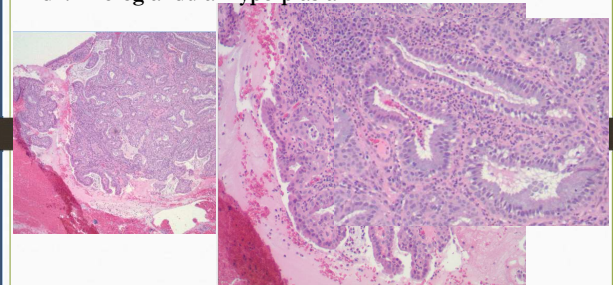
Squamous metaplasia

I had enough of this papillary bussines

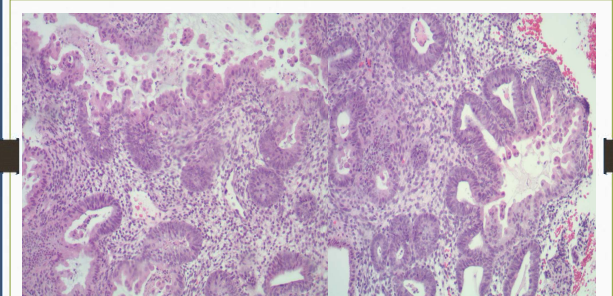
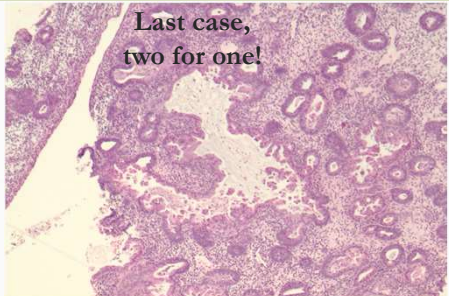
Papillary proliferation, complex follow up

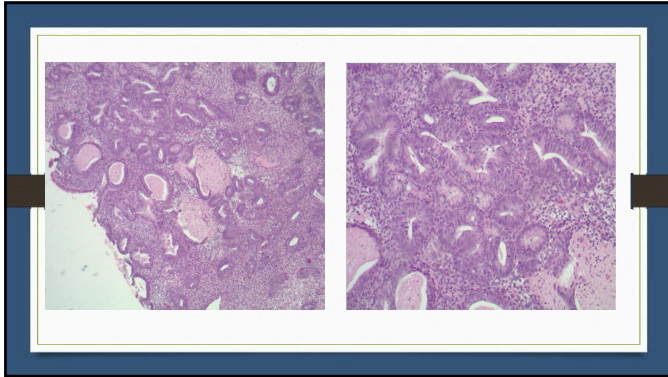
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Ddx: Microglandular hyperplasia



Last case, two for one!






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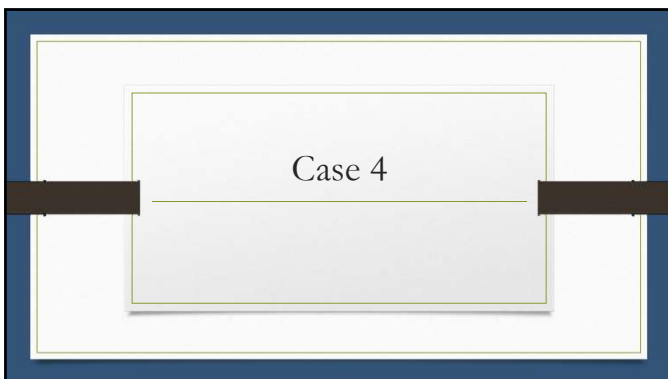
Department of
Pathology and
Laboratory
Medicine



EMORY

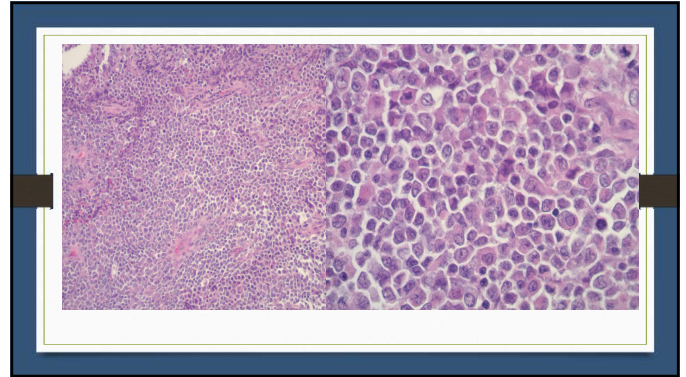
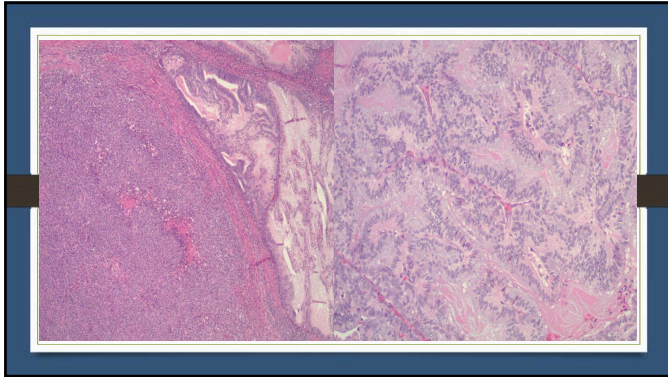
2020 Virtual
Pathology Course

Gynecologic Pathology
Krisztina Hanley, M.D.
Marina Mosunjac, M.D.



Case 4

- 47 y old female with vaginal bleeding,
- US endometrial thickness of 12.4 mm
- Endometrial biopsy in outside institution, not available for evaluation with the diagnosis of “carcinoma”
- Hysterectomy:
 - Endometrial cavity measures 4.0 x 2.1 cm with the thickness of endometrium measuring 0.2 cm. There is a 2.5 x 1.0 cm polypoid lesion arising from the anterior endometrium in the fundal region.



What is your diagnosis ?

Carcinosarcoma

Endometrioid carcinoma FIGO grade 3

Plasmacytoma and endometrioid carcinoma FIGO grade 1

Dedifferentated endometrial carcinoma

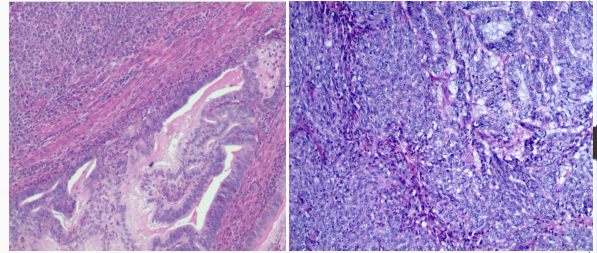
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Undifferentiated and dedifferentiated endometrial carcinoma (UDEEC)

- Dedifferentiated endometrial carcinoma
 - **Biphasic tumor** composed of **undifferentiated component** in combination with endometrioid carcinoma either **FIGO 1 or 2**
- Undifferentiated endometrial ca
 - Malignant epithelial neoplasm without morphological evidence of epithelial differentiation

Epidemiology and clinical features of (UDEEC)

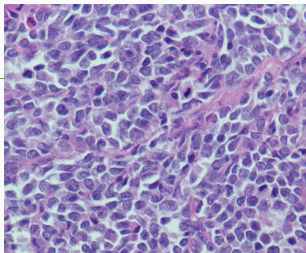
- Rare
- Younger women with median age of 55
- Higher association with Lynch syndrome
 - Abnormal MMR expression (up to 50%)
- Presents with postmenopausal bleeding
- Most are large polypoid intrauterine masses, often involving LUS
- Highly aggressive with recurrence and death in 55-95%



Dedifferentiated endometrial carcinoma: Key morphological features

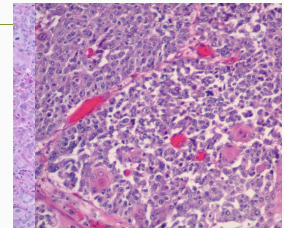
Common features

- Monomorphic population of cells
- No obvious differentiation
- Small to medium size
- Discohesive pattern
- Associated with myxoid stroma



Less common morphological features of undifferentiated portion

- Alveolar, nested or trabecular growth pattern
- Larger cells with abundant pink cytoplasm
- Marked pleomorphism
- Multinucleation
- Abrupt keratinization
- Presence of heterologous elements



Undifferentiated endometrial adenocarcinoma Immunohistochemistry

High rate of positivity	Rare focal positivity	Negative
NONE!!!! Abnormal MMR expression	EMA CK18 Vimentin Neuroendocrine markers C-Kir ER/PR	Cytokeratin AE3/AE1 Vimentin PAX8 E-cadherin P16 S100 LGA Desmin SMA p53

List of markers used in our case

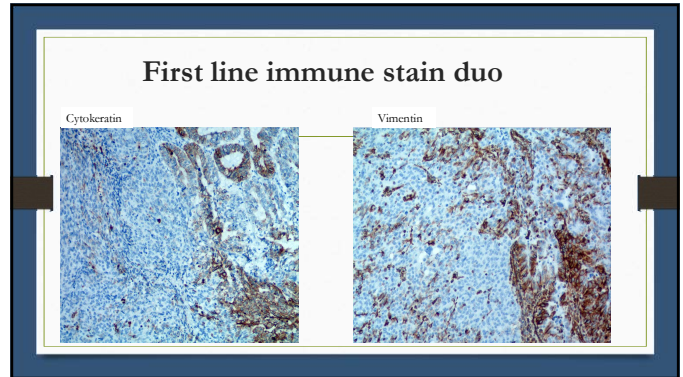
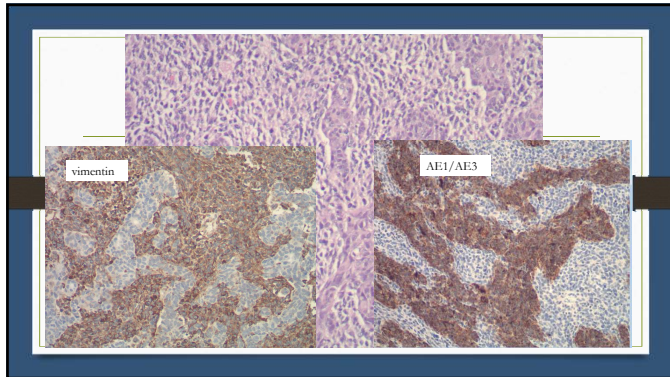


DDx for dedifferentiated carcinoma

- Carcinosarcoma
- Endometrioid carcinoma grade 2 or 3
- Serous carcinoma of uterus

DDx: Carcinosarcoma

- Low power biphasic look
- Epithelial and non epithelial component intermixed
- Epithelial component usually high grade
- Solid component rarely monotonous and discohesive
- ***Vimentin and cytokeratin positive***
- PAX 8 negative in mesenchymal component
- Abnormal MMR expression is rare



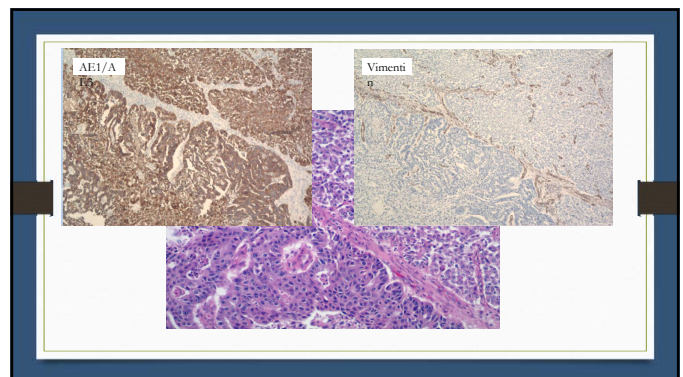
DDx: endometrioid carcinoma grade 2/3

Morphology

- Glandular and solid components usually intermixed
 - but can be distinct
- Solid and glandular component with similar degree of atypia

Immunohistochemistry

- Cytokeratin
- PAX 8
- ER and PR
- Vimentin can be focally positive
- E-cadherine



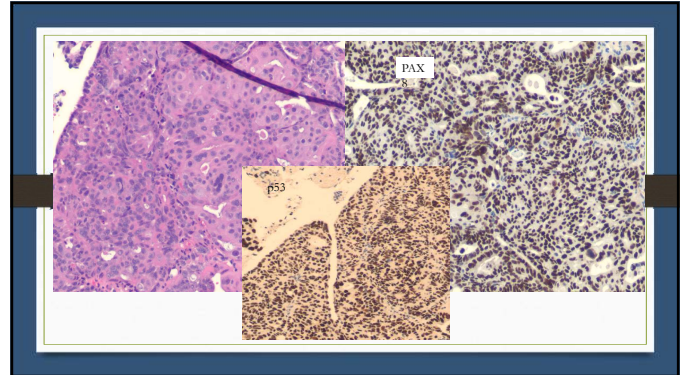
DDx: serous carcinoma solid type

Morphology

- Higher pleomorphism and atypia
- Cohesive
- Slit like spaces
- Focal papillary arrangement

Immunohistochemistry

- AE1/AE3
- PAX8
- p53 mutation
- E-cadherin



Immunohistochemical stains that can help further subclassify endometrial high grade carcinomas.

Characteristic	FIGO 3	Undifferentiated	Serous carcinoma
CK18	Strong	Focal and patchy	Strong
ER and PR	Strong	Weak or absent	Weak or absent
EMA	Strong	Focal and patchy	Strong
Vimentin	Strong	Negative	Negative
E-cadherin	Strong	Negative	Strong
p53	Wild type pattern*	<10% Aberrant expression	Aberrant expression
p16	Negative, rare cases positive	Negative, rare cases positive	Strong
PAX8	Positive	Negative	Positive
Pancytokeratin	Positive	Negative	Positive
Ck7	Positive	Negative	Positive
Microsatellite instability	Positive	Positive	Negative

*Up to 1/3 of high grade endometrioid carcinomas can have aberrant expression CK18 - cytokeratin 18, ER- estrogen receptor, PR- progesterone receptor, EMA- epithelial membrane antigen, Ck7-cytokeratin7

Hanley, Birdsong and Mosunjac. Arch Pathol Lab Med—Vol 141, April 2017

DDx: for undifferentiated endometrial carcinoma

- Lymphoma
- Melanoma
- Plasmacytoma
- High-grade neuroendocrine carcinoma
- Undifferentiated (SMARCA4 deficient) uterine sarcoma

DDx: SMARCA4-deficient uterine sarcoma

- Recently described entity with overlapping morphology with UDEC
- Sheets of medium to large epithelioid cells
- Rhabdoid morphology common
- Corded and phyllodiform architecture
- Members of the switch/sucrose non-fermenting complex which is involved in chromatin remodeling
- SMARCB1 (INI1)
 - Found in tumors with rhabdoid feature
- SMARCA4 (BRG1)
 - Small cell carcinoma of the ovary, hypercalcemic type

SMARCA4-deficient Uterine Sarcoma and Undifferentiated Endometrial Carcinoma Are Distinct Clinicopathologic Entities

David L. Kolin, MD, PhD,* Charles M. Quick, MD,† Fei Dong, MD,‡ Christopher D.M. Fletcher, MD, FRCPath,§ Colin J.R. Stewart, MD,§ Anita Soria, MChB, FRCPA,§ Jason L. Hornick, MD, PhD,¶ Maria R. Nucci, MD,† and Brooke E. Traut, MD||

(Am J Surg Pathol 2020;44:202-210)

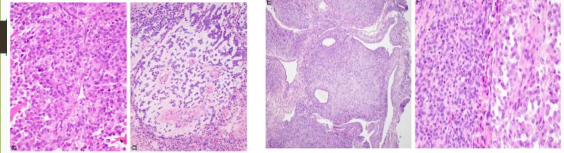
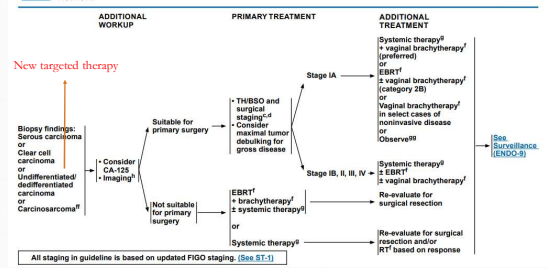


FIGURE 1 and 2. SMARCA4-deficient uterine sarcoma is typically composed of sheets of medium to large epithelioid cells, often with rhabdoid morphology (case 1). Other less common morphologic patterns include corded architecture with stromal hyalinization (C, 3), case 3), focal phyllodiform architecture (F, case 2) and biphasic growth, composed of small and large cell components (G, case 4).

DDx: SMARCA4-deficient uterine sarcoma

- Prominent nuclear pleomorphism
- Phyllodiform architecture present
- p53 and MSI less common
- SMARCA4 and SMARCB1 more common

NCCN Guidelines Version 2.2020 Endometrial Carcinoma



Take home message

- Think of undifferentiated endometrial adenocarcinoma when features of epithelial differentiation are absent
- It is a diagnosis of exclusion
- Exclude non-epithelial tumors
 - melanoma, lymphoma, plasmacytoma, sarcoma
- First line immunos : Cytokeratin and Vimentin
- When differential dx include FIGO 3
 - Loss of PAX8 and loss of E-cadherin is helpful

Thank you!



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GAP
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