第 102 回日本病理学会総会

コンパニオンミーティング１０（CM-10）

日本婦人科病理学会　『外陰・膣の病理』

座長：　笹島ゆう子（帝京大学医学部病理学講座）

佐藤勇一郎（宮崎大学医学部病理学　構造機能病態学分野）

講演１　外陰部扁平上皮病変

大石善丈　九州大学大学院医学研究院保健学部門検査技術科学

講演２　外陰部における色素細胞性疾患の病理診断 ABC

泉　美貴　東京医科大学　医学教育学講座

講演３　外陰・膣の軟部腫瘍

福永真治　東京慈恵会医科大学附属第三病院　病院病理部

平成 25 年 6 月 7 日（金）　18：40～20：40

R3 会場（ロイトン札幌 2 階リージェント）

Vulvar Squamous Neoplasia

Department of Anatomic Pathology
Kyushu University
Yoshihiro Ohishi

Content

1. Overview of vulvar squamous neoplasia
2. VIN (histology, IHC, malignant potential)
3. VSCC (histology, IHC, prognosis)
4. Special type (verrucous, BCC)
5. Condyloma vs papilloma

Histopathology 2013; 62; 161-175

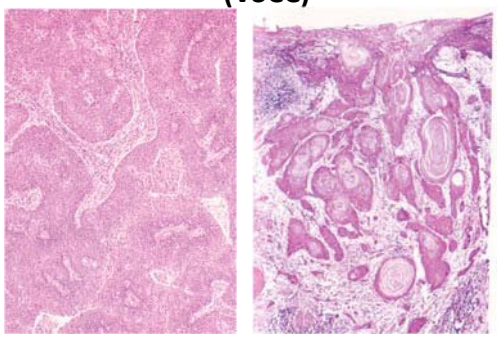
Vulvar Squamous Cell Carcinoma (VSCC)

- < 5% Gynecologic malignancies
- > 90% Vulvar malignancies

HPV-related VSCC
(HPV+)
basaloid/warty SCC

HPV-independent VSCC
(HPV-)
Keratinizing SCC

Vulvar Squamous Cell Carcinoma (VSCC)



Basaloid SCC Keratinizing SCC WHO, 2003

Vulvar Intraepithelial Neoplasia (VIN, precursor of VSCC)

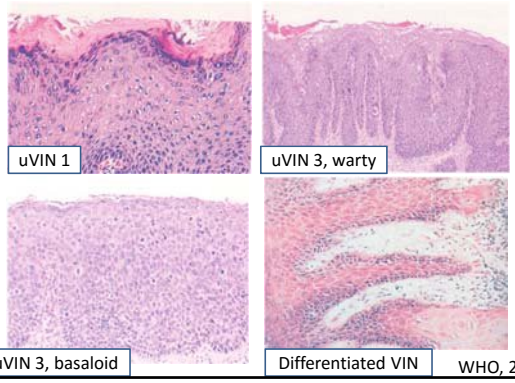
HPV-related VSCC
(HPV+)
usual VIN

(classic VIN)
(bowenoid VIN)

HPV-independent VSCC
(HPV-)
differentiated VIN

(simplex VIN)

Vulvar Intraepithelial Neoplasia (VIN)

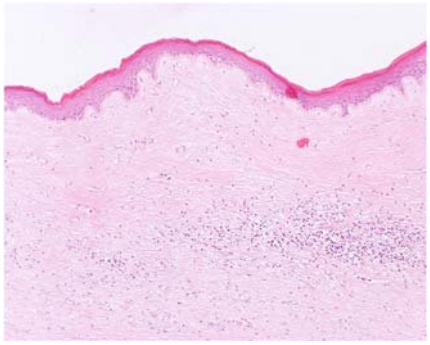


uVIN 1 uVIN 3, warty uVIN 3, basaloid Differentiated VIN WHO, 2003

Lichen Sclerosis

- Precursor of HPV-indepependent VSCC
- Lichen sclerosis << differentiated VIN

Lichen Sclerosis



HPV in VSCCs

Authors	Year	*n*	HPV typing test	HPV (%)	HPV16 (%)
Monk	1995	55	PCR L1 consensus primers	60	49
Kim	1996	18	PCR L1 consensus primers	39	71
Pinto	1999	16	PCR L1 consensus primers	50	–
Carter	2001	38	PGMY9/11	79	55
Riethdorf	2004	71	GP5+/GP6+ and $p16^{INK4a}$	35	76
van der Nieuwenhof	2009	130	Short PCR fragment L1	35	44
Kowalewska	2010	46	Linear array HPV test	15	71
Alonso	2011	98	SPF10 and $p16^{INK4a}$	19	74
Gargano	2012	121	PGMY9/11	69	81
Tsimplaki	2012	6	PapilloCheck HPV	50	100

Histopathology 2013; 62; 161-175

HPV in VINs

Authors	Year	*n*	HPV typing test	Type of VIN	HPV (%)	HPV16 (%)
Trimble	1996	54	Omniprobe Assay (Digene)	NOS	89	–
Pinto	1999	16	PCR L1 consensus primers	uVIN	67	–
Carter	2001	18	PGMY9/11	NOS	91	74.6
Riethdorf	2004	67	GP5+/GP6+ and $p16^{INK4a}$	NOS	52	88
van der Avoort	2006	37	SPF10	uVIN	66	65
van der Nieuwenhorf	2009	13	Short PCR fragment L1	uVIN	100	44
Garland	2009	62	PCR	uVIN	84	42
Smith	2009	65	PGMY09/11	NOS	98	50
Alonso	2011	48	SPF10	uVIN	83	–
Gargano	2011	66	PGMY9/11	NOS	94	48
Tsimplaki	2012	28	PapilloCheck HPV	uVIN	71	65

Histopathology 2013; 62; 161-175

HPV in VSCCs & VINs

- 1/5 ~ 1/2 VSCCs ・・・・・・・ HPV+
- > 4/5 VINs ・・・・・・・・・・・ HPV+

Most VSCCs are HPV-
Most VINs are HPV+

HPV in vulvar squamous lesion

- VSCC & VINs ・・・・・・ HPV16 >>>>>18,31,33,45
- Condyloma acuminatum ・・・・・ HPV6,11
- Verrucous carcinoma ・・・・・・・・ HPV6?

Epidemiology

HPV- squamous lesion		HPV+ squamous lesion
• Elderly		• Young
• Keratinizing SCC (common)	>	• Basaloid SCC (rare)
• Differentiated VIN (rare)	<	• Usual VIN (common)
• Lichen sclerosis (+)		• Lichen sclerosis (-)
• Multifocal lesion (-)		• Multifocal lesion (+)
• p16-; p53+		• p16++; p53-

Histological features of VIN

uVIN‥‥‥similar to CIN/VAIN

- Thickened epidermis
- Hyperkeratosis/parakeratosis
- Loss of maturation
- N/C ratio↑
- Hyperchromasia
- Mitosis↑

Histological features of VIN

uVIN

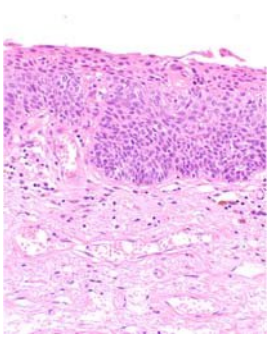
Basaloid VIN (undifferentiated)

- Flat
- Non-papillomatous

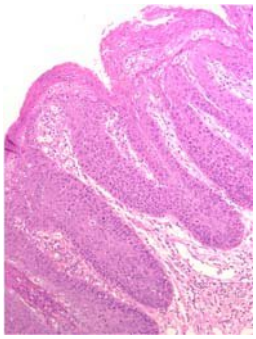
Warty VIN (condylomatous)

- Condylomatous
- papillomatous

Basaloid and warty VINs

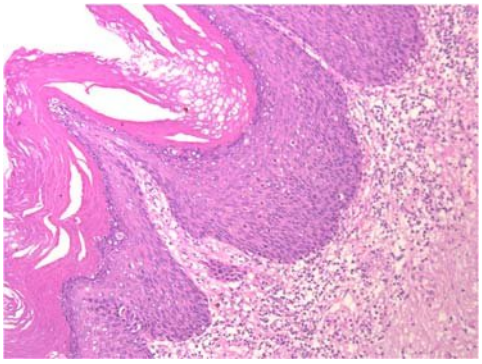


Basaloid VIN 3



Warty VIN 3

Overlap between basaloid and warty

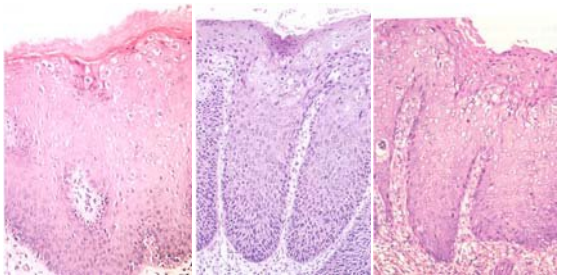


Histological feature of VIN

- Morphological overlaps ; basaloid & warty VINs
- Basaloid & warty VINs ; single category

usual VIN

Histological features of VIN



VIN 1, warty | VIN 2, warty | VIN 3, warty

Blaustein's textbook, 6th edition

Histological features of VIN
WHO terminology

uVIN (classic VIN)

- VIN1
- VIN2 ↕ subjective
- VIN3

Histological features of VIN
ISSVD recommendation

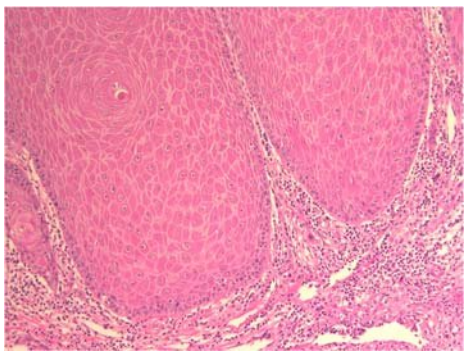
- ~~VIN1~~ → Condyloma
- VIN2
- VIN3

} uVIN

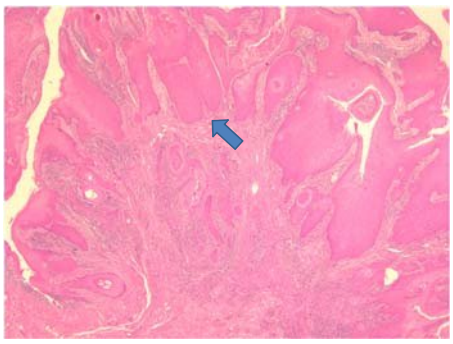
Histological features of VIN
differentiated VIN (dVIN)

- Subtle morphological change
- Thick epidermis
- Elongated rete ridges
- Large vesicular nuclei, macronucleoli
- Abundant, brightly eosinophilic cytoplasm
- Intercellular bridge (++)

Differentiated VIN



Differentiated VIN



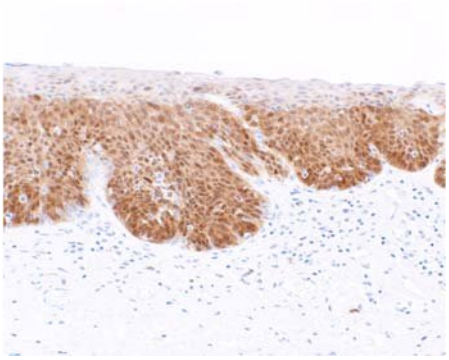
Differentiated VIN

- Interobserver reproducibility↓
- dVIN alone ····· rare diagnosis
- Confused with benign lesion
- "differentiated" but "high-grade"

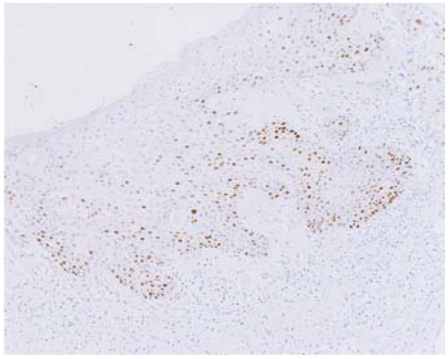
Immunohistochemistry of VIN

- uVIN ····· p16 (+, diffuse staining), p53 (-)
- dVIN ····· p16 (-), p53 (+, suprabasal extension)

p16 staining in uVIN



p53 staining in dVIN



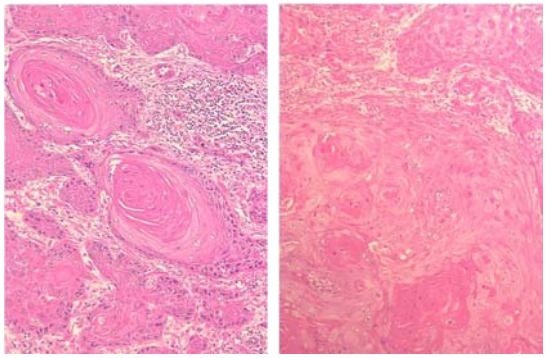
Malignant potential of VIN

- uVIN ····· 9-16% progress to SCC
- dVIN ····· higher% progress to SCC
  (underdiagnosis, transient lesion)

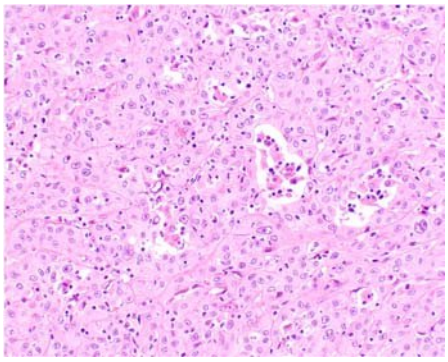
Histological features of VSCC
WHO classification

- Basaloid
- Warty
- Nonkeratinizing
- Keratinizing ····· most common

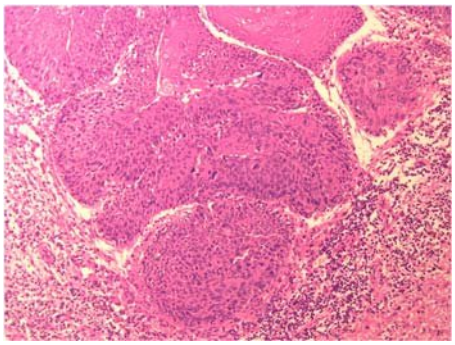
Keratinizing SCC



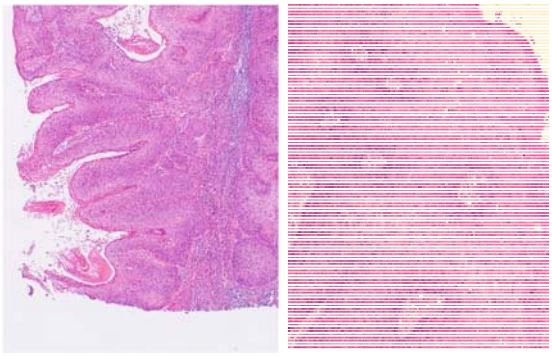
Nonkeratinizing SCC



Basaloid SCC



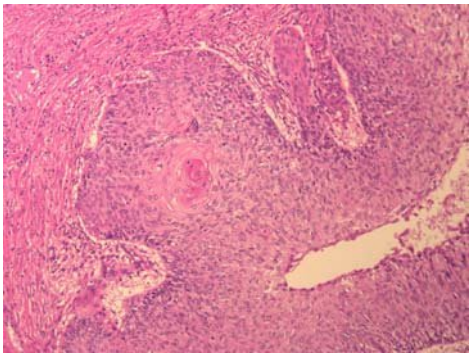
Warty SCC



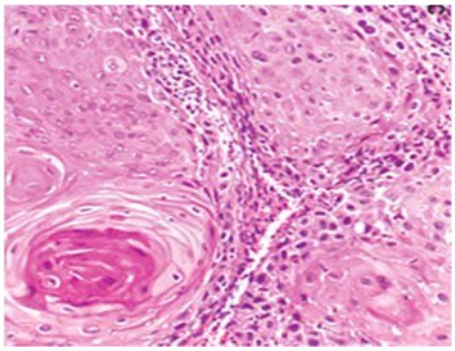
Histological features of VSCC

- Basaloid & warty → HPV+
- Keratinizing → HPV-

Basaloid & keratinizing SCC



Keratinizing SCC, HPV+



Histopathology 2013; 62; 161-175

Histological features of VSCC

- Basaloid & warty → HPV+
- overlap+
- Keratinizing → HPV-

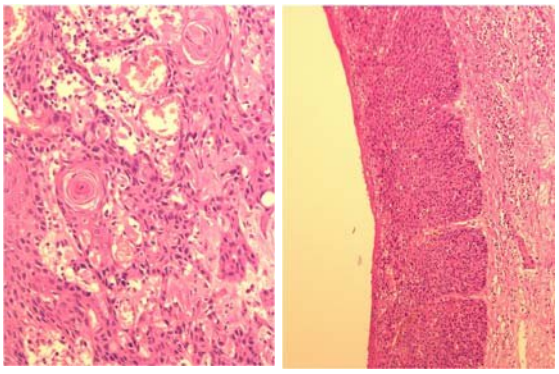
HPV+ VSCC *vs* HPV- VSCC

- dVIN/Lichen sclerosis + ····· HPV-
- uVIN+ ····· HPV+

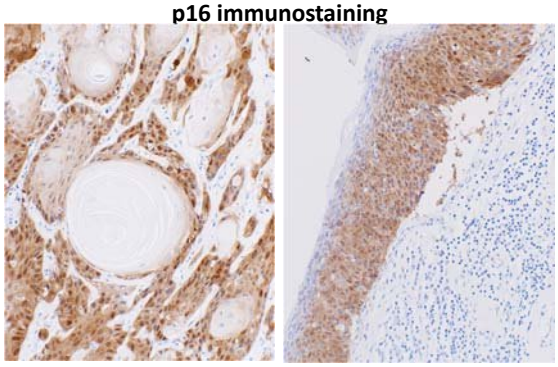
HPV+ VSCC *vs* HPV- VSCC
immunohistochemistry (most reliable)

- HPV+ VSCC ····· **p16 (++)**, p53 (-)
- HPV- VSCC ····· **p16 (-)**, p53 (+, 50-70%)

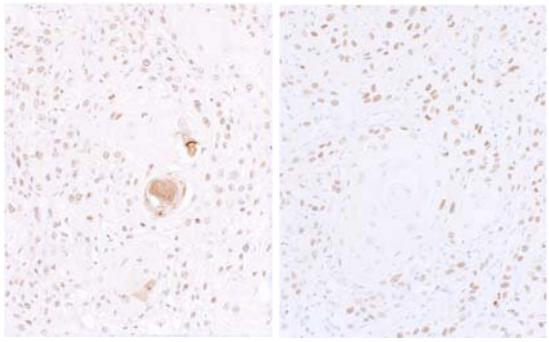
Keratinizing SCC + uVIN



Keratinizing SCC + uVIN
p16 immunostaining



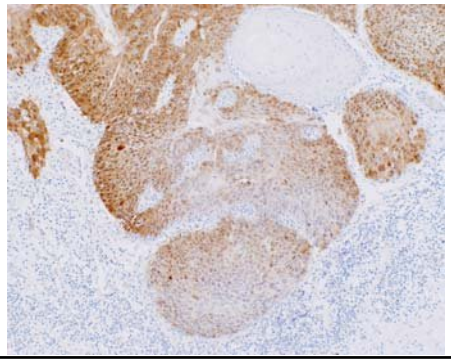
Keratinizing SCC



p16 IHC p53 IHC

Basaloid SCC

p16 immunostaining



Prognosis of VSCC

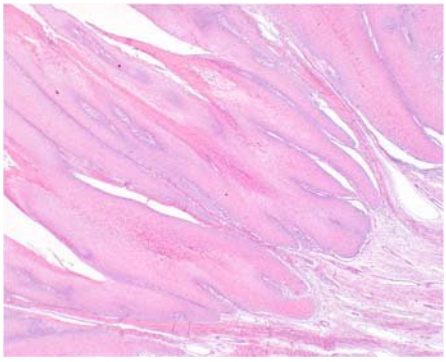
Authors	Year	*n*	Overall survival at 5 years (%)		*P*
			HPV+	HPV−	
Monk	1995	55	72	44	0.01
Pinto	2002	16	63	71	0.447
van der Nieuwenhof	2009	130	80	78	0.646
Lindell	2010	75	85	40	0.03
Alonso	2011	98	67	71	0.789
Choschzic	2011	39	40	75	>0.05

Histopathology 2013; 62; 161-175

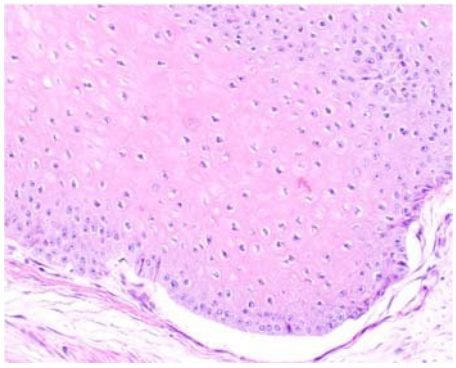
Verrusous carcinoma

- 1-2% of VSCC
- Undulating warty surface
- Hyperkeratosis
- Pushing border
- Minimal atypia
- HPV 6+?
- Favorable prognosis

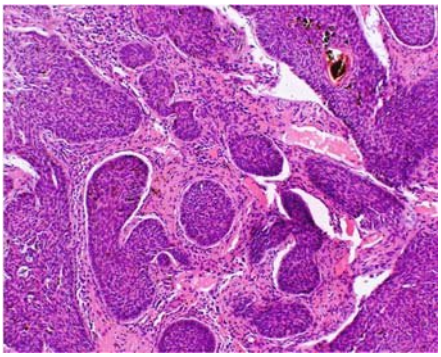
Verrucous carcinoma



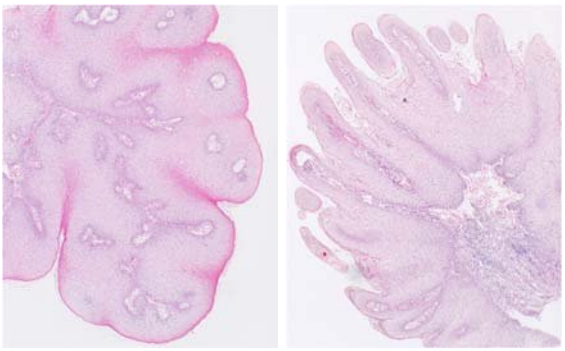
Verrucous carcinoma



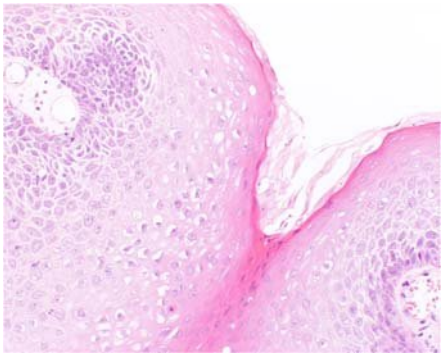
Basal cell carcinoma



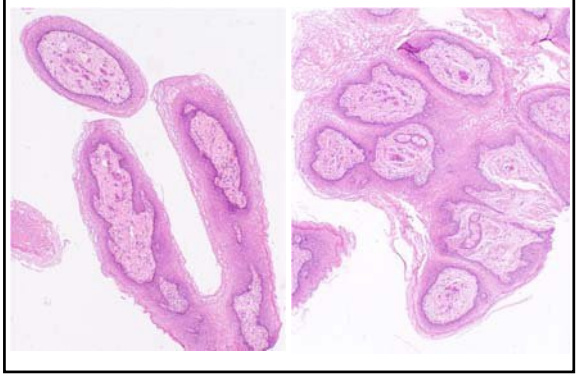
Condyloma acuminatum



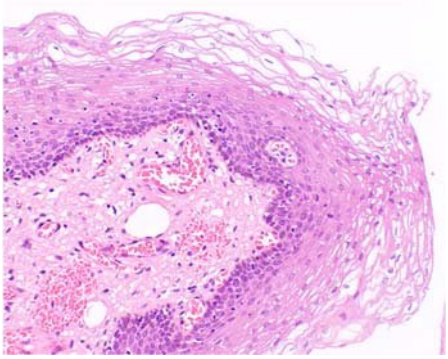
Condyloma acuminatum



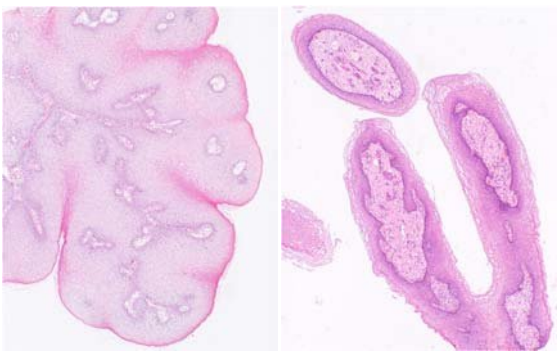
Papilloma



Papilloma



Condyloma *vs* papilloma



Summary
Vulvar squamous neoplasia

	(p53+/**p16-**)		(p53-/**p16+**)
• VSCC	HPV-	>>	HPV+
	SCC-k		**SCC-b/w**
• Precursor	HPV-	<<	HPV+
	dVIN		**uVIN**

第102回日本病理学会総会 コンパニオンミーティング
＜日本婦人科病理学会＞
外陰・膣の病理

外陰・膣における色素細胞性疾患の病理診断ABC

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ロイトン札幌　2013年（平成25）年6月7日

外陰・膣における色素性疾患：目次

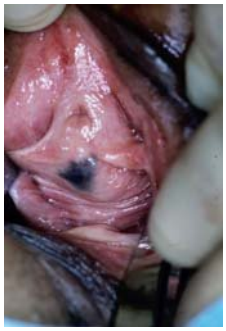
1. 良性疾患：
   メラノーシス
   色素細胞性母斑:“Nevus of special site”
1. 悪性黒色腫:
2. 色素細胞性疾患以外の黒色病変，
   “Melanocyte colonization”共生：
   乳房外Paget病，脂漏性角化症，Bowenoid papulosis，etc.

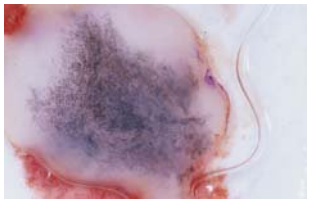
1.良性疾患

外陰・膣のメラノーシス：Vulvar melanosis
Atypical genital macule

- 本質：炎症後の色素沈着（？）：硬化性萎縮性苔癬の後
- 発生部位：粘膜～modified mucous membrane（小陰唇最多．皮膚には稀）
- 臨床像：単発～しばしば多発，茶色～黒色，不規則形で境界不明瞭な色素斑
- 時期：閉経前の若い女性，小児であれば他の症候群の合併を考慮（Peutz-Jeghers症候群., Laugier-Hunziker-Baran症候群., Cockayne症候群., LEOPARD症候群. Carney症候群, Cushing病）
- 偶然に発見（自覚症状なし）
- 病理像：表皮の肥厚と基底層のメラニンの増加，メラノサイトの増数は様々＋上皮下のメラノファージ
- 治療：必要ない（MMとの鑑別のため生検は必須）

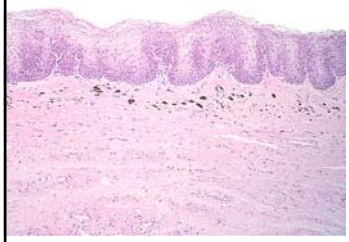
外陰・膣のメラノーシス－１
Atypical genital macule

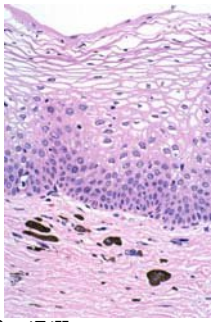




左右非対称性だが，色調均一

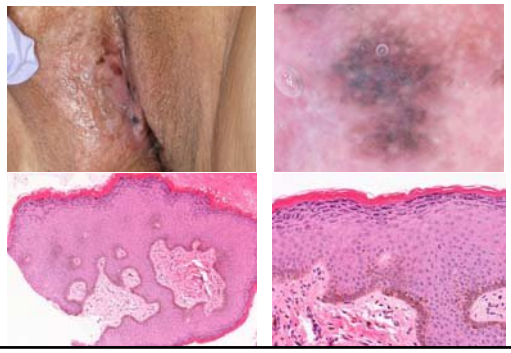
外陰・膣のメラノーシス－１
Atypical genital macule





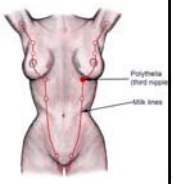
上皮の肥厚，上皮下はメラノファージの浸潤

外陰・膣のメラノーシス－２
Atypical genital macule



外陰・膣の色素細胞性母斑
左右非対象，異型性，ascentがある

1. 特別な部位
   - ①“Nevus of special sites”（Milk line）
   - ② 間擦部（腋窩，外陰部）
   - ③ 粘膜：膣，口唇・口腔内，眼瞼，鼻腔
   - ④ 掌蹠（手掌・足底）
2. 特別な母斑
   - ① 先天性母斑
   - ② Spitz母斑
   - ③ 青色母斑
3. 特別な時期：新生児・乳幼児，妊娠中



“Nevus of special sites”
外陰・膣の色素細胞性母斑

- 病理所見が悪性様：
  “Atypical melanocytic nevi of genital type”
  “Nevi of site related atypia”
- 臨床的には良性所見：左右非対象でも境界明瞭，色調均一
- 年齢：閉経前の女性（平均23歳）
- 偶然に発見：妊娠・出産，子宮筋腫の手術時など
- 部位：皮膚に多い（通常の母斑は粘膜と皮膚両方），小児は小陰唇と陰核

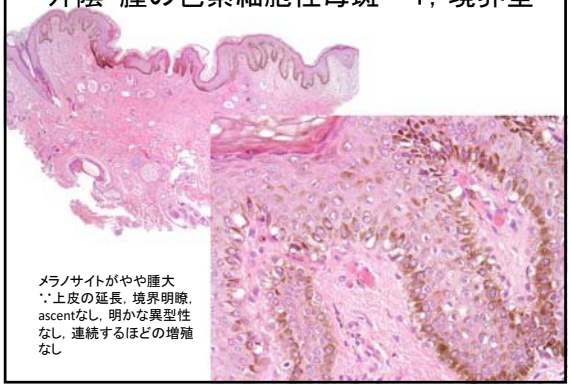
外陰・膣の色素細胞性母斑
“Atypical melanocytic nevi of genital type ”
“ Atypical genital nevi”

- **悪性と間違える：先天性母斑様（案外多い），異形成母斑様**
  - 大型： 10 mm～（先天性）
  - 不整形：胞巣が不整・多形・分布が不規則，炎症細胞，メラニンの分布
  - 表皮の増生：（表皮突起の延長，癒合(DN)，乳頭状，偽癌性表皮過形成）
  - 付属器に沿う配列（先天性）
  - 細胞が大型（特に表皮内や真皮浅層），異型性，多形性（先天性）
  - 明瞭な核小体
  - 多少のAscent
  - 高度の炎症細胞浸潤（DN）
  - Lamellar fibroplasia（層状で好酸性の線維化）（DN）

外陰・膣の色素細胞性母斑
“Atypical melanocytic nevi of genital type ”
“ Atypical genital nevi”

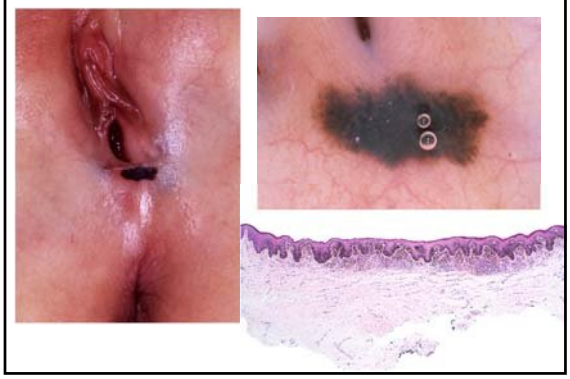
- **良性と判断できる所見：**
  - 潰瘍はない
  - 表皮内病変は真皮内病変を超えない（shoulder lesionはない）
  - 境界が明瞭
  - 構造異型は目立つが細胞異型は乏しい
  - 多少のascentはあっても，Paget様進展はない
  - 壊死はない
  - 核分裂像はない（特に上皮下にはない）
  - 深部への成熟を示す
  - 細胞周囲の密な線維化やリンパ球浸潤はない

外陰・膣の色素細胞性母斑－１，境界型

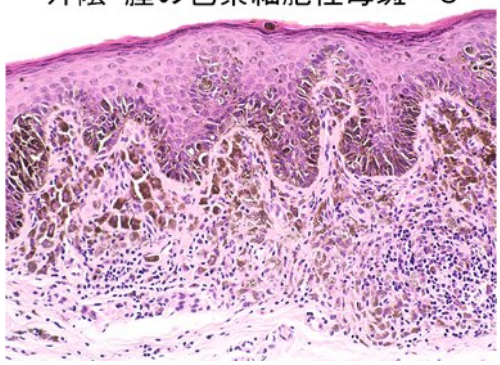


メラノサイトがやや腫大
∵上皮の延長，境界明瞭，ascentなし，明かな異型性なし，連続するほどの増殖なし

外陰・膣の色素細胞性母斑－２

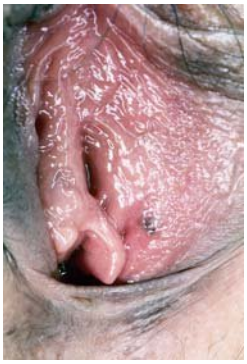


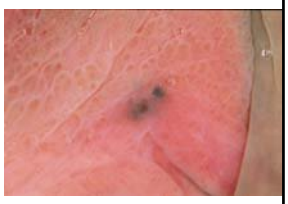
外陰・膣の色素細胞性母斑－３



異形成母斑様のlamellar fibroplasiaとリンパ球浸潤

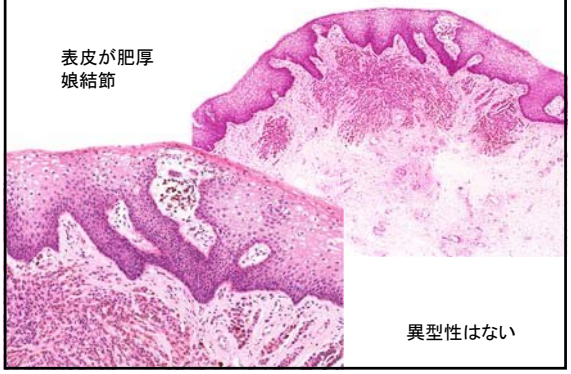
外陰・膣の色素細胞性母斑－３





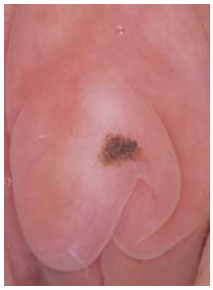
左右非対象性だが境界は明瞭，色調も均一

外陰・膣の色素細胞性母斑－３



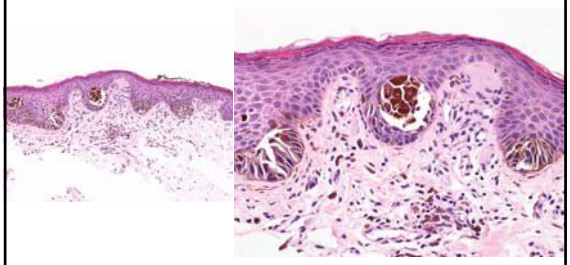
異型性はない

外陰・膣の色素細胞性母斑－４



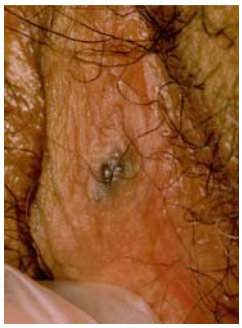
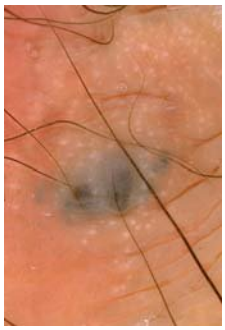
5歳女児，陰核：典型例

外陰・膣の色素細胞性母斑－４



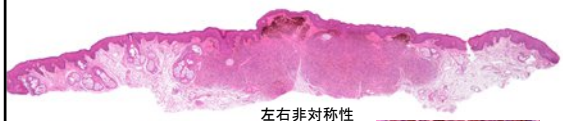
大型の胞巣，細胞接着が緩い

外陰・膣の色素細胞性母斑－5

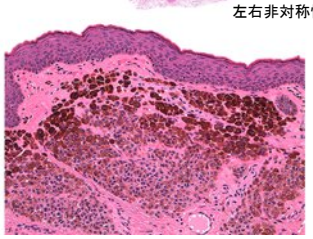
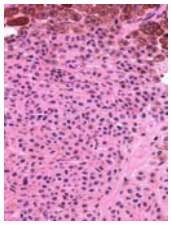



臨床的には不規則，左右非対象，隆起あり，娘結節？　ただし境界は明瞭，色調も均一

外陰・膣の色素細胞性母斑－5

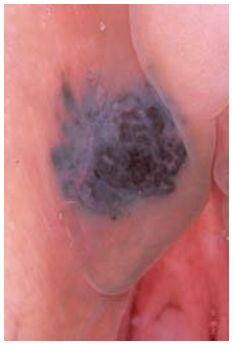


左右非対称性

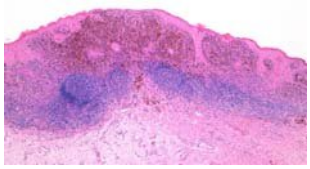



上皮直下は細胞が大型　　∵深部は成熟あり

外陰・膣の色素細胞性母斑－6

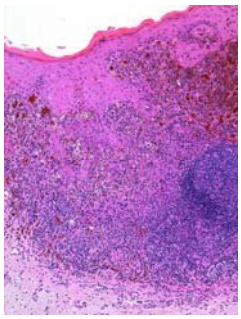



左右非対称性，境界は明瞭

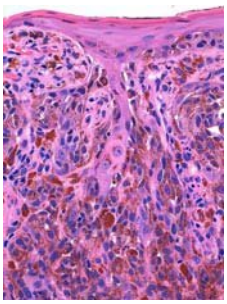


高度の炎症細胞浸潤，

外陰・膣の色素細胞性母斑－6

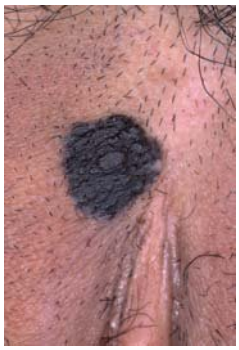


表皮の偽癌性過形成，著しいリンパ球浸潤



表皮突起の不規則な延長
∵母斑細胞に異型性はない．

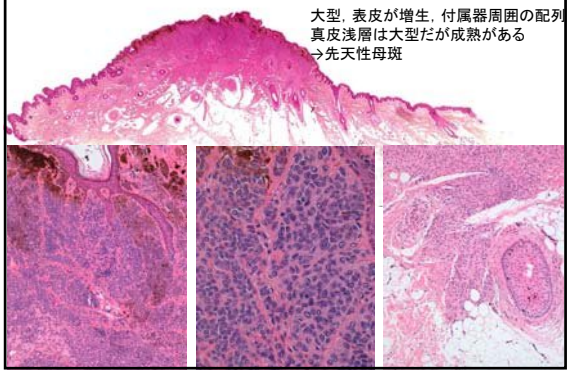
外陰・膣の色素細胞性母斑－7




若い女性の外陰部（有毛部）の境界明瞭な色素性病変：母斑の典型

外陰・膣の色素細胞性母斑－7

大型，表皮が増生，付属器周囲の配列
真皮浅層は大型だが成熟がある
→先天性母斑



2.悪性黒色腫

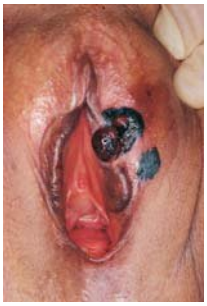
外陰部悪性黒色腫の臨床

- 患者：閉経後の女性，平均68歳
- 頻度：外陰部の悪性腫瘍でSCCに次ぎ5%，悪性黒色腫の，1～2.3%
- 部位：Atypical NZNと異なり，無毛部の大陰唇，陰核
- 臨床像：境界不明瞭，色調不均一（amelanotic melanomaは稀），しばしば多発(>20%)
- 大きさ：≧7mm
- 生検，excisional biopsy，（shave biopsyは禁忌：深達度不明，取り残し必至）
- 組織像：表皮は潰瘍～萎縮，明瞭な構造異型・細胞異型，境界不明瞭，ascent/Pagetoid進展，核分裂像
- Breslow thickness：平均3.2 mm，in situは極めて稀
- 予後因子：年齢．Stage（潰瘍あり，深達度深い，amelanosis）．LN転移の有無，深達度は再発に関与しても生存率には無関係とも．
- 予後：悪い（平均生存期間5.2年，1/5/10年生存率＝85/50/30%）
- 治療：切除・リンパ節郭清

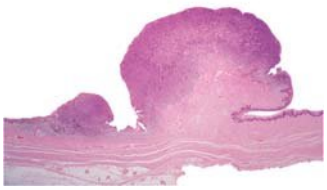
膣の悪性黒色腫の臨床

- 患者：閉経後(80%)の女性，平均60歳前後
- 頻度：非常に稀，報告300例余り，膣悪性腫瘍の<3%
- 発生母地：成人女性3%の膣にメラノサイト＋
- 部位：膣外側1/3
- 症状：出血，結節
- 臨床像：潰瘍形成，易出血性，黒色調(amelanoticは稀)，20%が多発
- 予後因子：①大きさ≧3cm 12ヶ月，<3cm 41ヶ月生存．②リンパ節転移がない．深達度は関与しないとも
- 予後：40%が局所再発，転移：肺，肝臓，骨
- 治療：切除（拡大手術と最小限のマージンでも予後に差は無い）＋放治
- 予後：5年生存率 0～21%

外陰悪性黒色腫－1

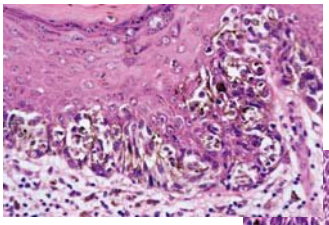


臨床的に悪性

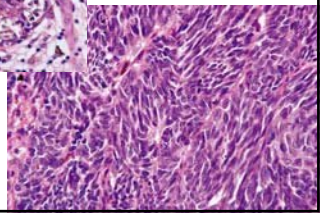


潰瘍，腫瘤の形成

外陰悪性黒色腫－1

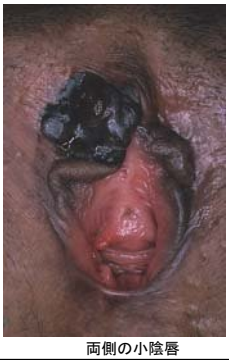


表皮内病変あり

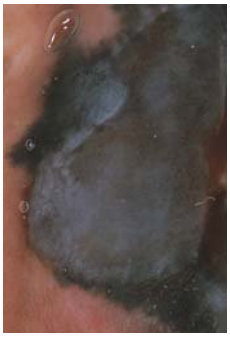


短紡錘形の異型細胞
高いN/C比，クロマチンの濃縮

外陰悪性黒色腫－2

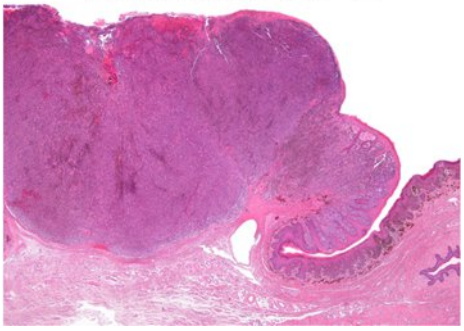


両側の小陰唇



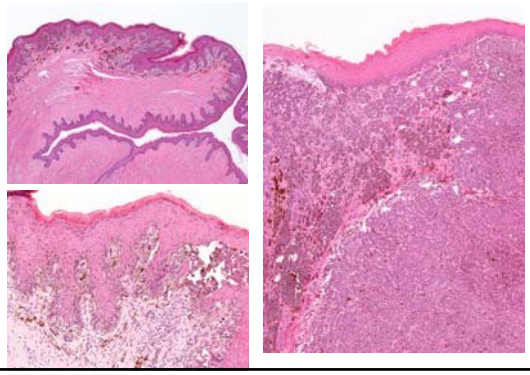
辺縁にシミ出し

外陰悪性黒色腫－2

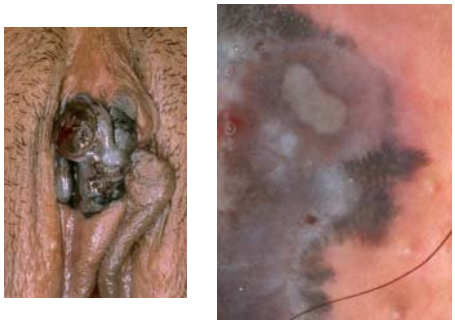


皮膚の結節型黒色腫と同様

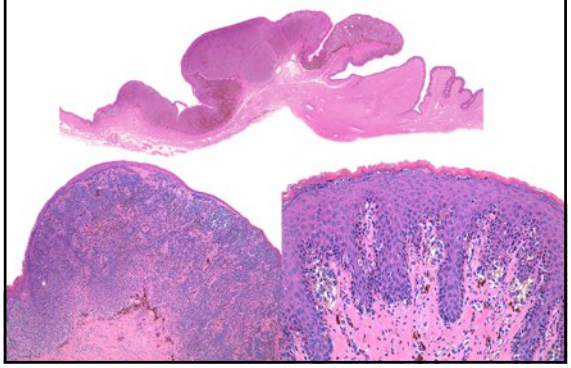
外陰悪性黒色腫－2



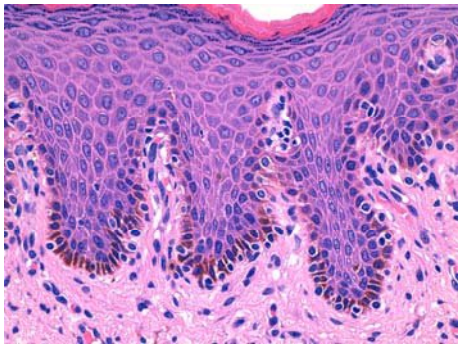
外陰悪性黒色腫－3



外陰悪性黒色腫－3

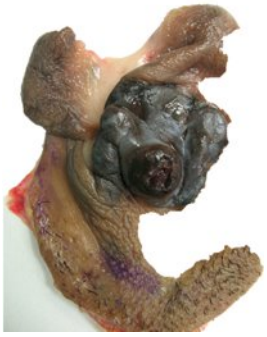


外陰悪性黒色腫－3

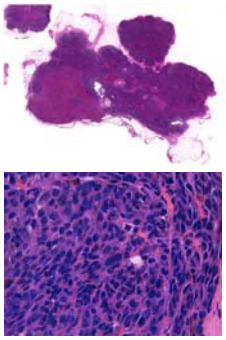


Atypical melanocytic hyperplasiaがmelanomaの周辺に広がる(14%)

外陰悪性黒色腫－3

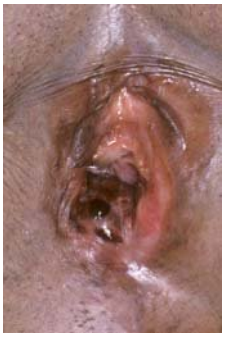


Vulvectomy施行するも

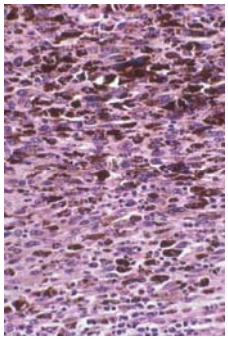


左右の鼠径リンパ節に転移

膣悪性黒色腫－1

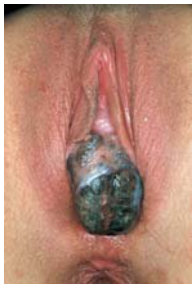


膣壁複数の斑～小丘疹

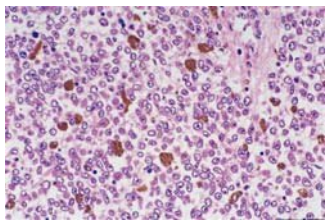


浸潤部は紡錘形細胞

膣悪性黒色腫－2



膣壁の大型腫瘤，ヘルニア状



類円形異型細胞，びまん性に増殖

3.メラノサイトの共生
Melanocyte colonization

“Melanocyte colonization”

●定義：メラノサイト系病変でないにも拘わらず，メラノサイトが混在しメラニンの沈着する病態．

●歴史：1977年，AzzopardiとEusebiが乳癌の癌細胞胞巣中にメラノサイトとメラニンが混在することを発表

●メラノサイト：樹枝状．S-100蛋白+，MART-1+

●病因：メラノサイトの滴落？

脂漏性角化症

A）1929 年，Bloch：「**Melanoepithelioma**」

1. Melanoepithelioma type I
   ≒ Inverted follicular keratosis
2. **Melanoepithelioma type II**
   Bloch良性非母斑性黒色上皮腫第II 型

B）1960 年，Pinkus & Mishima
「**Melanoacanthoma**」：

•脂漏性角化症のうち，メラノサイトが増加し，メラニン沈着の多い病態

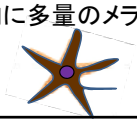
•皮膚，口腔内（口唇，歯肉，口蓋，頬粘膜）

Melanoepithelioma Bloch type II
Melanoacanthoma
“Melanocyte colonization”

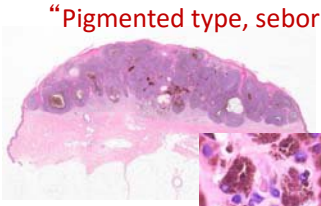
メラノサイト

“Pigment blockade melanocyte”
“Blockade melanocyte”

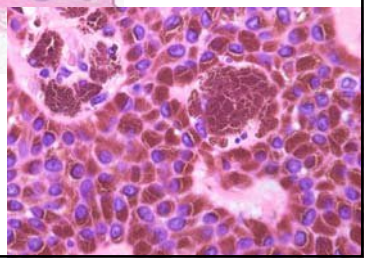
メラノサイトから角化細胞へメラニンの移送が障害され，メラノサイトの細胞質内に多量のメラニンを貯留した状態



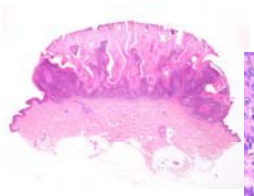
色素型の脂漏性角化症
“Pigmented type, seborrheic keratosis”



➢メラノサイトは少数
➢メラニンが豊富

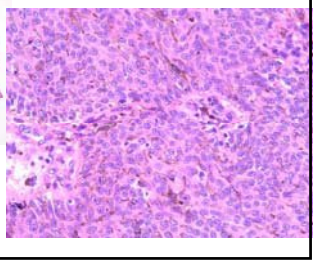


脂漏性角化症
Melanoepithelioma, Bloch type II
Melanoacanthoma

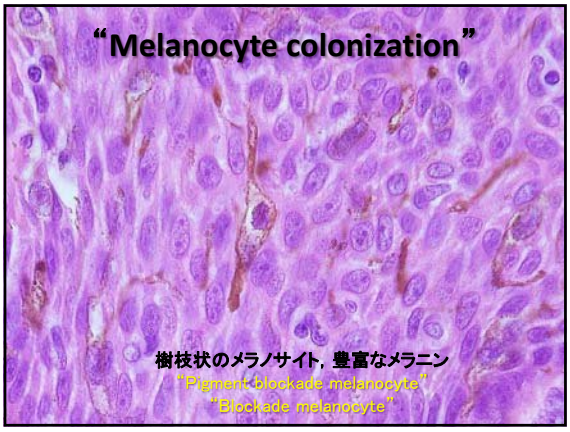


“ボタンを置いたような”

➢メラノサイトが増加
➢メラニンが豊富



“Melanocyte colonization”



樹枝状のメラノサイト，豊富なメラニン
“Pigment blockade melanocyte”
“Blockade melanocyte”

Melanocyte colonizationを来す疾患

＜腫瘍性疾患＞	＜非腫瘍性病変＞
●乳癌	● 尋常性疣贅
●基底細胞上皮腫（癌）	● 尖圭コンジローマ
●乳房外Paget病	● Bowenoid papulosis
●SCC(転移)	
●ボーエン病(日光角化症)	
●脂漏性角化症	
●石灰化上皮腫	
●汗孔腫，汗孔癌	
●Apocrine hidrocystoma	
●神経線維腫(Pigmented)	
●DFSP(Bednar tumor)	

Melanocyte colonizationを来す疾患

＜腫瘍性疾患＞	＜非腫瘍性病変＞
●乳癌	● 尋常性疣贅
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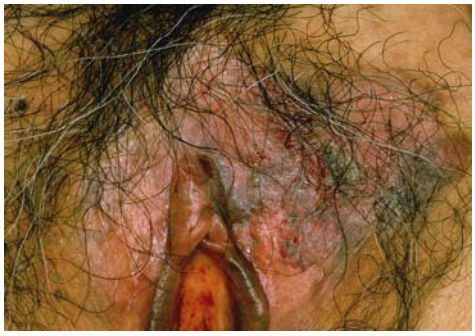
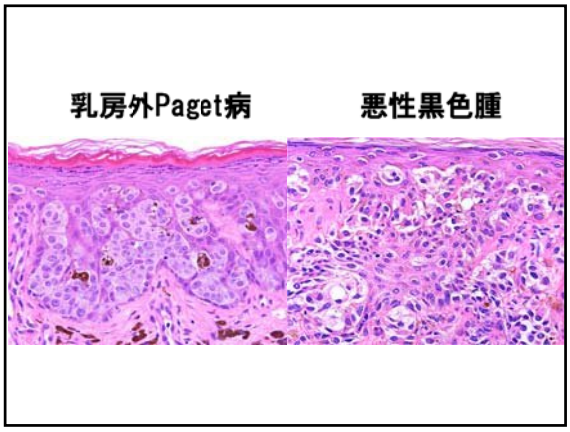
●汗孔腫，汗孔癌	
●Apocrine hidrocystoma	
●神経線維腫(Pigmented)	
●DFSP(Bednar tumor)	

乳房外Paget病

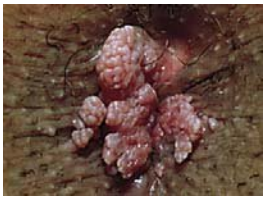


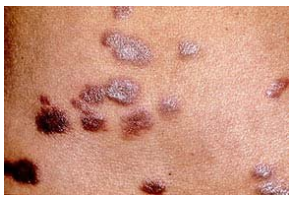


特殊染色・免疫染色による鑑別法

		乳房外Paget病	悪性黒色腫
特殊染色	DPAS	+	−
	アルシアン青	+	−
免疫染色	AE1/AE3	+	−
	CAM5.2	+	−
	サイトケラチン 7	+	−
	サイトケラチン 20	−	−
	CEA	+	−
	MUC1	+	−
	GCDFP-15 (BRST-2)	+	−
	c-erb B-2 (Her-2)	+	−
	Androgen receptor (AR)	+	−
	S-100蛋白	−	+
	MART-1/Melan-A	−	+

Bowenoid papulosis(HPV)



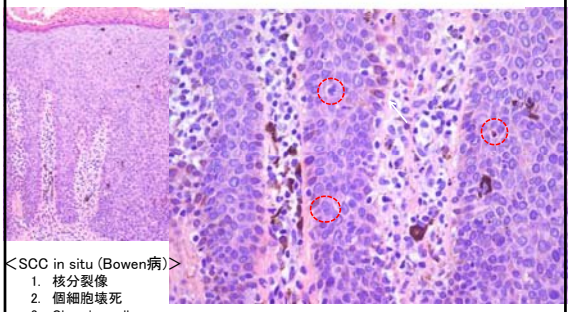


Condyloma acuminatum
肌色，乳頭状集簇性

Bowenoid papulosis
褐色局面～乳頭状，孤立性

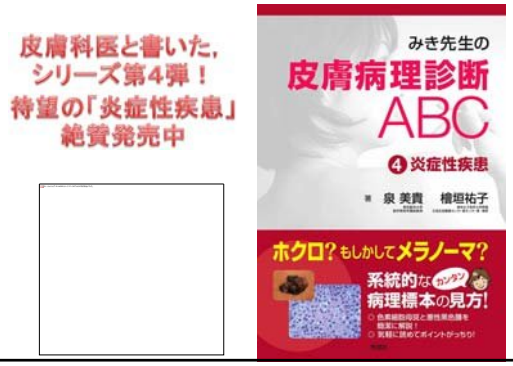
＜HPV 16感染＞
- コイロサイトーシス
- 錯角化を伴う過角化柱
- 多顆粒細胞症

Bowenoid papulosis



＜SCC in situ (Bowen病)＞
1. 核分裂像
2. 個細胞壊死
3. Clumping cells

ご清聴ありがとうございました



Pathologic Diagnosis of Vulvovaginal Mesenchymal Tumors

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Department of Pathology
Jikei University Daisan Hospital,
Tokyo, Japan

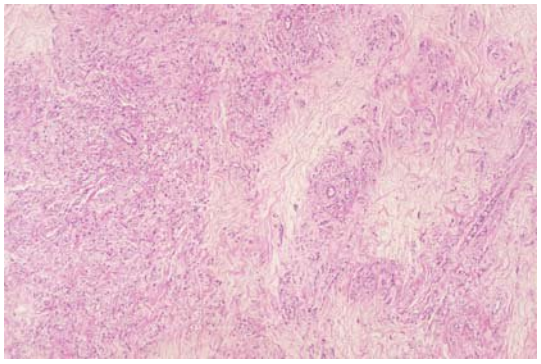
A. Site-specific or characteristic vulvovaginal mesenchymal lesion

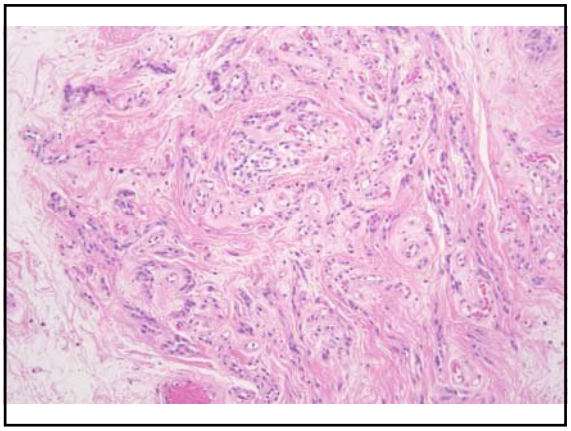
B. Miscellaneous mesenchymal lesions with diagnostic difficulties

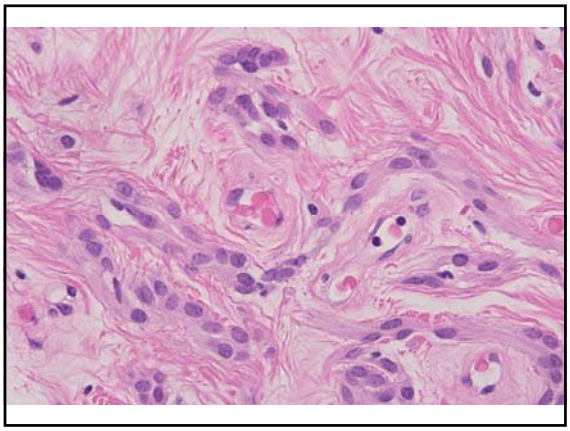
Site-specific or characteristic vulvovaginal mesenchymal lesion

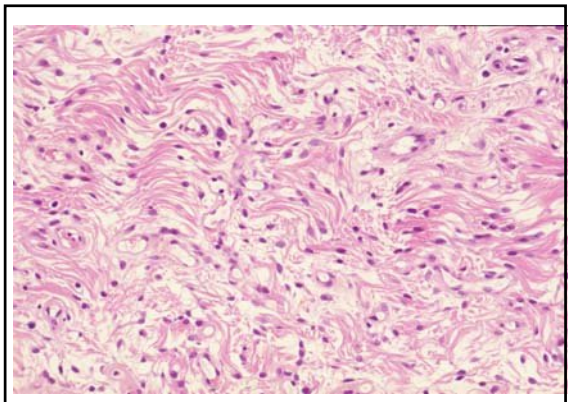
- Angiomyofibroblastoma
- Aggressive angiomyxoma
- Superficial angiomyxoma
- Superficial (cervicovaginal) myofibroblastoma (of the lower uterine genital tract)
- Cellular angiofibroma
- Fibroepithelial stromal polyp
- Prepubertal vulval fibroma
- (Vaginal tubulo-squamous polyp)

A right vulva mass in a 46-year-old female.
Clinical diagnosis: Bartholin gland cyst









Angiomyofibroblastoma

- Reproductive age women (and men)
- Vulva (20%), vagina, inguinal area and scrotum
- Typically small (<5cm), circumscribed, non-recurring superficial soft tissue benign tumor.
- Preoperative diagnosis: Bartholin's gland cyst.

Immunohistochemistry

- ER + (AR+ in men)
- PR +
- Desmin, actin, CD34:+/-
- S100 -

Histology

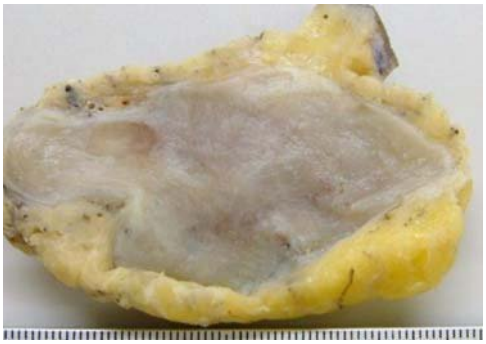
1. Well-circumscribed tumor
2. Alternating hypercellular and hypocellular edematous areas.
3. A vascular proliferation and a perivascular proliferation of spindled and rounded cells showing perivascular epithelioid arrangements
4. A short fascicular or wavy proliferation of predominantly spindle cell
5. Vascualr proliferations
6. Absence of cellular atypia and mitotic figures

Differential diagnosis

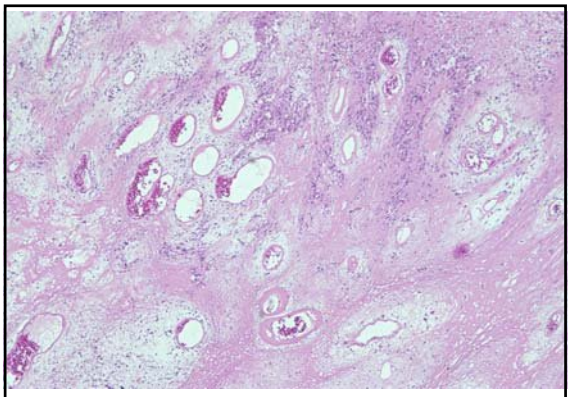
1. Aggressive angiomyxoma
2. Superficial angiomyxoma
3. Cellular angiofibroma
4. Fibroepithelial stromal polyp
5. Benign nerve sheath tumor
6. Myxoid epithelioid leiomyoma

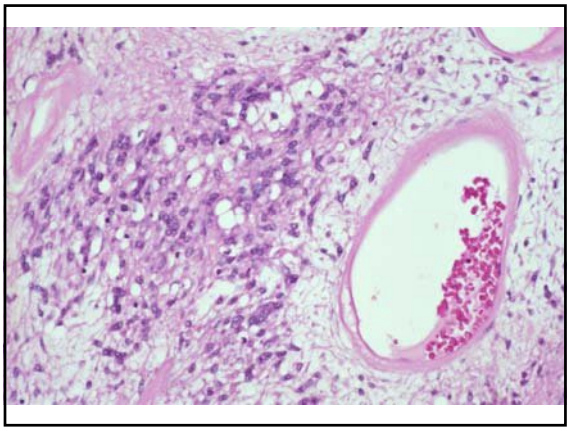
Aggressive angiomyxoma

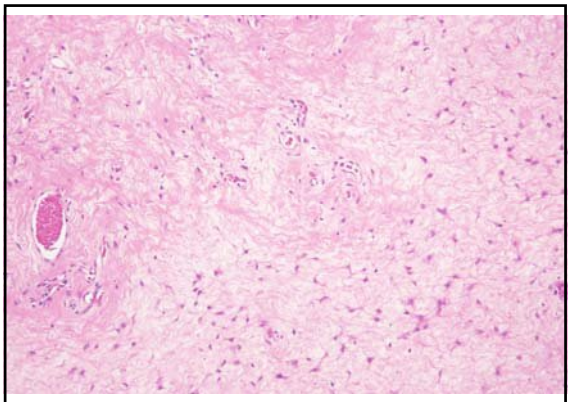
- Subcutaneous or deep soft tissue
- Large (>5cm), gelatinous or myxoid mass with infiltrative margins.
- Bland spindle cell, no nuclear atypia, low mitotic index
- Small to medium sized blood vessels with may be thick walled and hyalinized.
- Condensation of fibrillary collagenous material or bundles of smooth muscle around blood vessels.



Aggressive angiomyxoma



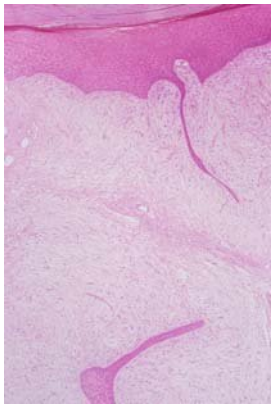


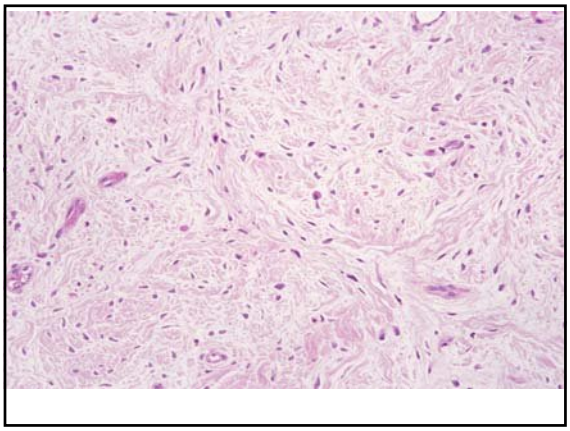


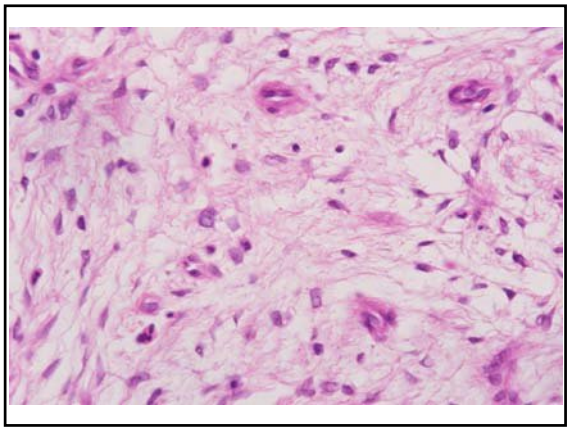
Superficial angiomyxoma

- Superficial, small (>5cm), circumscribed, with multilobulated pattern.
- Neutrophil infiltrates.
- Epithelial or adnexal component (1/3)
- Significant risk for local (nondestructive recurrence (up to 40%).

Vulva
Superficial angiomyxoma

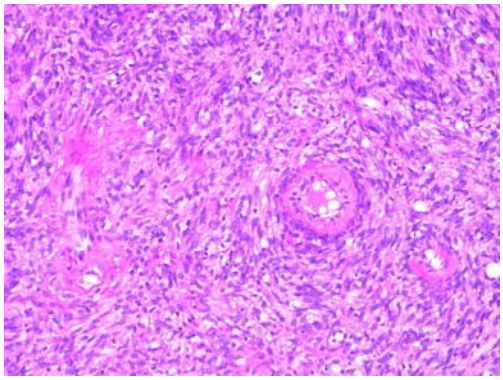






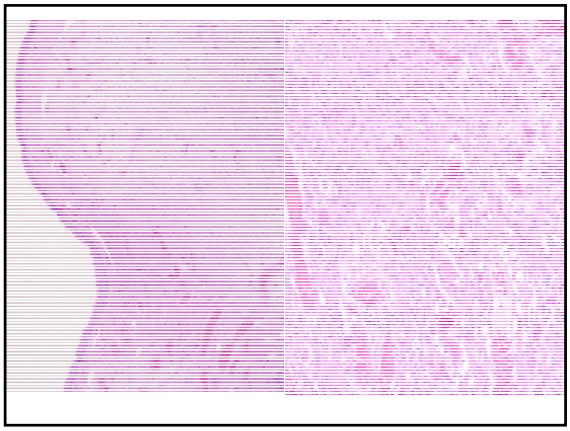
Cellular angiofibroma

- Rare, small (<5cm), superficial soft tissue tumor in middle age women (and men) in the vulvovaginal region and the inguinoscrotal or paratesticular region.
- Numerous small to medium sized vascular vessels with hyalinization.
- Uniform spindle cell proliferation
- Variable mitotically active.
- CD34 +



Superficial cervicovaginal myofibroblastoma

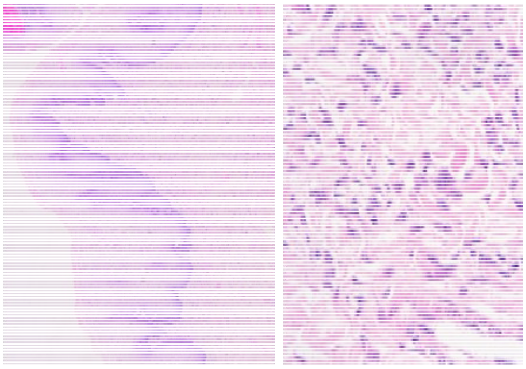
- Cervix, vagina, vulva
- Well-demarcated polypoid or nodular benign lesion
- A well-circumscribed but unencapsulated lesion. The presence of Grenz zone.
- Bland spindle cell proliferation in a fibrous or myxoid stroma
- Fascicular, lacelike, silve-like patterns.
- Immunostaining: No-characteristic: Vimentin, ER, PgR :+. CD34, aSMA: + some cases
- Fibroepithelial stromal polyp : same spectrum?



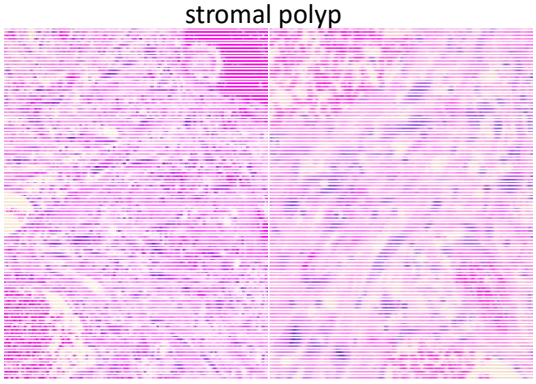
Fibroepithelial stromal polyp

- Small, superficial exophytic or polypoid mass in reproductive aged women.
- Vagina, vulva, cervix.
- No Grenz zone.
- Multinucleate cells, enlarged bizarre nuclei.
- May have high mitotic index (>10/10HPF)
- Pale, edematous and myxoid stroma.
- Variable vascular component with thick-walled vessels in middle.

Fibroepithelial stromal polyp



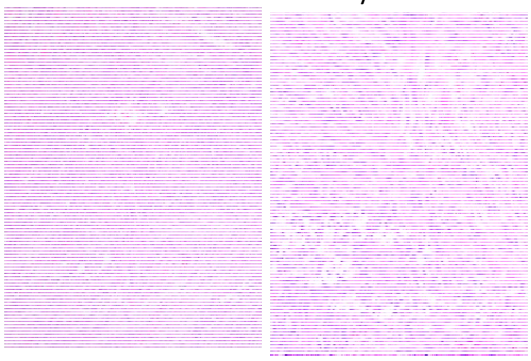
Cellular pseudosarcomatous fibroepithelial stromal polyp



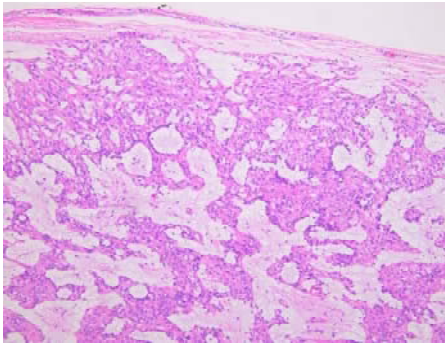
B. Miscellaneous Mesenchymal lesions with diagnostic difficulties

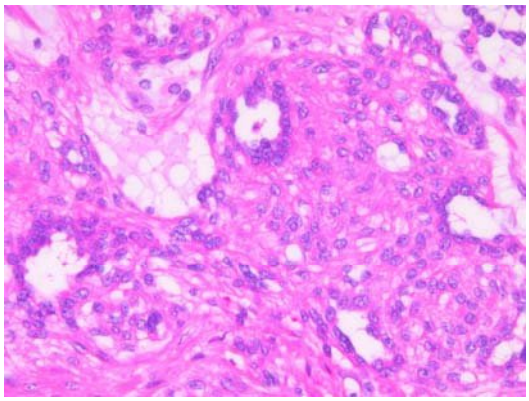
- **Reactive, proliferative lesions**
- **Epithelioid/Biphasic tumors**
- **Myxoid tumors**
- **Others**

A 1.5cm vulva mass in a 28-year-old female



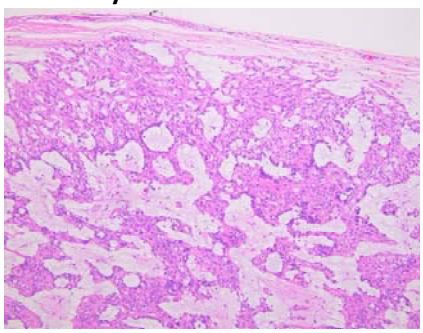
Case: A 2.5cm vaginal mass in a 50-year-old female

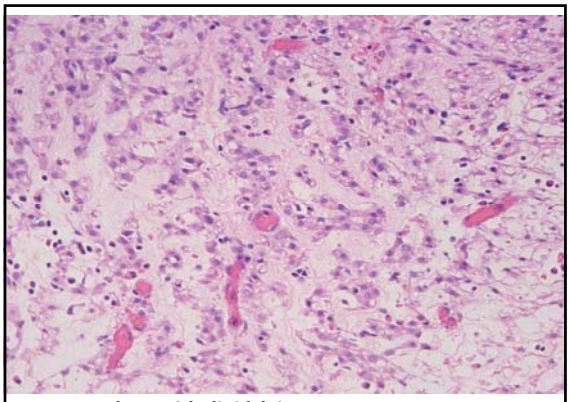




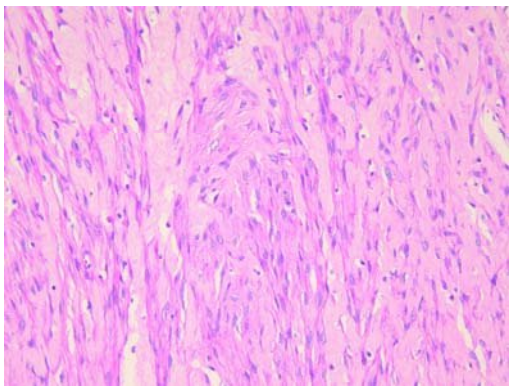
Case: A 2.5cm vaginal mass in a 50-year-old female

Epithelioid leiomyoma

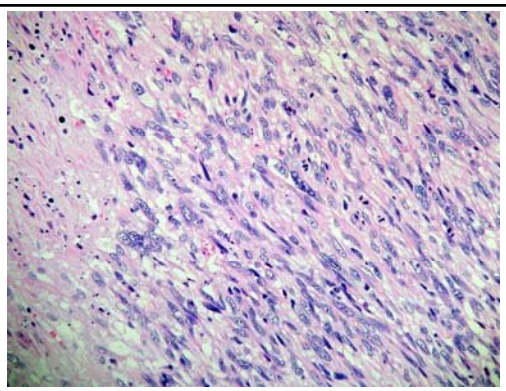




Vulva. epithelioid leiomyoma



Vulva leiomyoma with myxohyaline change



Vulva. Leiomyosarcoma

Vulvovaginal smooth muscle tumors

- Premenopausal women
- Vagina more common than vulval
- Vagina usually benign, but recurrence seen when mitotic index>5/10HPF
- Vulval lesions recur locally and may metastasize to lungs (<25%)
- Main histologic patterns: spindles, myxohyaline and epithelioid.
- ER, PR:+

Vulval smooth muscle tumors

- **Main histologic patterns: spindles, myxohyaline and epithelioid.**

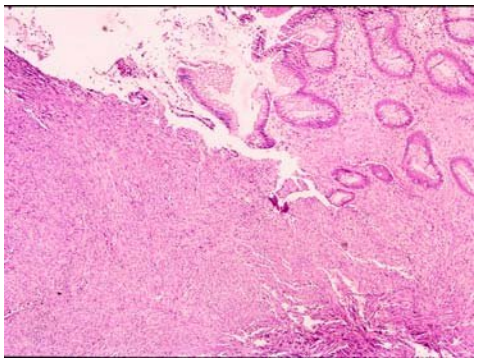
Vulvovaginal smooth muscle tumors: Criteria for malignancy

- Size>5cm*
- Infiltrative margins*
- Moderate to severe cytologic atypia*
- Mitotic index>5/10HPF*
- Tumor cell necrosis

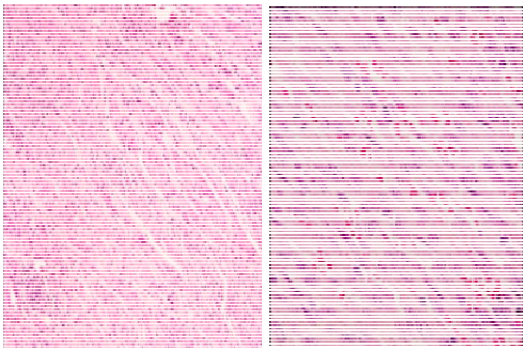
*Tumors with 3 of these features are classified as malignant (leiomyosarcoma).

Any single feature may indicate local recurrence and complete excision is needed.

A "vaginal" nodule in a 34-year-old "female"



A "vaginal" nodule in a 34-year-old "female"



Case: A 34-year-old female (originally male) with a vaginal nodule

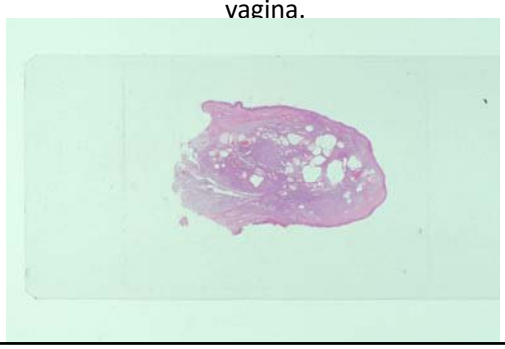
Homosexual, HIV (+)
Vagina was formed by rectum three weeks previously
A nodule at the operative site

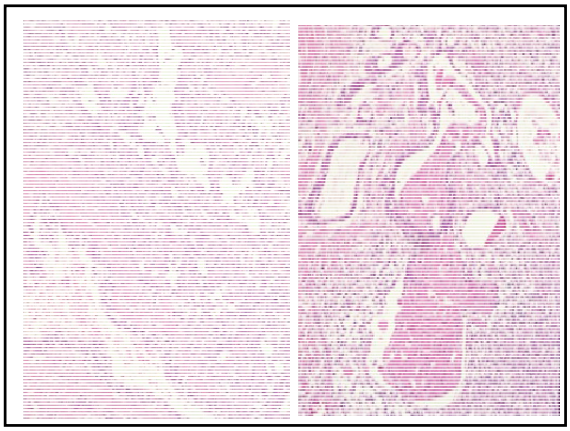
Diagnosis: Postoperative spindle cell nodule

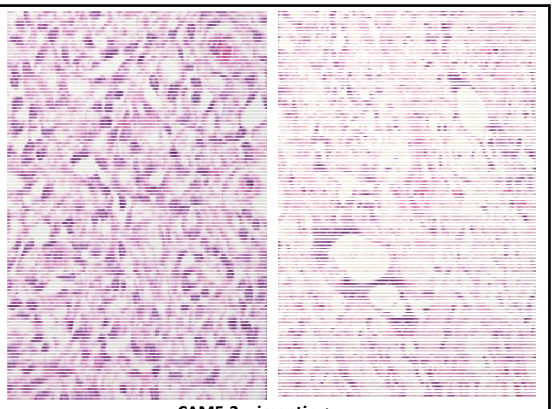
Postoperative spindle cell nodule

- A non-neoplastic localized lesion
- At the site of recent operation several weeks to several months postoperatively, especially in GU or GI areas.
- Closely packed proliferation of spindle cells and capillaries simulating a leiomyosarcoma. Inflammatory cell infiltrates.
- Diagnostic clue: History of a recent operation at the same site

A 33-year-old woman with a polypoid 2.5 cm mass in the posterior wall of the lower vagina vagina.





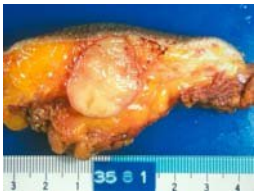


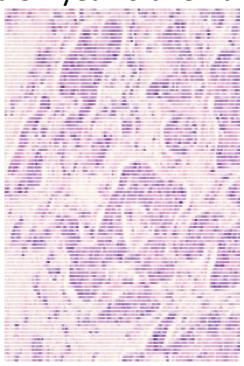
CAM5.2, vimentin:+

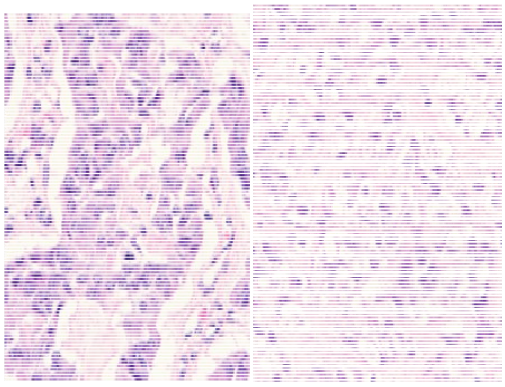
Mixed tumor of the vagina

1. women of reproductive age
2. Occurring proximal to the hymen
3. A non-encapsulated, well-circumscribed mass
4. A proliferation of small, bland stromal cells
5. A nest of well-differentiated squamous cells and occasional mucinous glands
6. A good prognosis

A 3cm vulva mass in a 52-year-old female







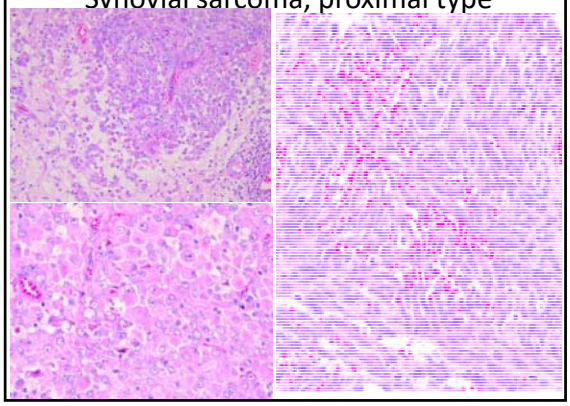
Malignant myoepithelioma of the soft tissue (myoepithelial carcinoma)

Tumor with moderate or severe nuclear atypia In soft tissue cases.

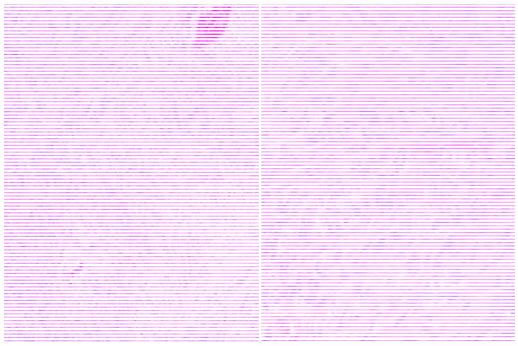
Hornick H, Fletcher CDM.

Am J Surg Pathol ;27:1183-96.

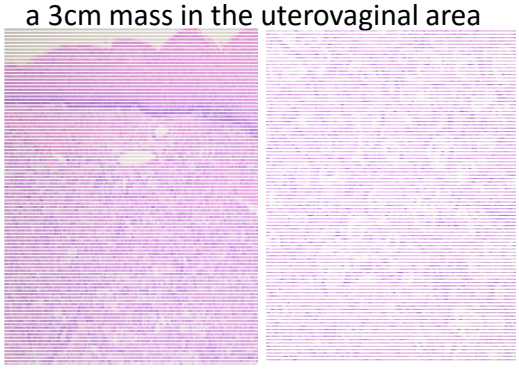
Synovial sarcoma, proximal type



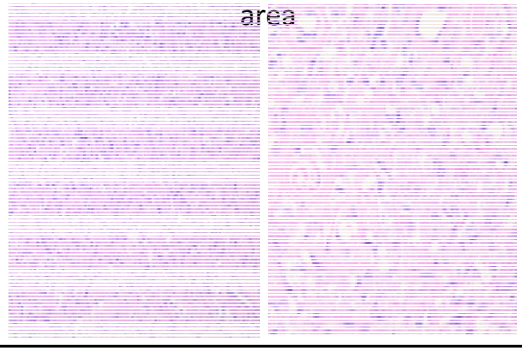
A 3cm vaginal tumor in 54-year-old female
Extra GI GIST



A 31-year-old female
a 3cm mass in the uterovaginal area



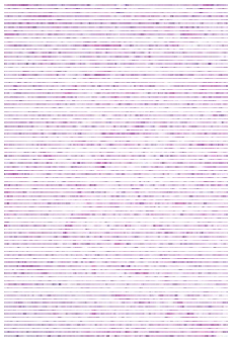
A 31-year- old female
a 3cm, mass tumor in uterovaginal area



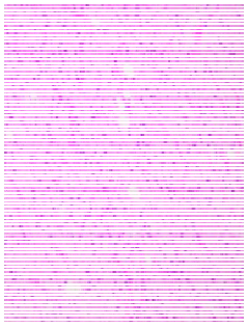
Sclerosing perivascular epitheliod cell tumor （PEComa)

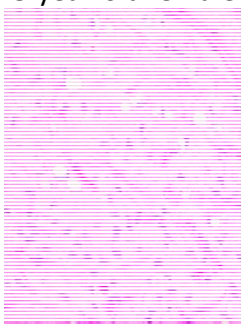
- PEComa with extensive stromal hyalinization
- Women, middle aged (mean, 49 yrs)
- Retroperitoneum, pelvic cavity, uterus
- Rarely recur or metastasize

Dermatofibrosarcoma protuberans, myxoid type



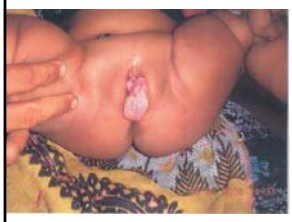
A vulvar mass in a 78-year-old female





Myxoid liposarcoma

A 2cm vaginal mass in a three month old female



Embryonal rhabdomyosarcoma
Sarcoma botryoid ブドウ状肉腫

***Miscellaneous mesenchymal lesions with diagnostic difficulties* (continued)**

- ***Reactive, proliferative lesion*: Nodular fasciitis. Postoperative spindle cell nodule, endometriosis**
- ***Epithelioid/Biphasic tumor:***

smooth muscle tumor
mixed tumor of vagina
myoepithelioma
synovial sarcoma
GIST
PEComa
(mesonephric adenocarcinoma with spindle cell component)

Miscellaneous mesenchymal lesions with diagnostic difficulties

- **Myxoid tumor: smooth muscle tumor, myxoid DFSP, myxoid liposarcoma**
- **Other mesenchymal tumors：embryonal rhabdomyosarcoma, Ewing sarcoma, SFT.**
- **Mammary type tumors: fibroadenoma, phyllodes tumor, myofibroblastoma**

Conclusions

- **If clinically benign , but not easily classified, consider "specialized (gonadal) stromal tumor"**

  Immuostains are not always useful
- **Exclude reactive and/or inflammatory processes.**
- **Take care a lot if smooth muscle tumor is diagnosed. The criteria of malignancy is not same as those in the uterus.**
- **Consider extension from retroperitoneum, pelvic, and mammary type lesions.**