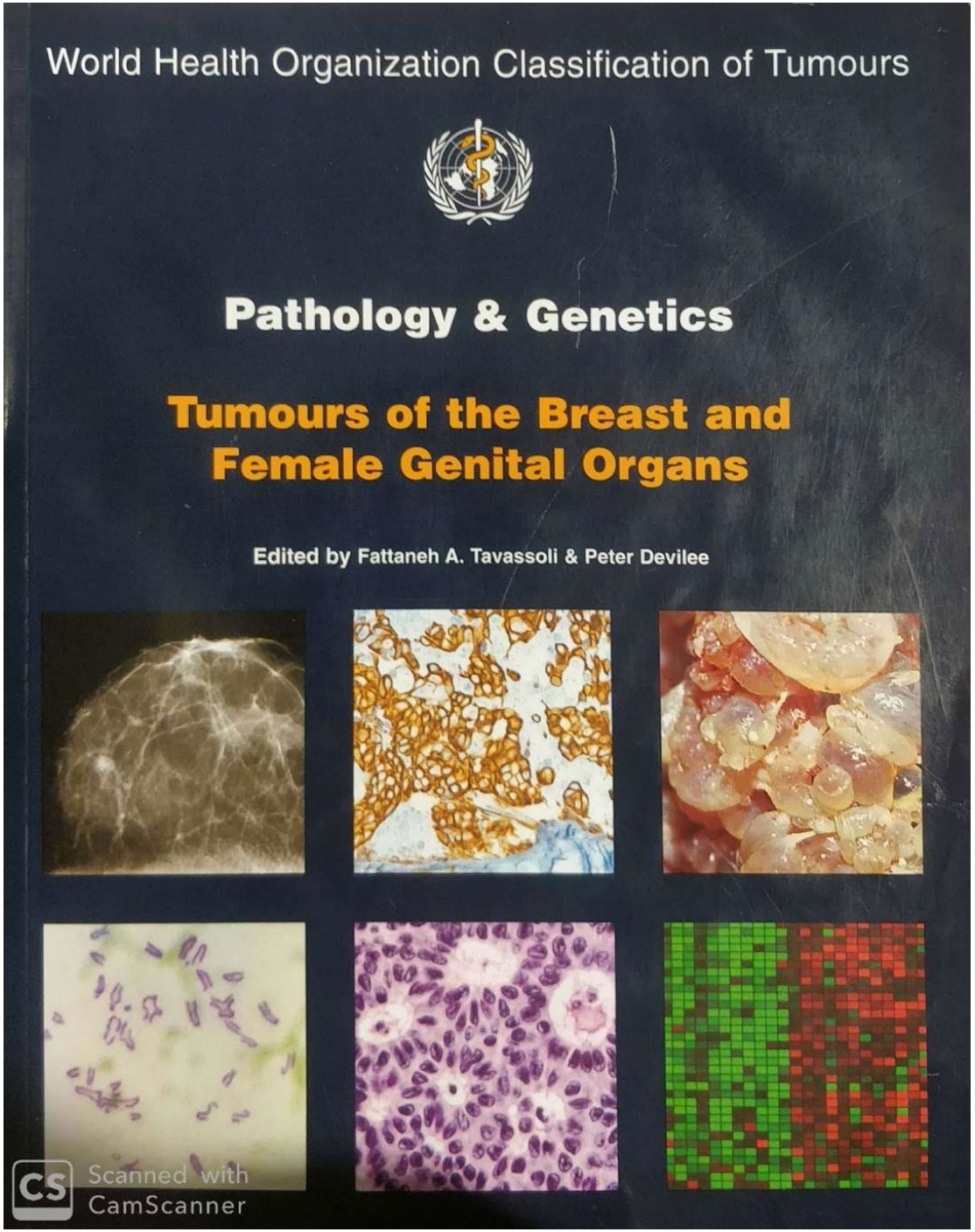
LESIONES INTRAEPITELIALES DE VULVA

Sebastián Ortiz Reina, Alejandra Isaac Montero y Tamara Ibarra Selva
Complejo Hospitalario Universitario de Cartagena

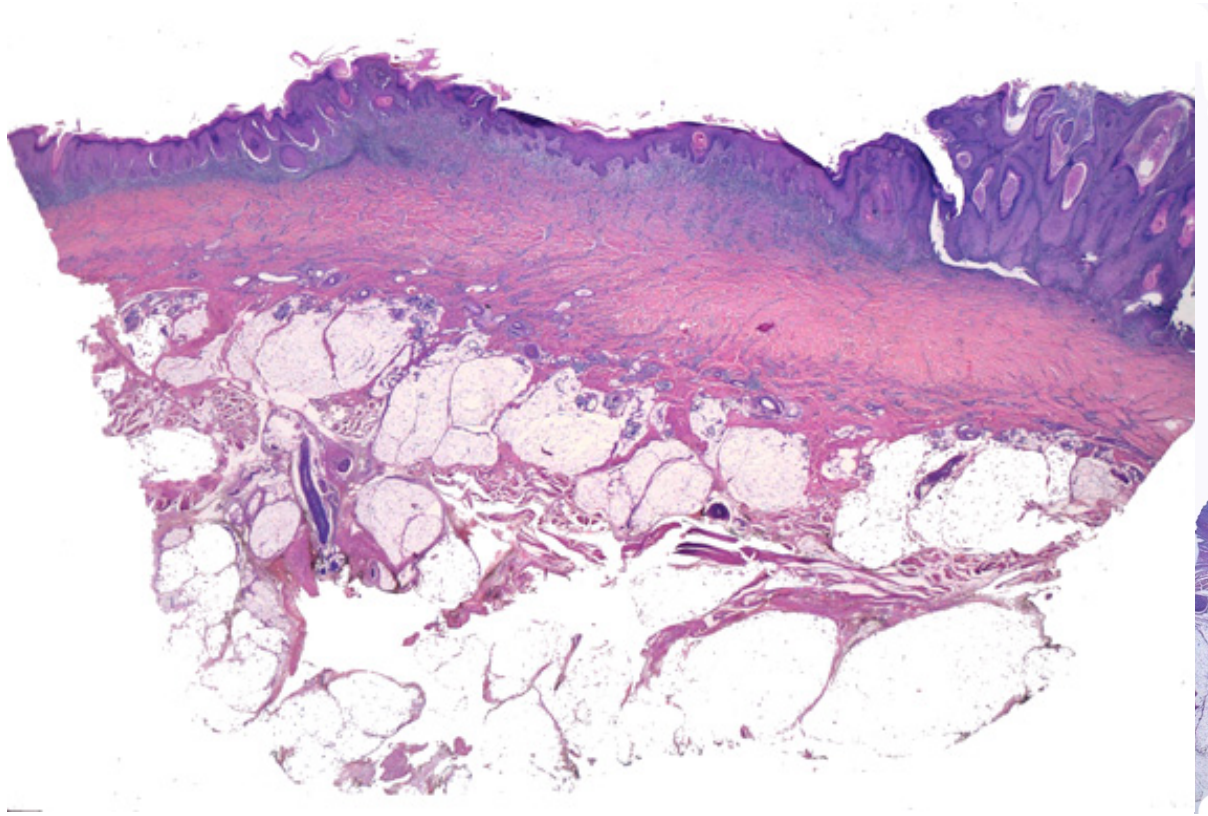
Sheela na Gigs

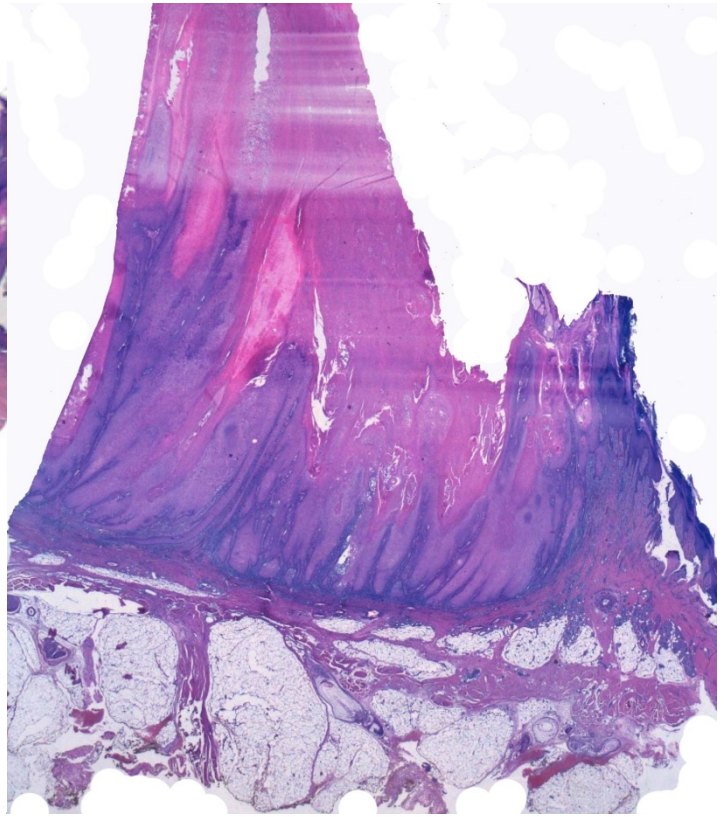


2003

Table 7.01
Currently recognized precursors of vulvar squamous cell carcinoma.

(1) Vulvar intraepithelial neoplasia (VIN) and associated human papillomavirus (HPV) infection.
(2) The simplex (differentiated) type of VIN not associated with HPV infection {1621,3175}.
(3) Lichen sclerosus {1621} with associated squamous cell hyperplasia {403}.
(4) Chronic granulomatous vulvar disease such as granuloma inguinale {2628}.





The Lower Anogenital Squamous Terminology Standardization Project for HPV-Associated Lesions:

Background and Consensus Recommendations from the College of American Pathologists and the American Society for Colposcopy and Cervical Pathology

Teresa M. Darragh, MD;[1] Terence J. Colgan, MD;[2] J. Thomas Cox, MD;[3] Debra S. Heller, MD;[3] Michael R. Henry, MD;[4] Ronald D. Luff, MD;[5,6] Timothy McCalmont, MD;[1] Ritu Nayar, MD;[7] Joel M. Palefsky, MD;[1] Mark H. Stoler, MD;[8] Edward J. Wilkinson, MD;[9] Richard J. Zaino, MD;[10] David C. Wilbur, MD,[11] for members of the LAST Project Work Groups

Arch Pathol Lab Med—Vol 136, October 2012

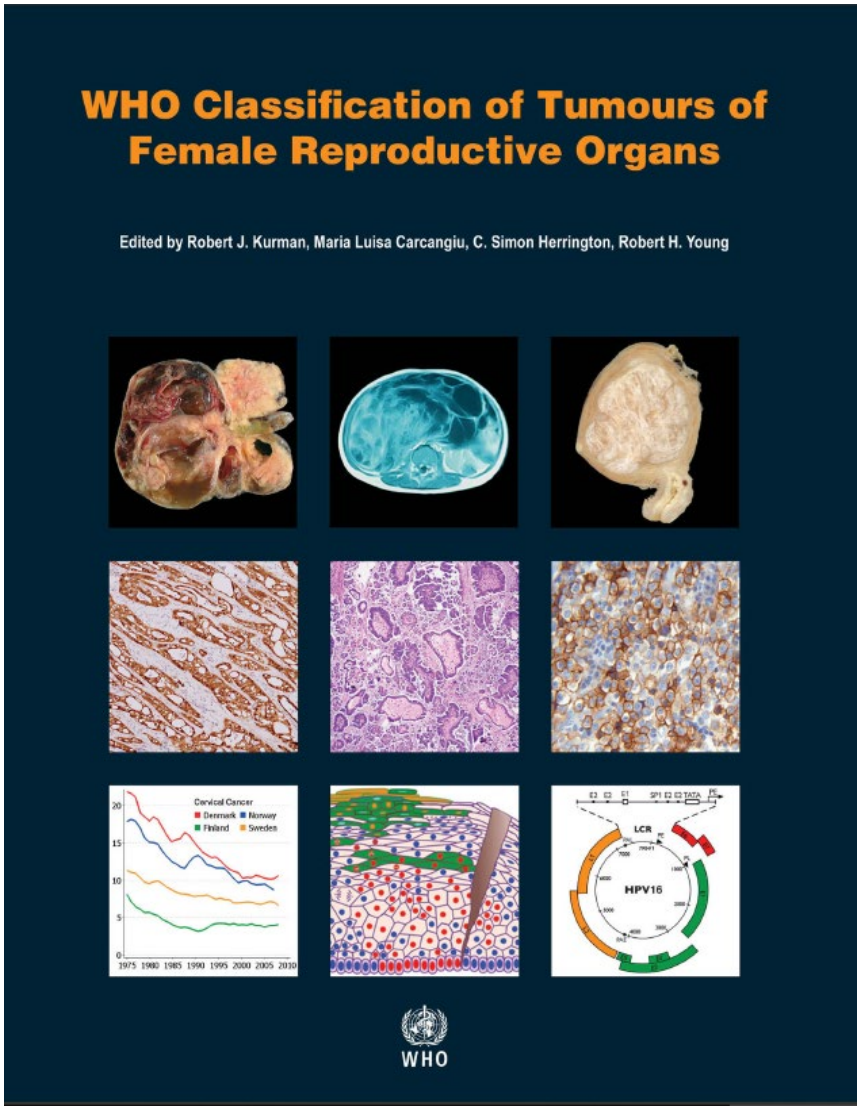
The following LAST Steering Committee members, Work Group members, and/or Conference Moderators have no perceived conflicts of interest to report: Jill Allbritton, Sarah Bean (advisor), Joel Bentz, Debra Heller, Gene Herbeck, Rodolfo Laucirica, Christopher Otis, Stanley Robboy, Mary Schwartz, Mark Welton, and Barbara Winkler.

Steering Committee: Dr Darragh serves on the advisory boards of OncoHealth and Arbor Vita Corporation; she owns stock in OncoHealth and receives grants from the National Institutes of

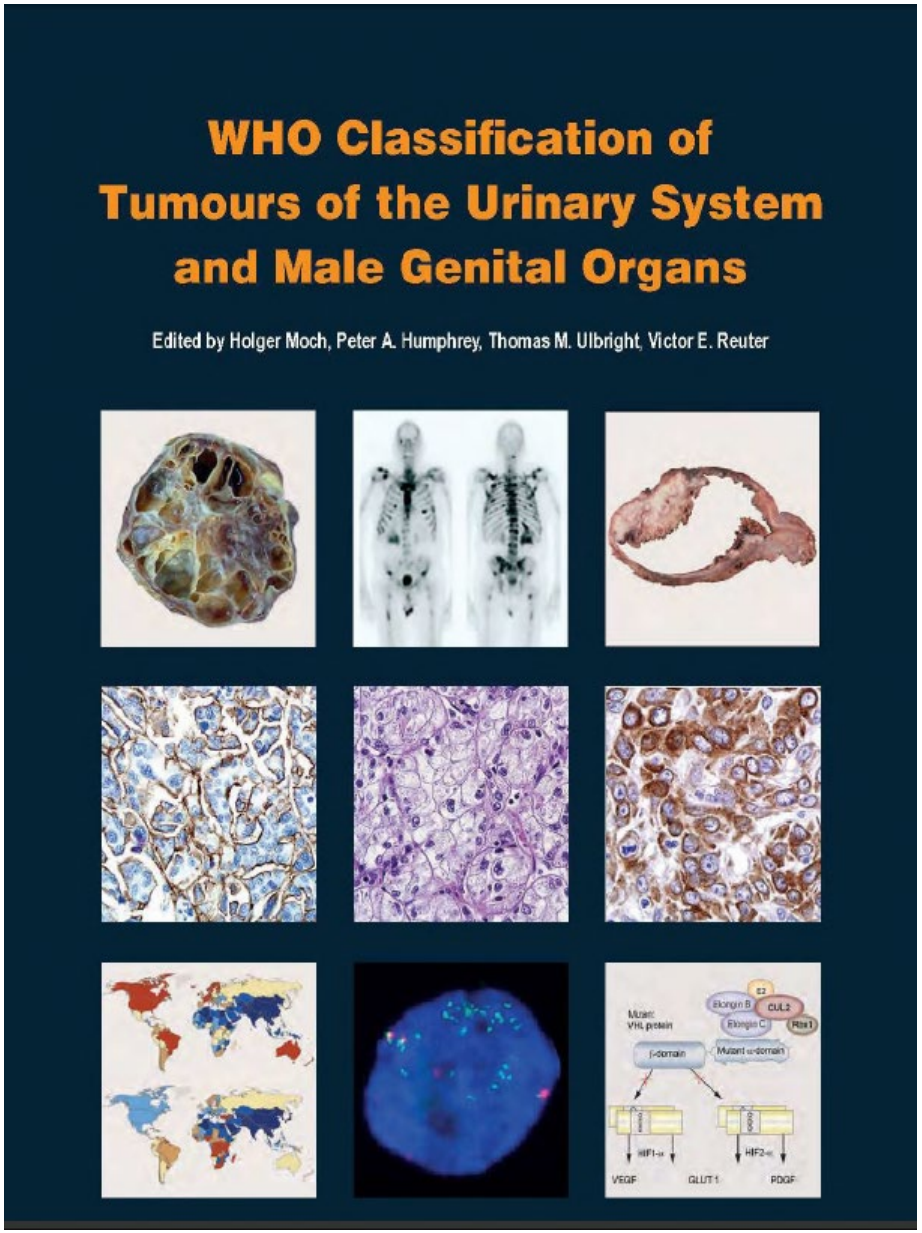
Recommendation
SQUAMOUS INTRAEPITHELIAL LESIONS, WG2
1. A unified histopathologic nomenclature with a single set of diagnostic terms is recommended for all HPV-associated preinvasive squamous lesions of the LAT.
2. A 2-tiered nomenclature is recommended for noninvasive HPV-associated squamous proliferations of the LAT, which may be further qualified with the appropriate –IN terminology.
3. The recommended terminology for HPV-associated squamous lesions of the LAT is LSIL and HSIL, which may be further classified by the applicable –IN subcategorization.

2012

2014



Epithelial tumours	
Squamous cell tumours and precursors	
Squamous intraepithelial lesions	
Low-grade squamous intraepithelial lesion	8077/0
High-grade squamous intraepithelial lesion	8077/2
Differentiated-type vulvar intraepithelial neoplasia	8071/2*
Squamous cell carcinoma	8070/3
Keratinizing	8071/3
Non-keratinizing	8072/3
Basaloid	8083/3
Warty	8051/3
Verrucous	8051/3
Basal cell carcinoma	8090/3
Benign squamous lesions	
Condyloma acuminatum	
Vestibular papilloma	8052/0
Seborrheic keratosis	
Keratoacanthoma	
Glandular tumours	
Paget disease	8542/3
Tumours arising from Bartholin and other specialized anogenital glands	
Bartholin gland carcinomas	
Adenocarcinoma	8140/3
Squamous cell carcinoma	8070/3
Adenosquamous carcinoma	8560/3
Adenoid cystic carcinoma	8200/3
Transitional cell carcinoma	8120/3
Adenocarcinoma of mammary gland type	8500/3
Adenocarcinoma of Skene gland origin	8140/3
Phyllodes tumour, malignant	9020/3
Adenocarcinomas of other types	
Adenocarcinoma of sweat gland type	8140/3
Adenocarcinoma of intestinal type	8140/3



2016

Table 5.03 Pathological classification of penile intraepithelial neoplasia (PeIN)

1. Non–HPV-related PeIN
   - Differentiated (simplex) PeIN
2. HPV-related PeIN
   - Basaloid PeIN
   - Warty PeIN
   - Warty–basaloid PeIN
3. Other rare patterns of PeIN
   - Pleomorphic
   - Spindle
   - Clear cell
   - Pagetoid

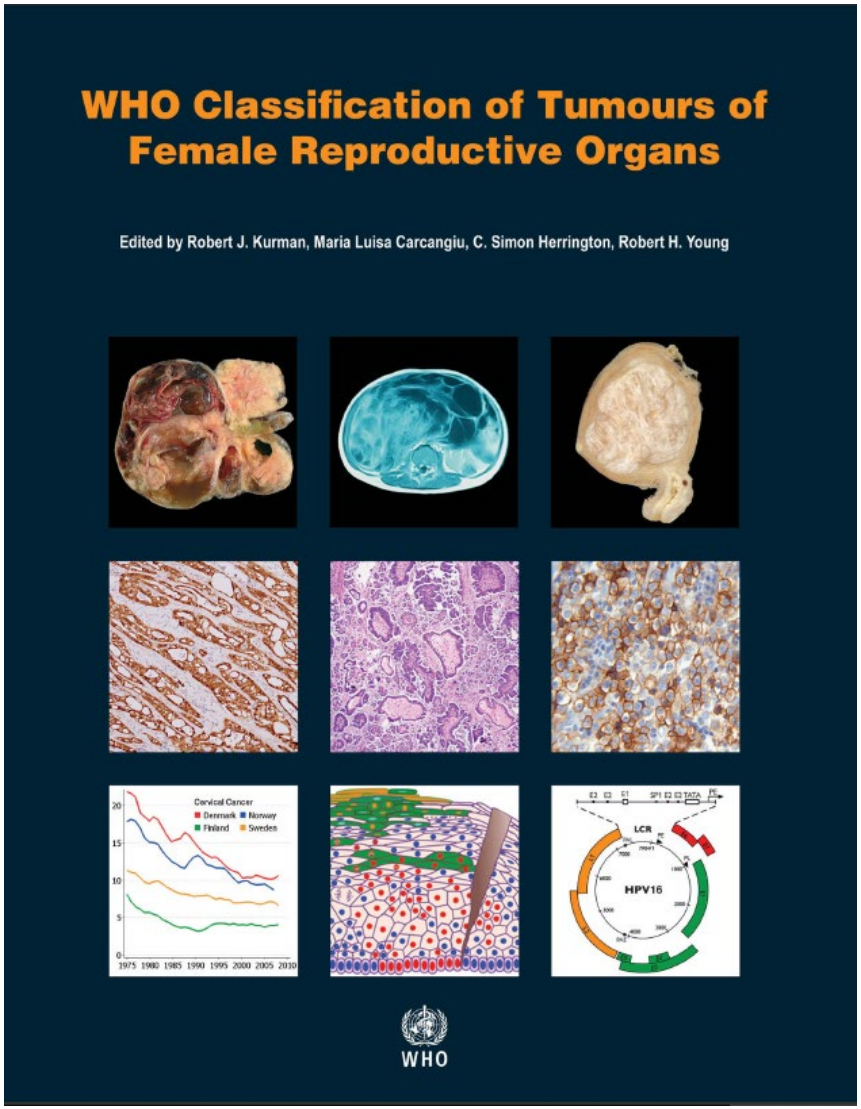
LESIONES ESCAMOSAS INTRAEPITELIALES.

CONDILOMAS MALIGNIZADOS.

ADENOCARCINOMAS DE VULVA CON EXTENSIÓN PAGETOIDE.

LESIONES ESCAMOSAS INTRAEPITELIALES

2014



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LESIONES ESCAMOSAS INTRAEPITELIALES HPV DEPENDIENTES.

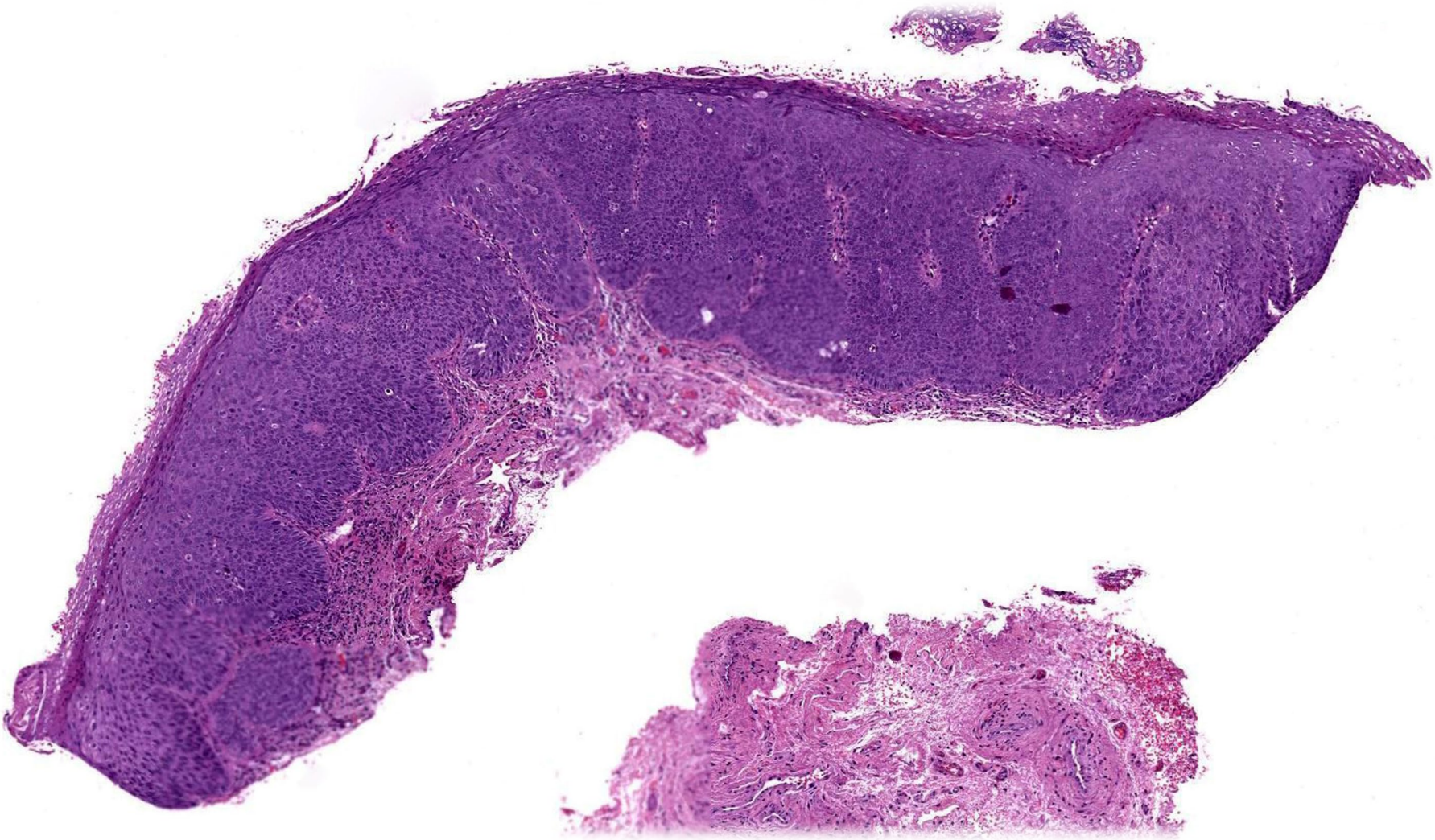
ISSVD 1986	WHO 2003	ISSVD 2005	WHO 2014
VIN 1	Displasia leve	Condiloma acuminado	SIL bajo grado (LSIL)
VIN 2	Displasia moderada	VIN clásico / usual	SIL alto grado (HSIL)
VIN 3	Displasia intensa		
VIN 3 diferenciado	CIS tipo simple	VIN diferenciado	VIN tipo diferenciado (d-VIN)

◇ HPV - dependiente

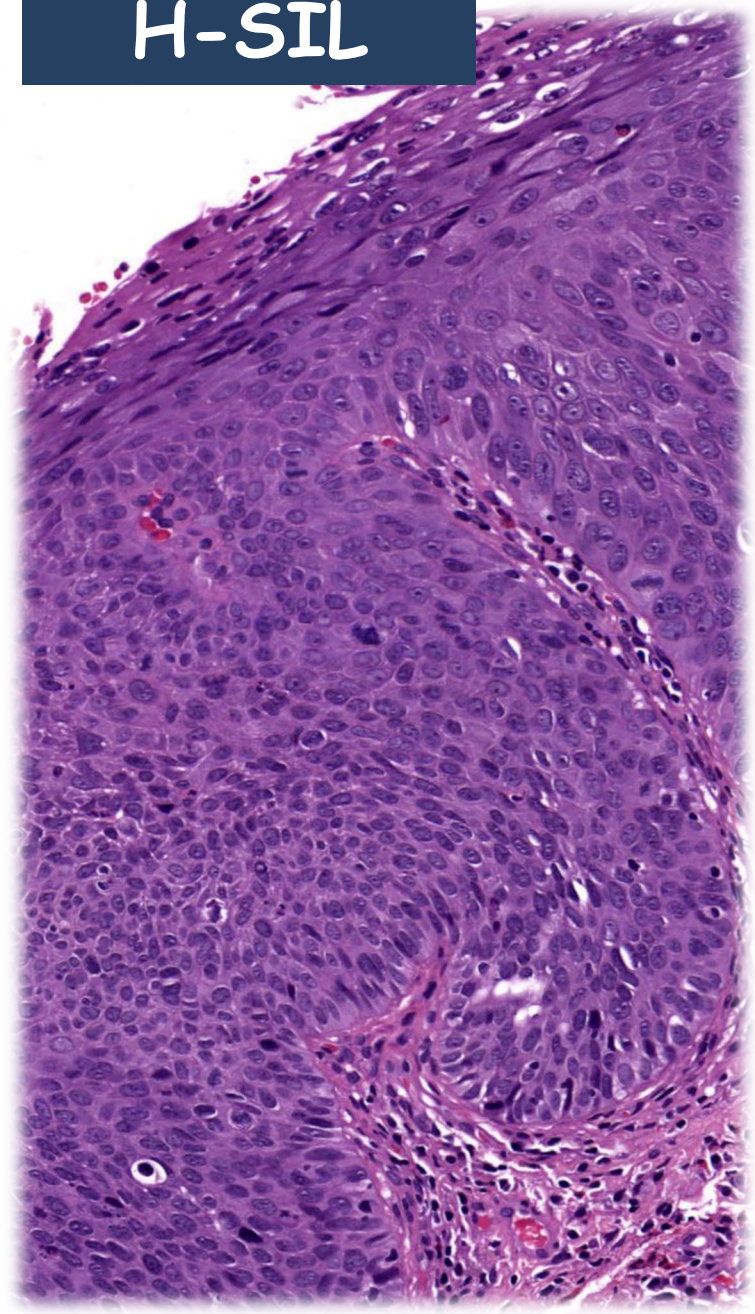
◇ HPV - independiente

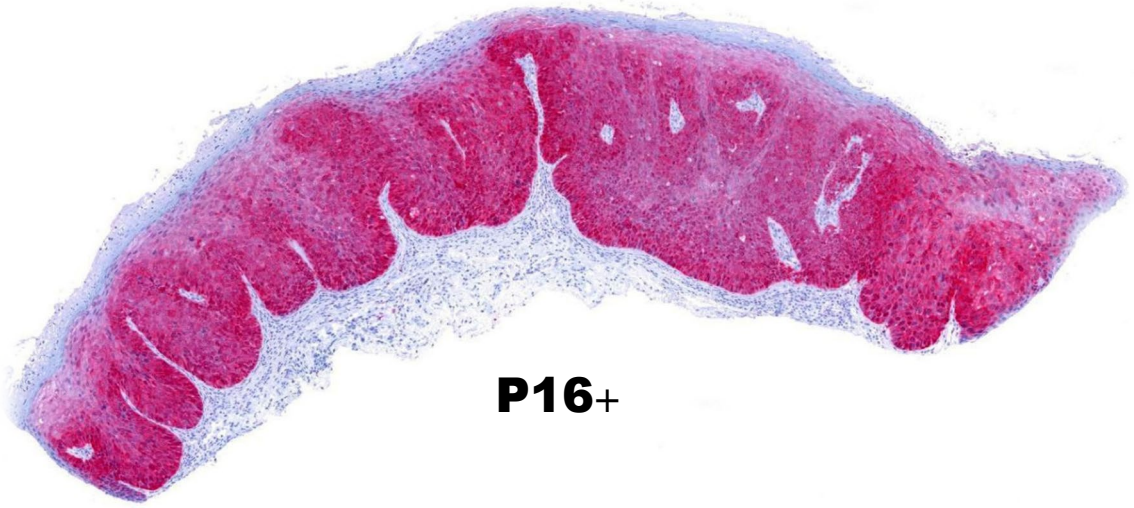
- En cara lateral inferior izquierda de introito vaginal presenta placa geográfica blanquecina, hiperqueratósica, sobreelevada, bien delimitada, sangrante al tacto y pruriginosa, de 4cm.

H-SIL



H-SIL





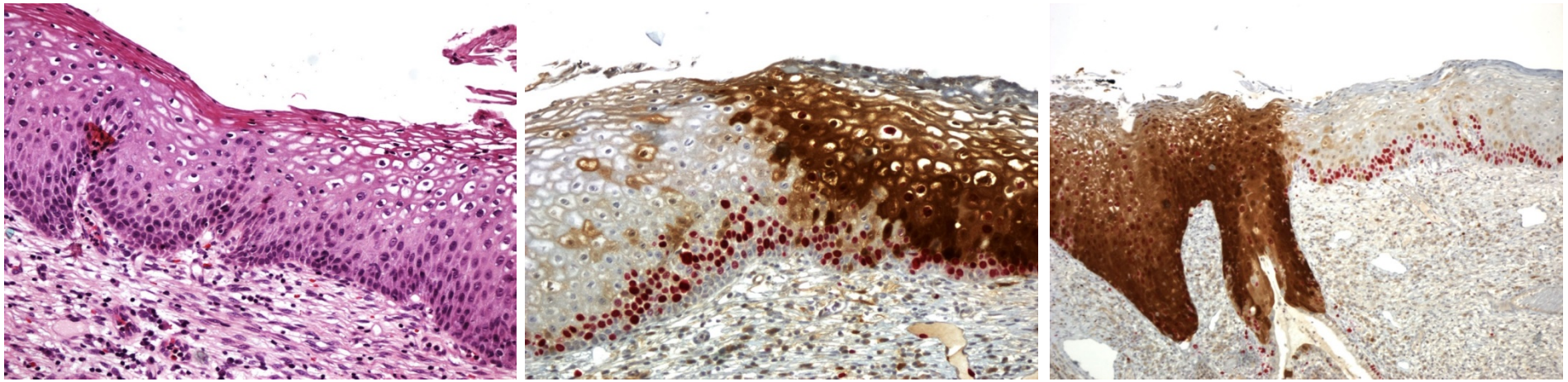
P16+

- Núcleos hipercromáticos y pleomorfos.
- Mitosis fuera del estrato basal. Pérdida de la normal estratificación y de la polaridad nuclear.
- Lesión intraepitelial pavimentosa de alto grado, con HPV 16+

La proteína p16, codificada por el gen supresor CDKN2A (MTS1, INK4A) situado en el cromosoma 9p21.

- Elevada sensibilidad para lesiones de alto grado.
- Alta especificidad.
- Es fácil de evaluar.

UTILIDAD p16



DUAL (p16 / Ki 67), vulva y cérvix

- Positivo: Patrón de tinción difuso: Intensa inmunotinción nuclear y citoplasmática, de distribución continua, localizada en capas basal y parabasal (1/3 INFERIOR) del epitelio escamoso, con o sin tinción de las células de capas superficiales.
- Negativo: Patrón de tinción negativo: No se tiñe el epitelio escamoso. Patrón de tinción focal: Se tiñen células aisladas o pequeños grupos (EN DAMERO).

The LAST Guidelines in Clinical Practice

Implementing Recommendations for p16 Use

Lani K. Clinton, MD, PhD,[1,2] *Kyle Miyazaki,*[1] *Asia Ayabe,*[1] *James Davis, PhD,*[2] *Pamela Tauchi-Nishi, MD,*[1,2] *and David Shimizu, MD*[1,2]

From the [1]Hawaii Pathologists' Laboratory, Queen's Medical Center, Honolulu, and [2]John A. Burns School of Medicine, Universi

Key Words: p16; LAST guidelines; Cervical pathology; Gynecologic pathology

Am J Clin Pathol December 2015;144:844-849

Recommendation 1: HSIL vs mimics

Recommendation 2: Possible CIN2

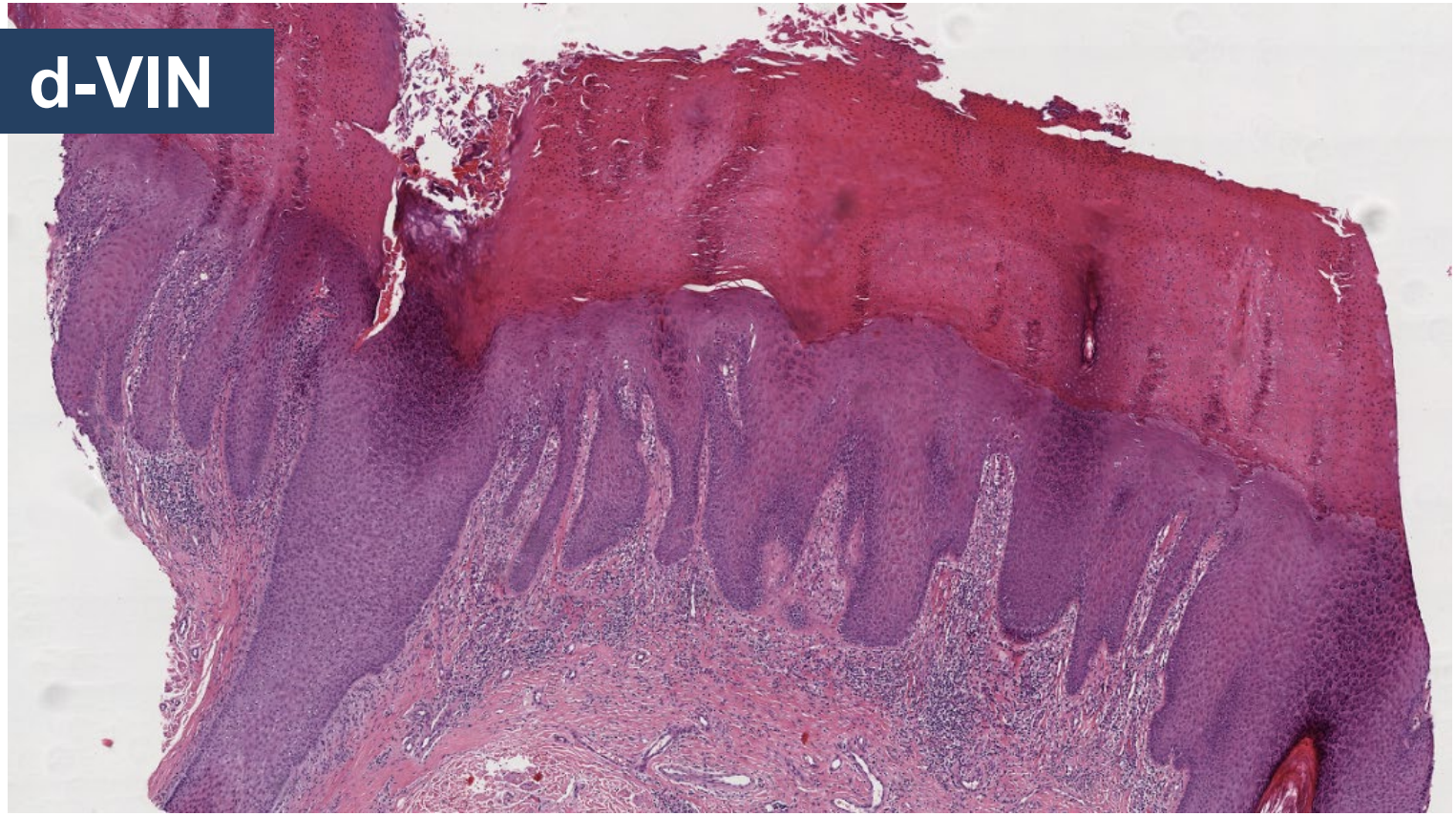
Recommendation 3: Professional disagreement

Recommendation 4a: High-risk colposcopic referral situations with H&E biopsy specimens initially LSIL or lower

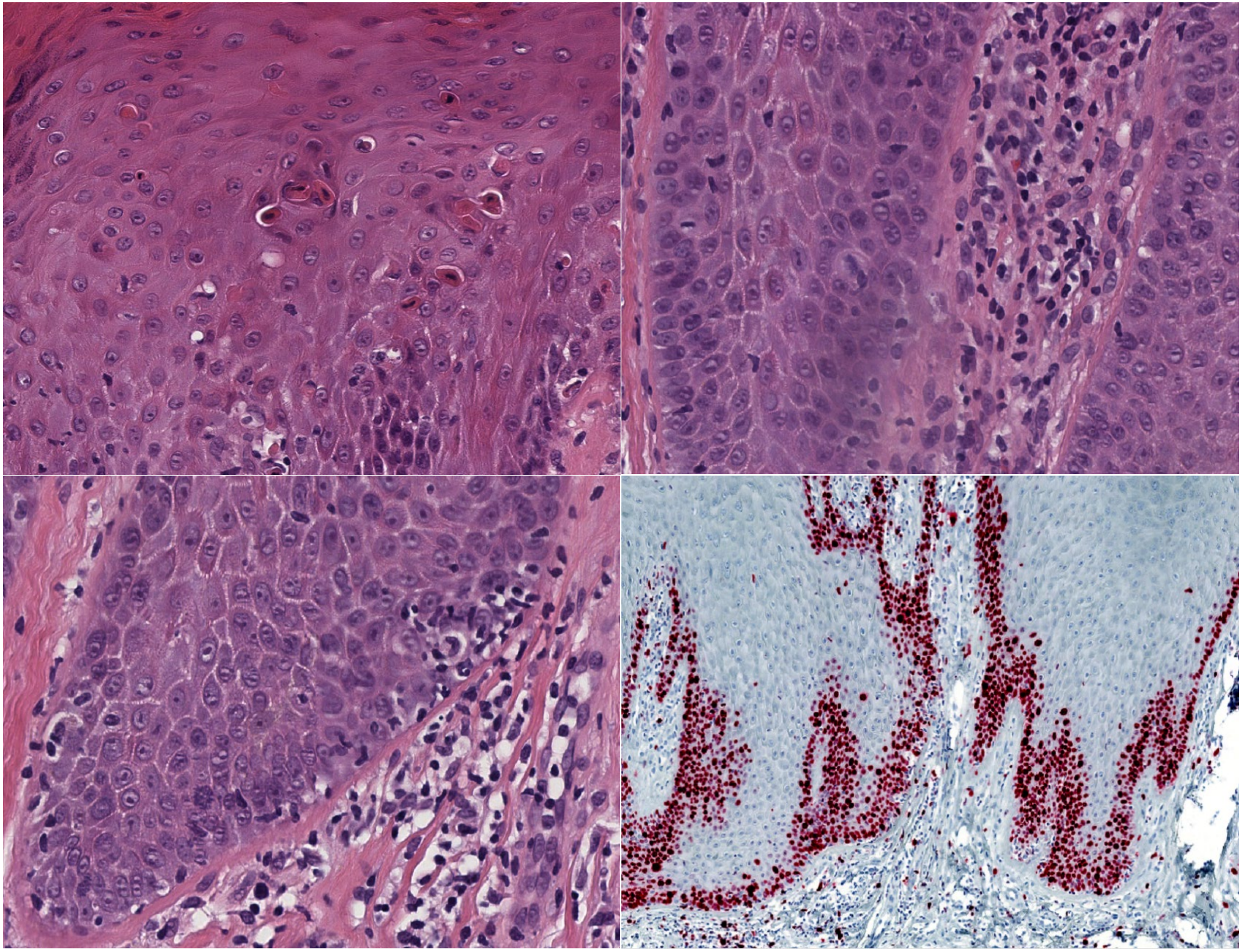
LESIONES ESCAMOSAS INTRAEPITELIALES HPV INDEPENDIENTES (d-VIN)

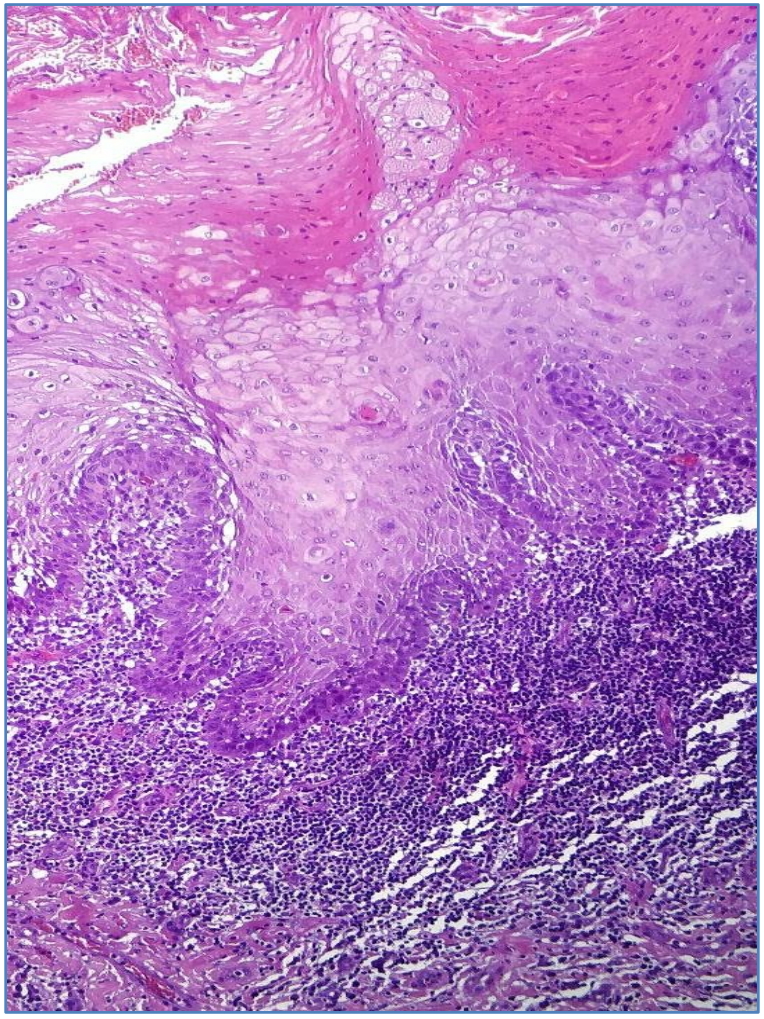
d-VIN

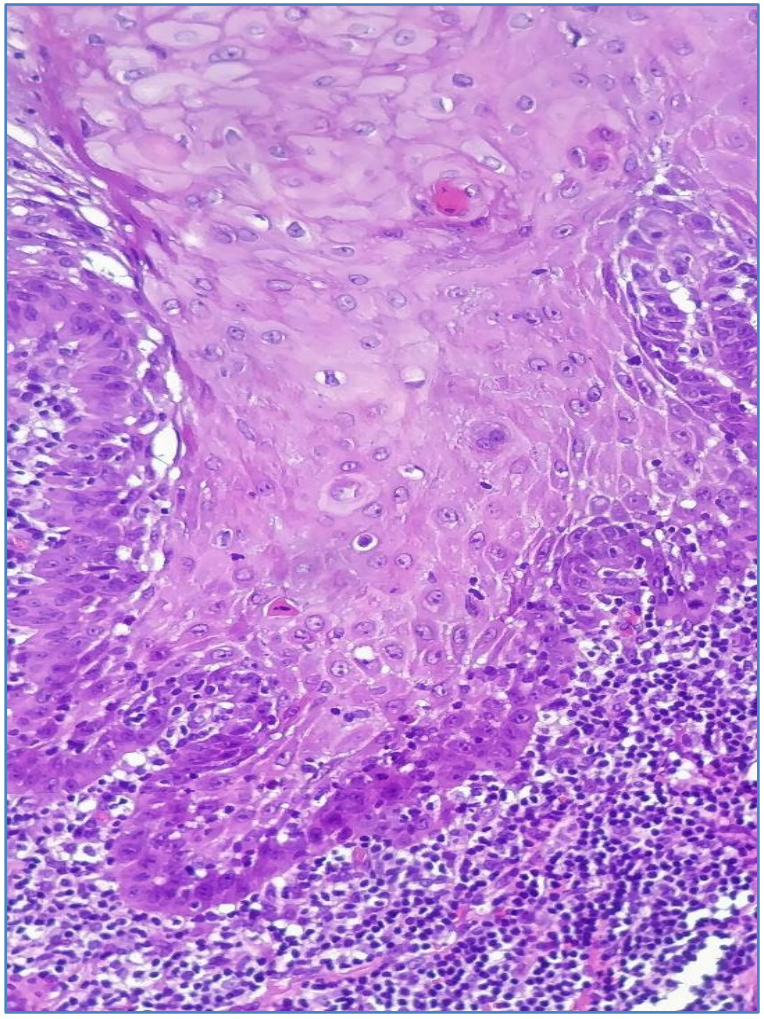
d-VIN



- APARIENCIA ADOQUINADA.
- ATIPIA NUCLEAR: HIPERCROMATISMO, ANGULACIÓN, MULTINUCLEACIÓN Y MACRONUCLEOLOS.
- MITOSIS SUPRABASALES.
- QUERATINIZACION PRECOZ E HIPEREOSINOFILICA (CÉLULAS REFRACTILES). PERLAS CORNEAS Y ESPONGIOSIS.
- HIPERQUERATOSIS, PARAQUERATOSIS.
- HIALINIZACIÓN DEL CORION SUBEPITELIAL.
- INFILTRADO EN BANDA CON ESCASAS PLASMÁTICAS.







Virchows Archiv (2018) 473:739–747
https://doi.org/10.1007/s00428-018-2436-8

ORIGINAL ARTICLE

Differentiated vulvar intraepithelial neoplasia (dVIN): the most helpful histological features and the utility of cytokeratins 13 and 17

Shatavisha Dasgupta[1] · Patricia C. Ewing-Graham[1] · Folkert J. van Kemenade[1] · Helena C. van Doorn[2] · Vincent Noordhoek Hegt[1] · Senada Koljenović[1]

Recently, the diagnostic utility of the immunohistochemical markers cytokeratin 13 (CK13) and cytokeratin 17 (CK17) has been established for oral epithelial dysplasia [15–17]. Loss of CK13 along with expression of CK17 has been reported in (high-grade) oral epithelial dysplasia [15–17]. Increased expression of CK17 has been reported for dVIN

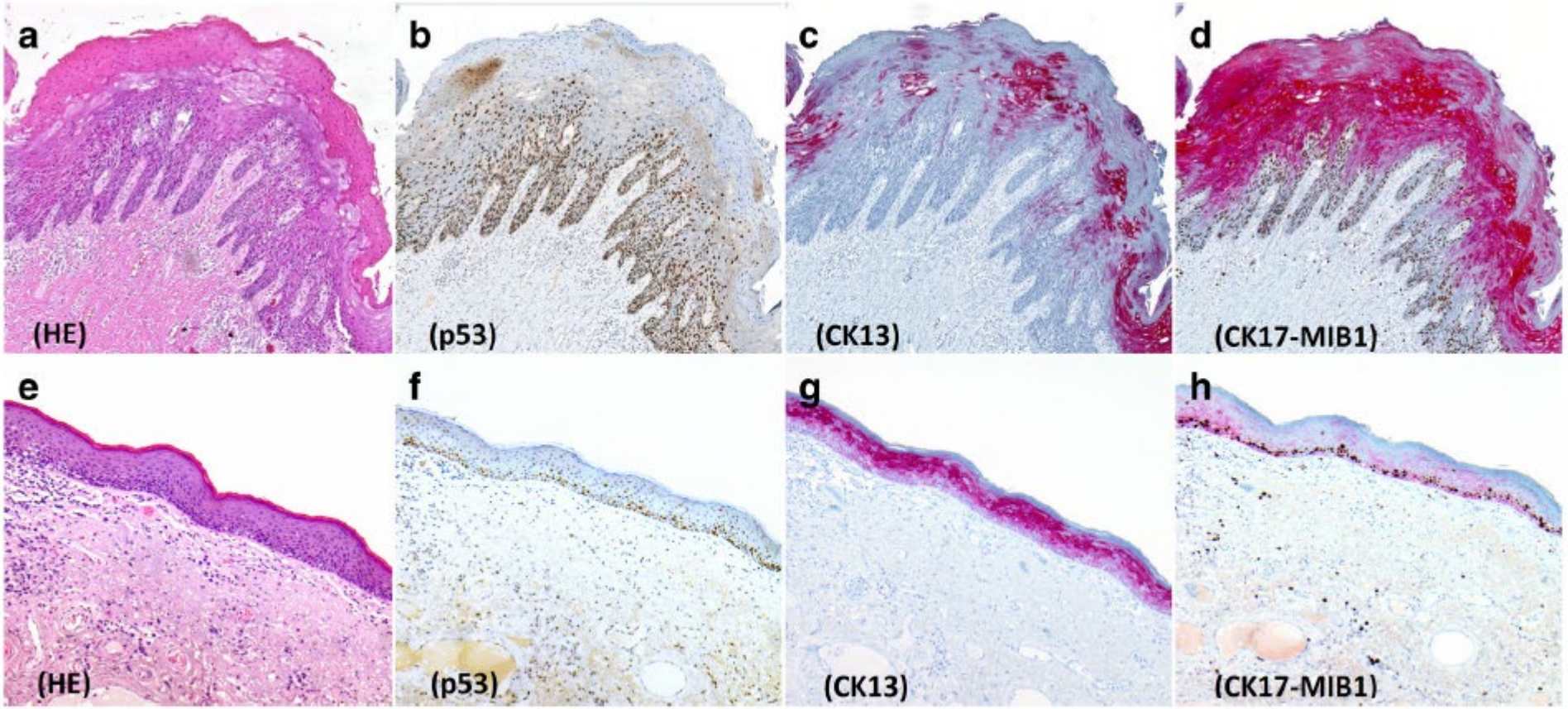
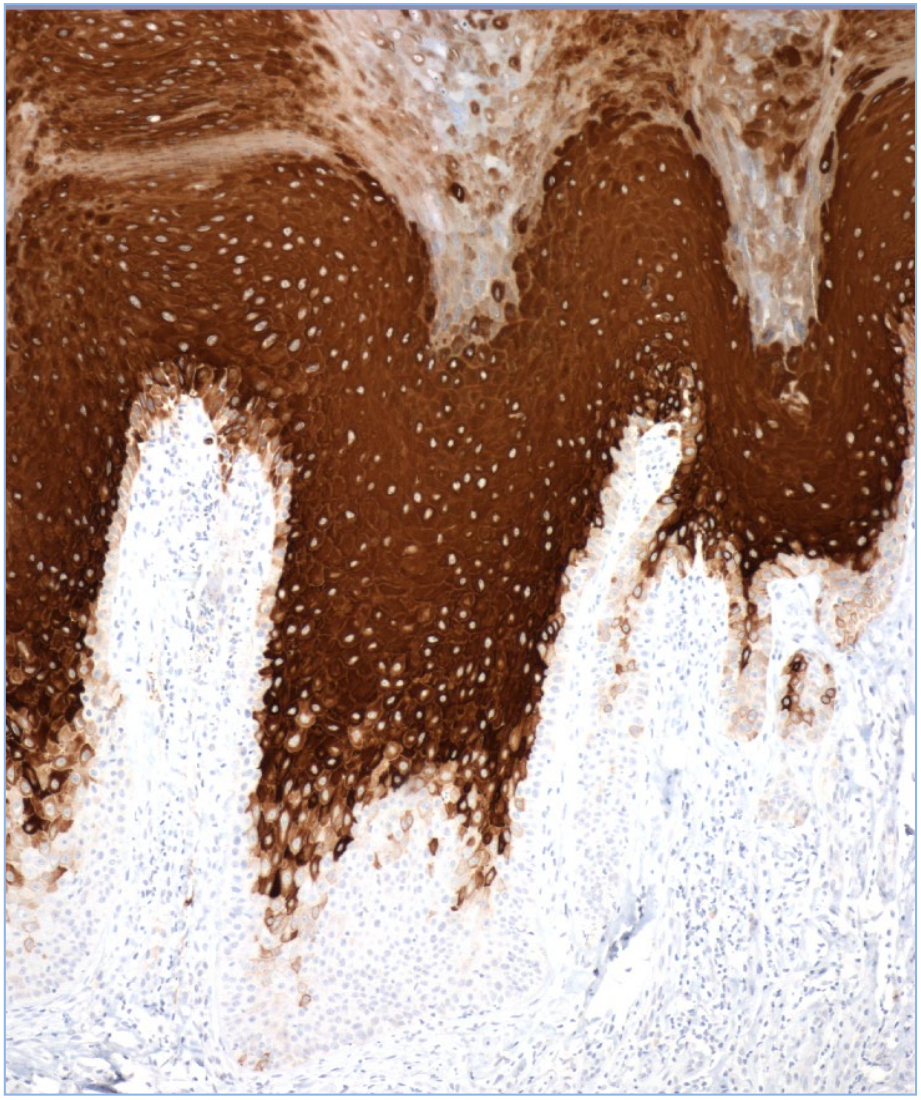
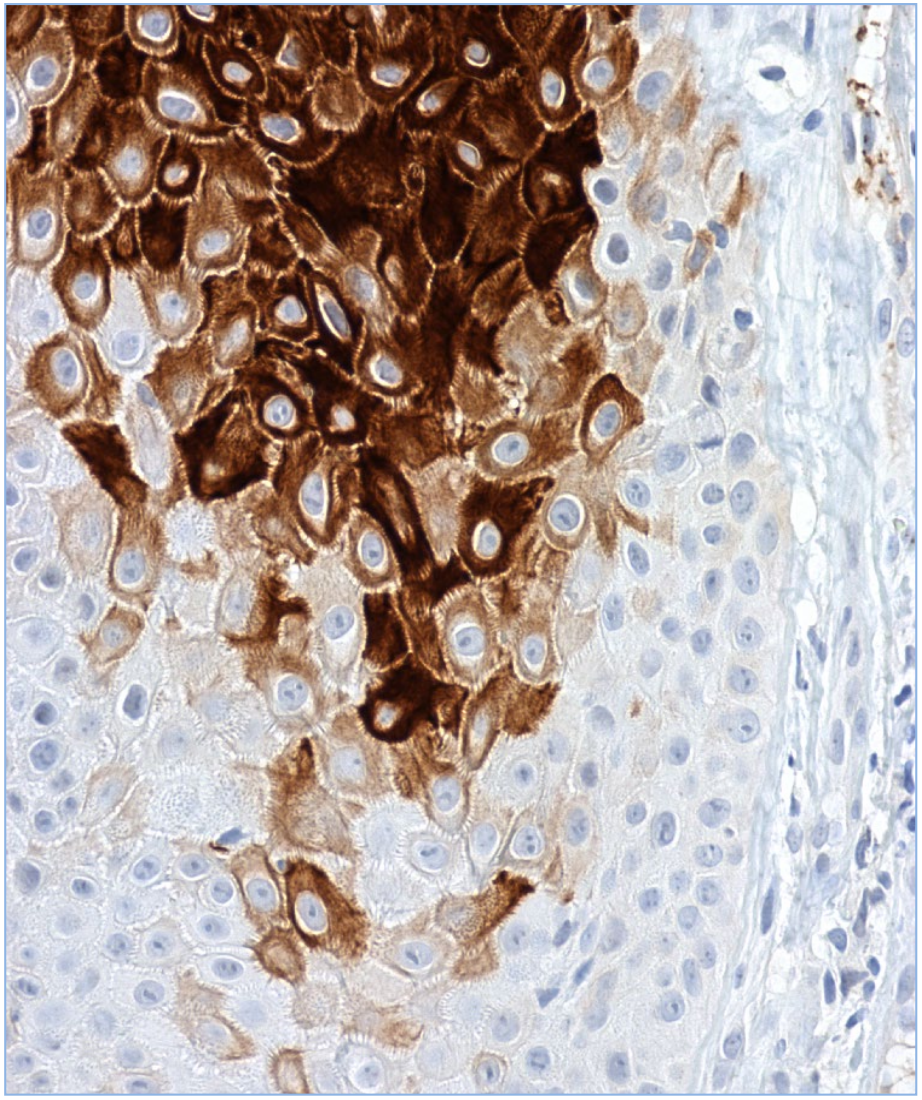
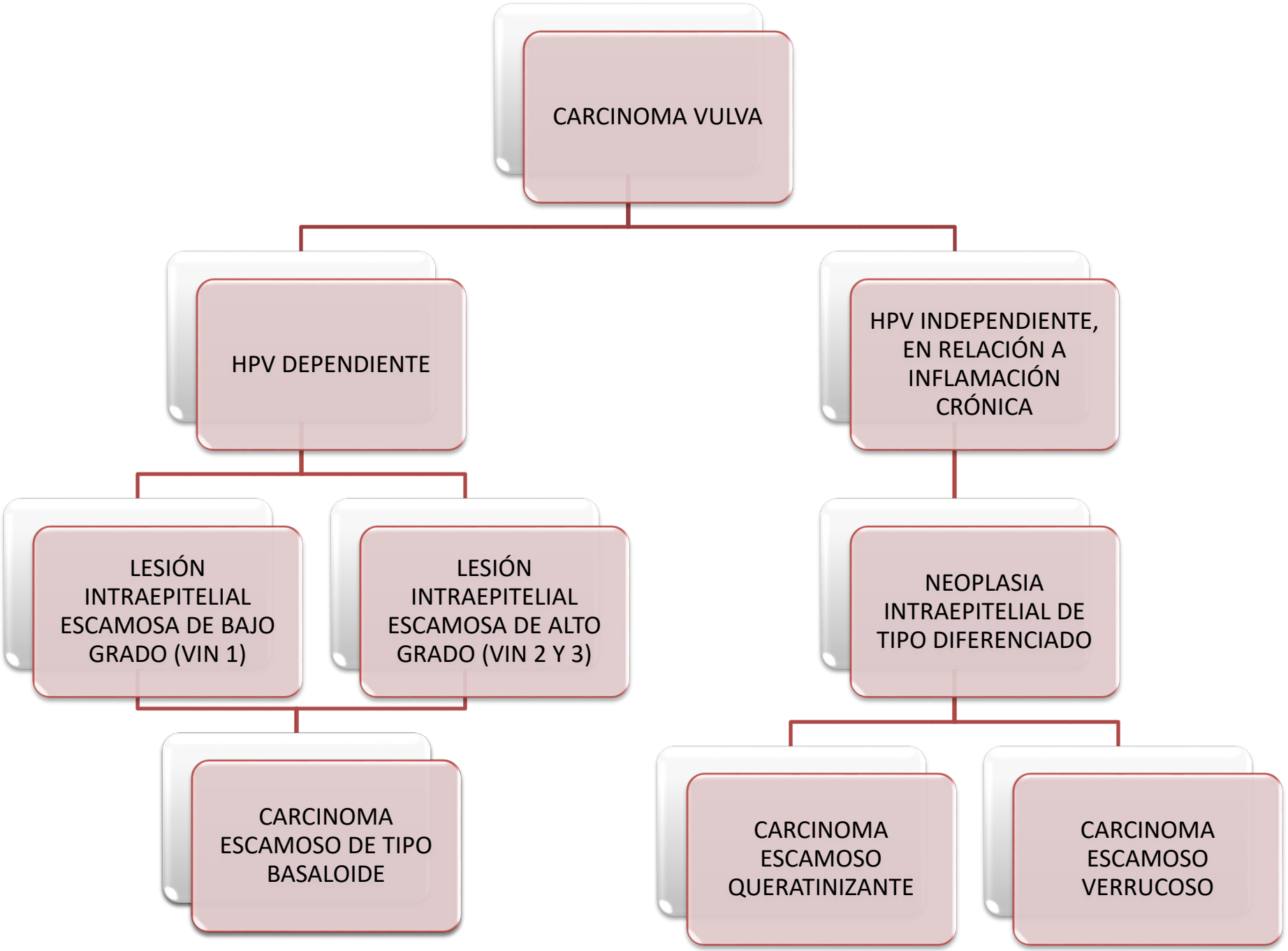


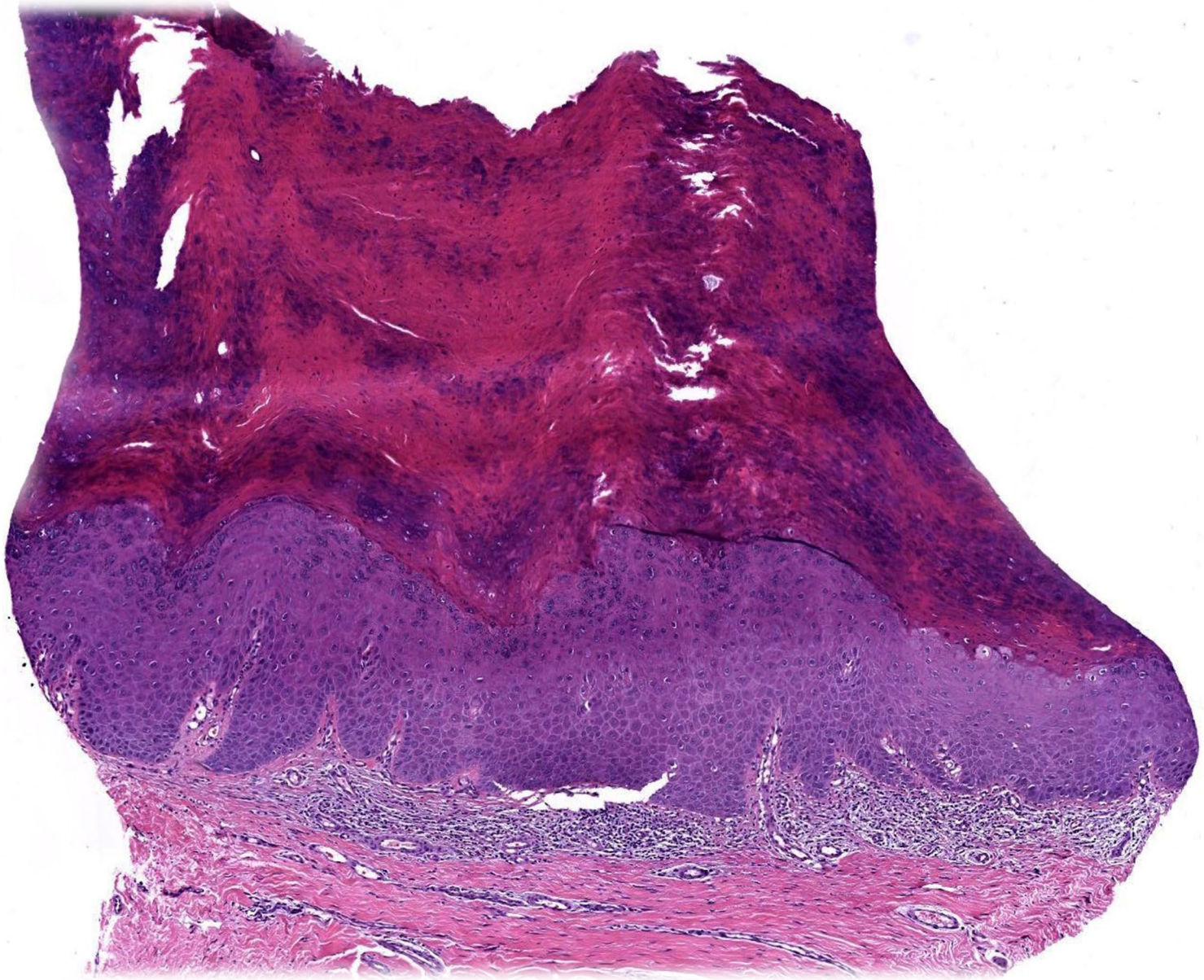
Fig. 3 Immunohistochemistry in differentiated VIN (**a–d**) and Lichen sclerosus (**e–h**). **a** Differentiated VIN, HE stain **b** Overexpression of p53. **c** Weak, patchy CK13 staining. **d** Strong and diffuse CK17 expression, with increased MIB-1. **e** Lichen sclerosus, HE stain. **f** Wild-type p53 expression. **g** Diffuse staining of moderate intensity with CK13. **h** Very weak, patchy CK17 staining with increased MIB-1

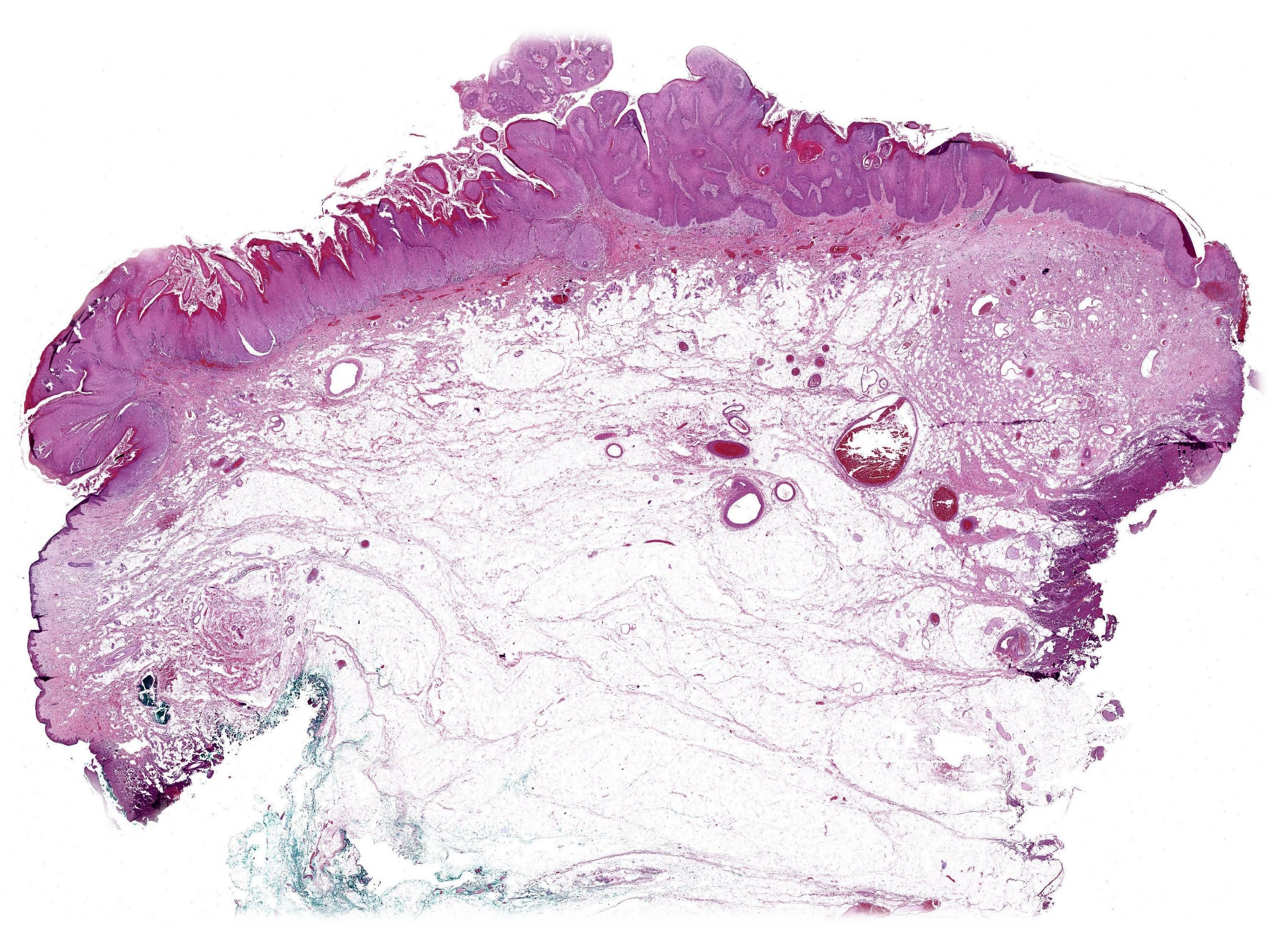
CK 17

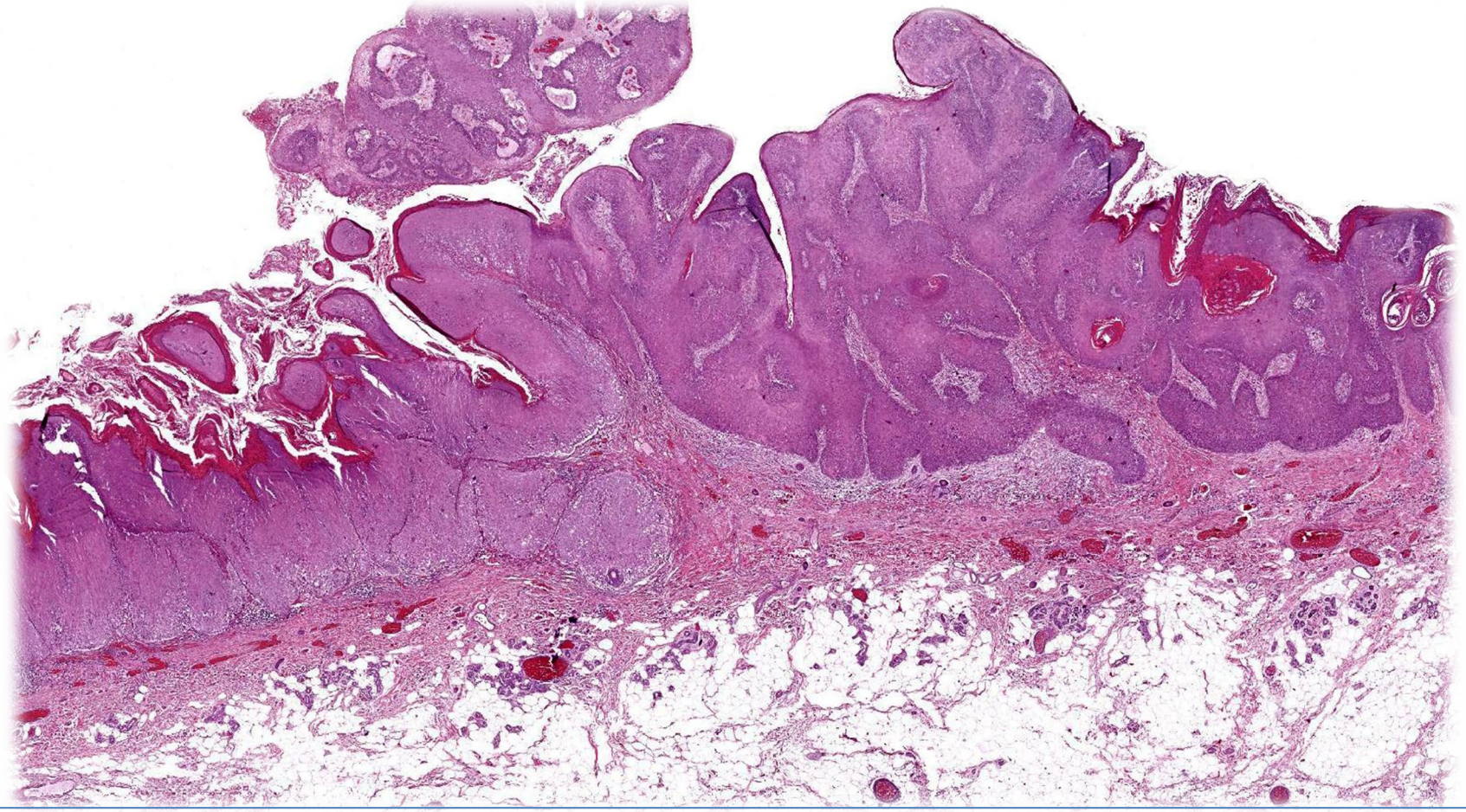





CARCINOMA VULVA
HPV DEPENDIENTE
HPV INDEPENDIENTE, EN RELACIÓN A INFLAMACIÓN CRÓNICA
LESIÓN INTRAEPITELIAL ESCAMOSA DE BAJO GRADO (VIN 1)
LESIÓN INTRAEPITELIAL ESCAMOSA DE ALTO GRADO (VIN 2 Y 3)
NEOPLASIA INTRAEPITELIAL DE TIPO DIFERENCIADO
CARCINOMA ESCAMOSO DE TIPO BASALOIDE
CARCINOMA ESCAMOSO QUERATINIZANTE
CARCINOMA ESCAMOSO VERRUCOSO







- Epidermis con hiperqueratosis, papilomatosis, hipergranulosis, acantosis.
- Las crestas son bulbosas con patrón "bulldozing"
- En profundidad proliferan grandes masas y bulbosas, que parecen invadir la dermis.
- Atipia mínima.

- d-VIN: Variabilidad diagnóstica.
- d-VIN: Atipias en capas bajas. Ojo con biopsias superficiales.
- d-VIN: Afecta a capas bajas, pero se considera una lesión de alto grado.
- Inmunohistoquímica útil CK 17, p53 y Ki 67.
- Se elimina el condiloma.
- d-VIN: No confundir con el liquen simple.

Human Papillomavirus–Independent Squamous Lesions of the Vulva

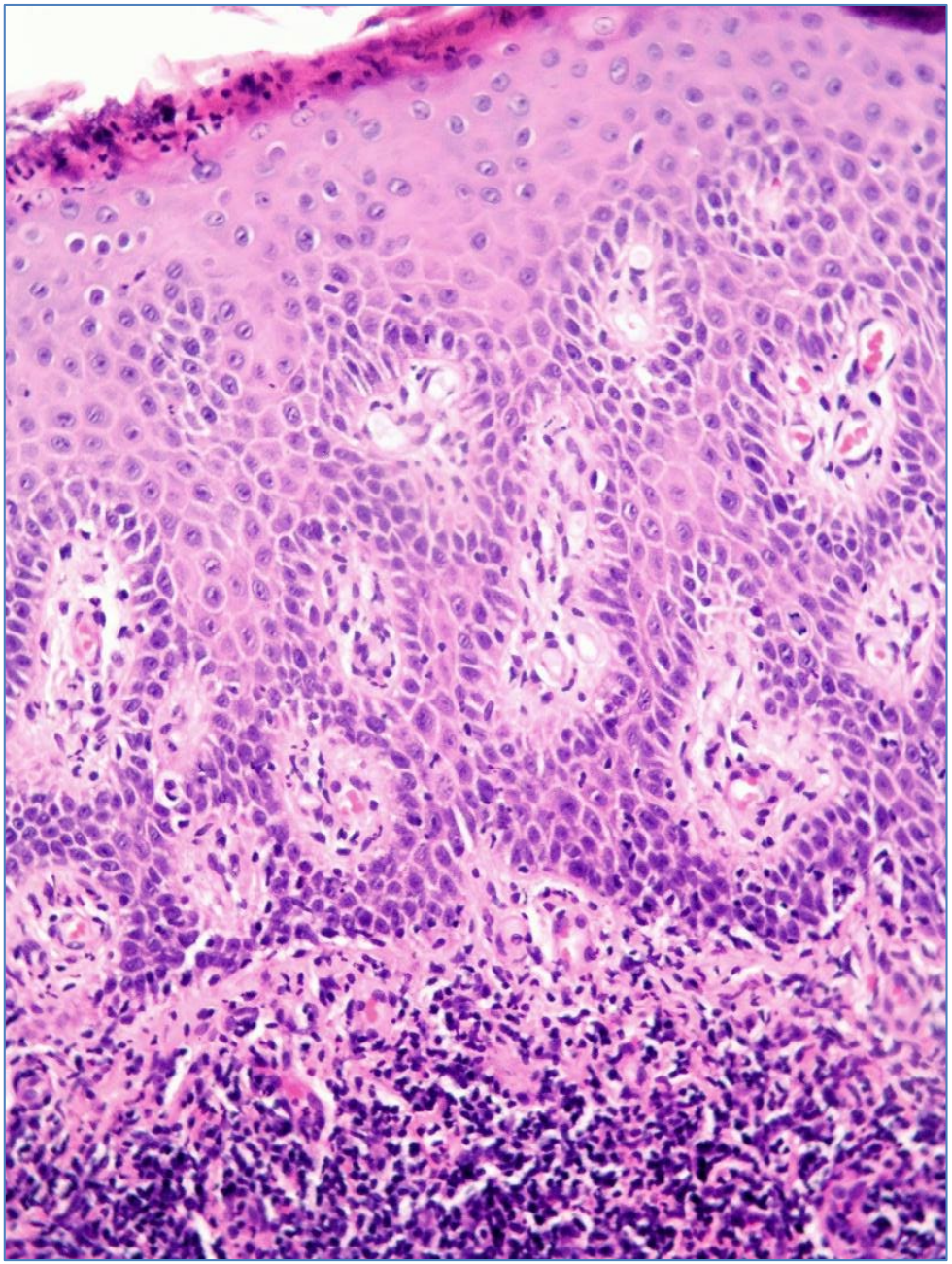
Jaclyn C. Watkins, MD, MS

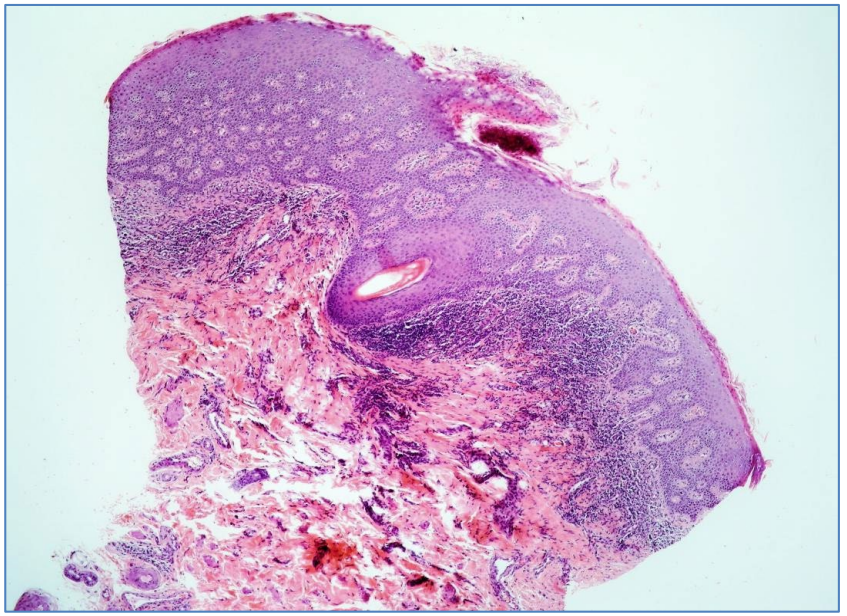
Surgical Pathology 12 (2019) 249–261
https://doi.org/10.1016/j.path.2019.01.001

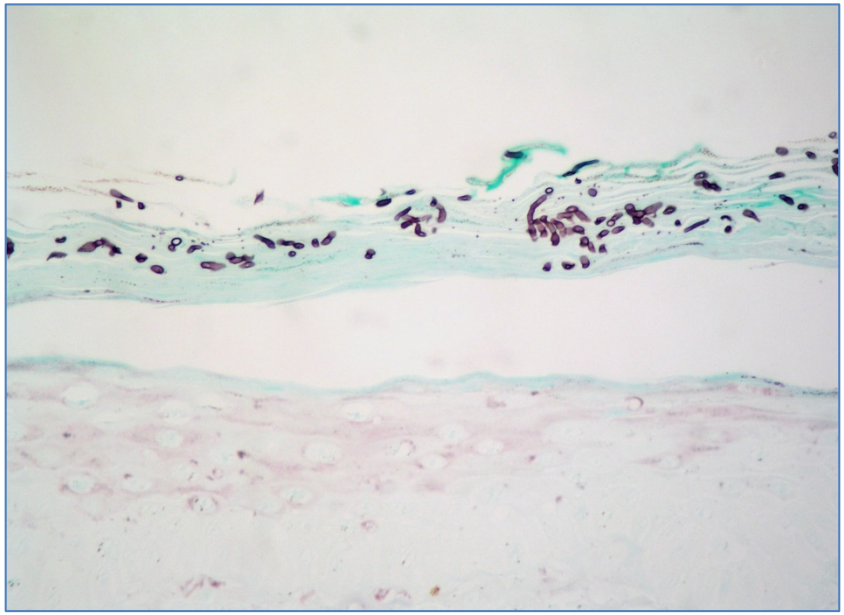
Key Features

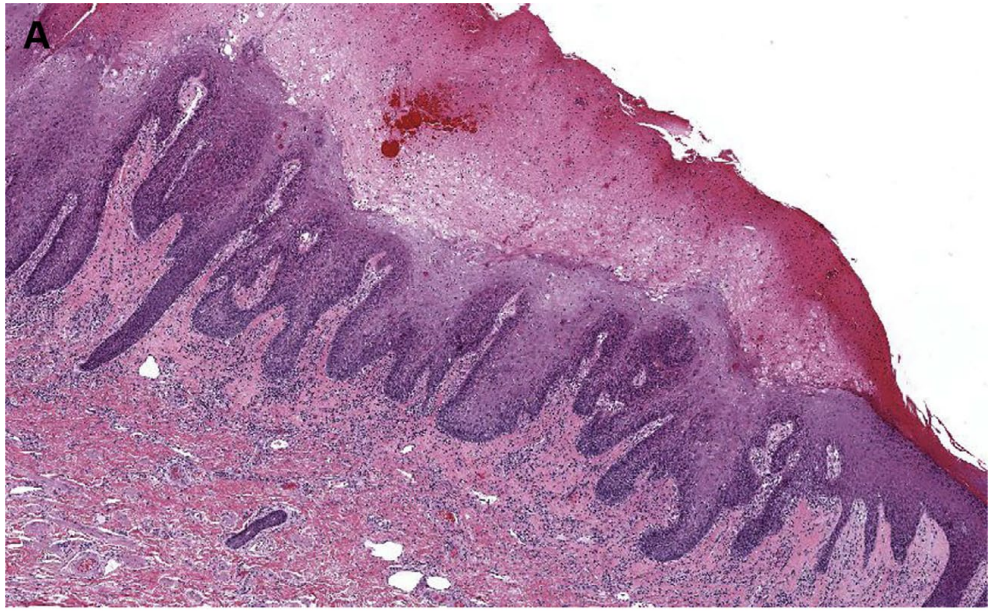
Lichen Simplex Chronicus

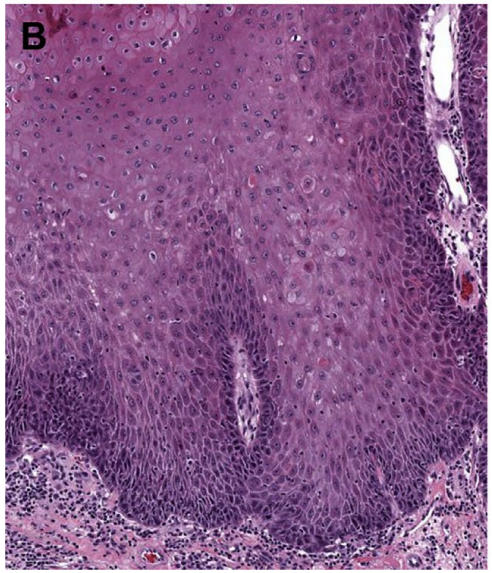
- Hyperkeratosis
- Psoriasiform epidermal hyperplasia (eg, elongated rete ridges)
- Hypergranulosis
- Vertical papillary dermal fibrosis
- Sparse chronic inflammation (typically perivascular)

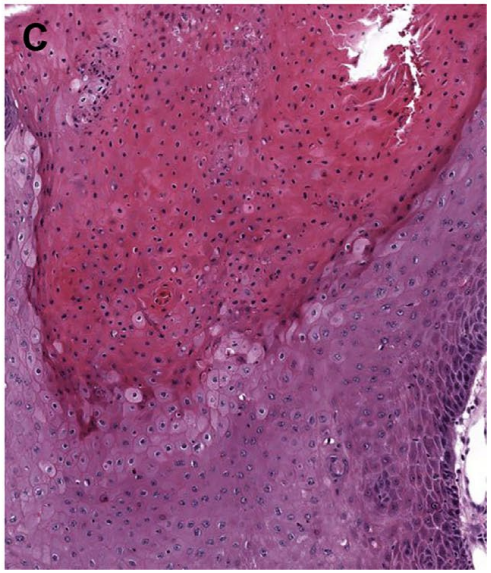












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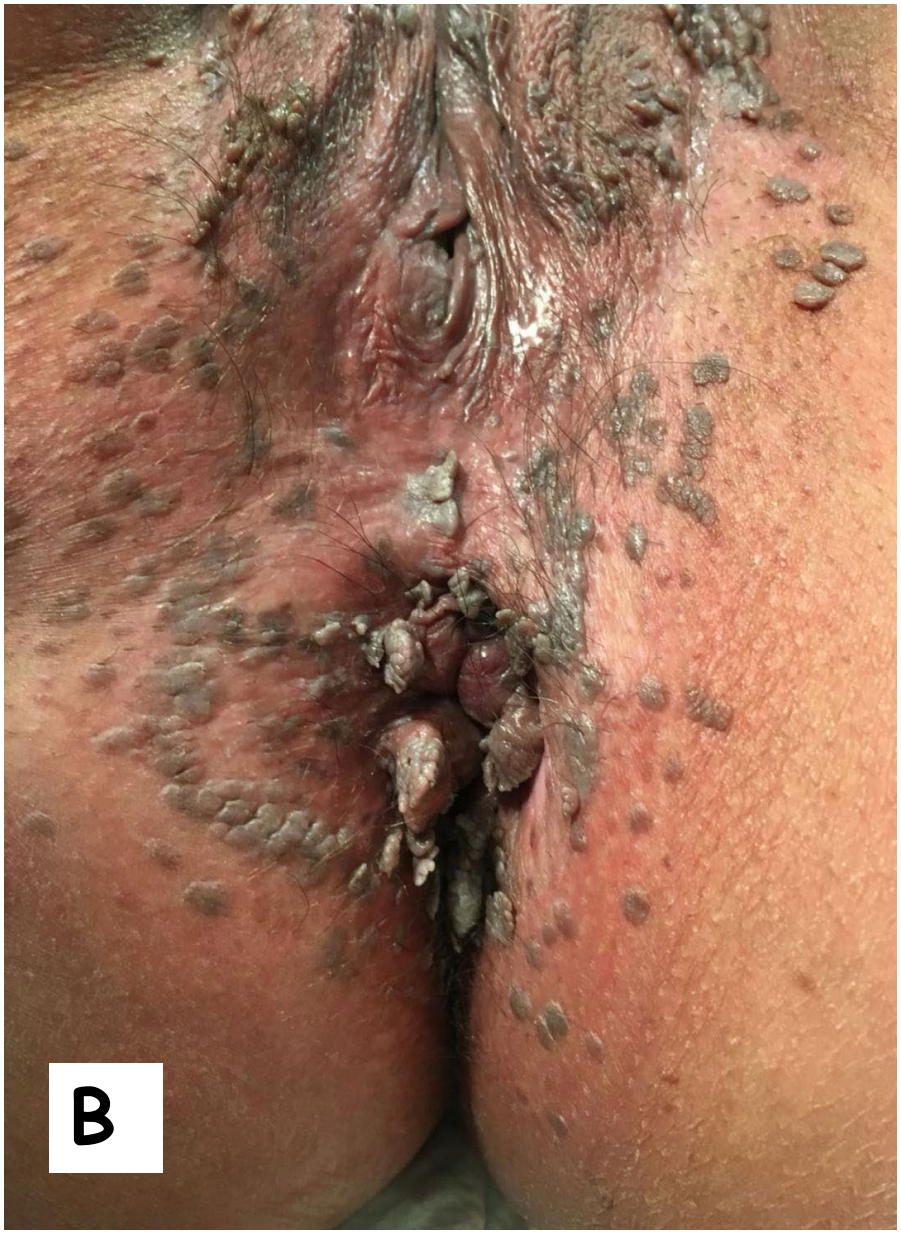
Surgical Pathology 12 (2019) 249–261
https://doi.org/10.1016/j.path.2019.01.001

Key Features
Vulvar Acanthosis with Altered Differentiation

- Epithelial pallor
- Absence of cytologic atypia
- Acanthosis
- Plaque-like parakeratosis
- Loss of the granular cell layer
- Variable verruciform architecture

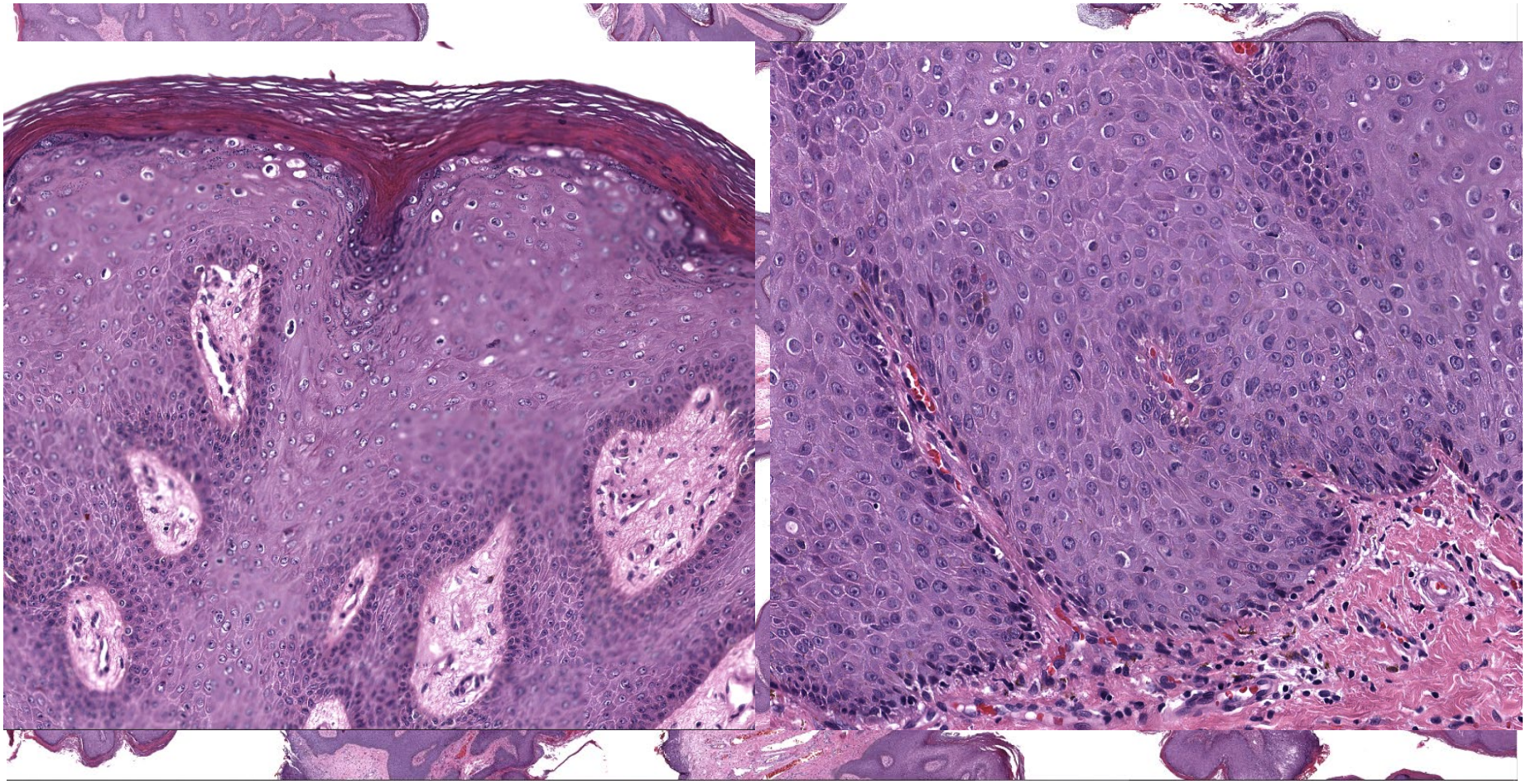
Tipo de Carcinoma de células escamosas (SCC)	SCC HPV+	SCC HPV-
Edad	35-65 años	55-85 años
Factores de riesgo	Verrugas anogenitales, tabaco, alcohol	Liquen escleroso y plano
Focalidad	Multifocal	Único foco
VIN asociado	LSIL y HSIL (antiguos VIN 1-3)	VIN diferenciado
Tipo histológico	SCC no queratinizante, basaloide, verrucoso +/-, condilomatoso	SCC queratinizante
P16	+	-
P53	-	+

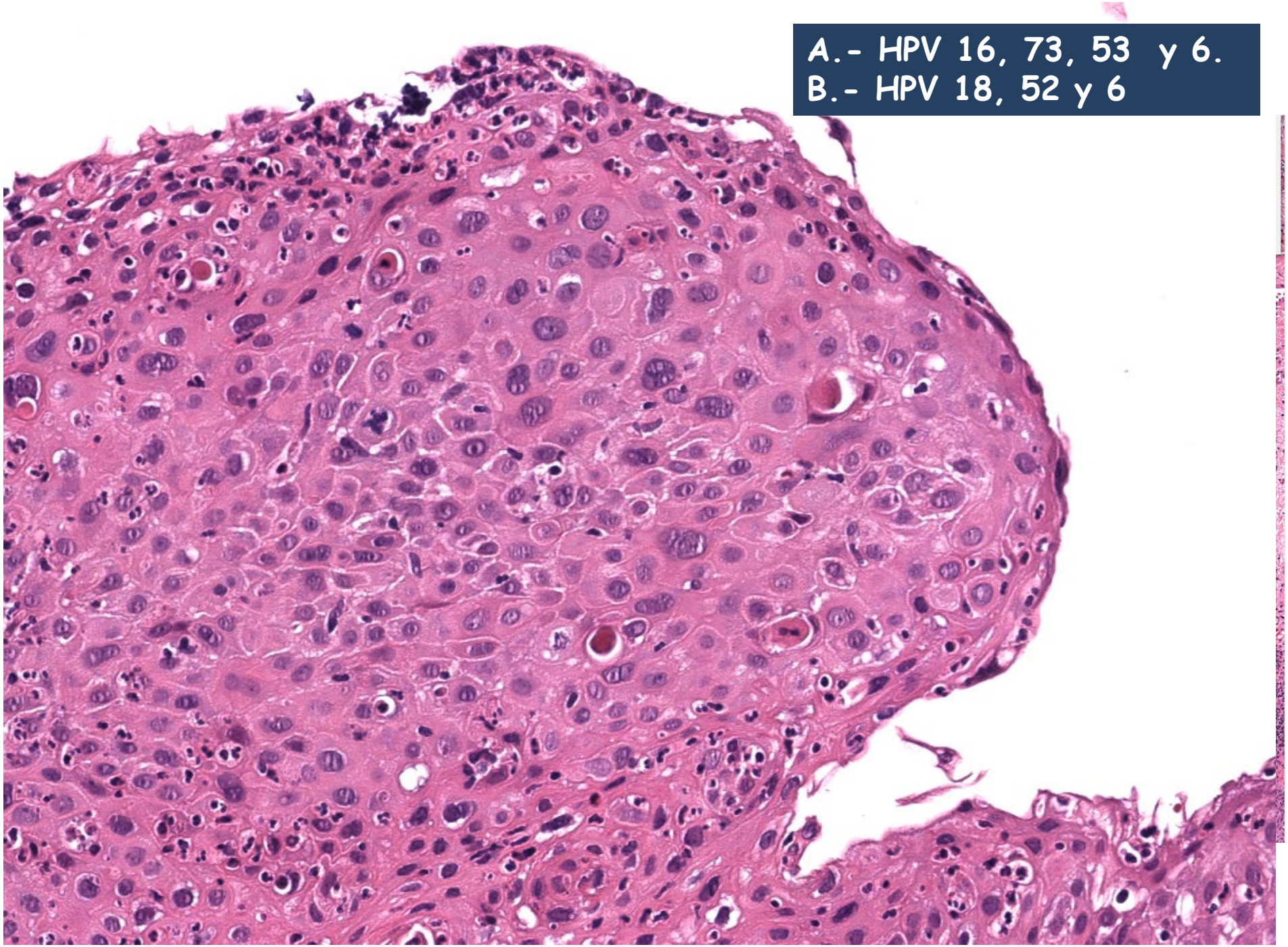
CONDILOMAS MALIGNIZADOS



A.- 24 años. B.- 30 años. CONDILOMATOSIS VULVAR FLORIDA.

A.- HPV 16, 73, 53 y 6.
B.- HPV 18, 52 y 6




A.- HPV 16, 73, 53 y 6.
B.- HPV 18, 52 y 6

Condyloma acuminatum

Definition
A benign verrucous papillary lesion associated with HPV infection.

Synonyms
Viral wart; genital wart; viral papilloma; low-grade squamous intraepithelial lesions (LSIL) with condylomata

cally preventable by the quadrivalent HPV vaccine {32,1852}.

Macroscopy
Papular or warty lesion may be seen on the introital, labial, perineal, and perianal mucosa. Lesions may be pruritic.

Histopathology
Acanthosis, papillomatosis, hyperkera-

Prognosis and predictive factors

The disease is managed by observation, local excision, topical imiquimod or trichloroacetic acid, and electro-cautery or superficial cryotherapy when larger. The majority resolve spontaneously or do not recur following removal. Recurrences are higher in immunosuppressed individuals in whom condylomata may co-exist with HSIL (VIN 2/3) {1159}.

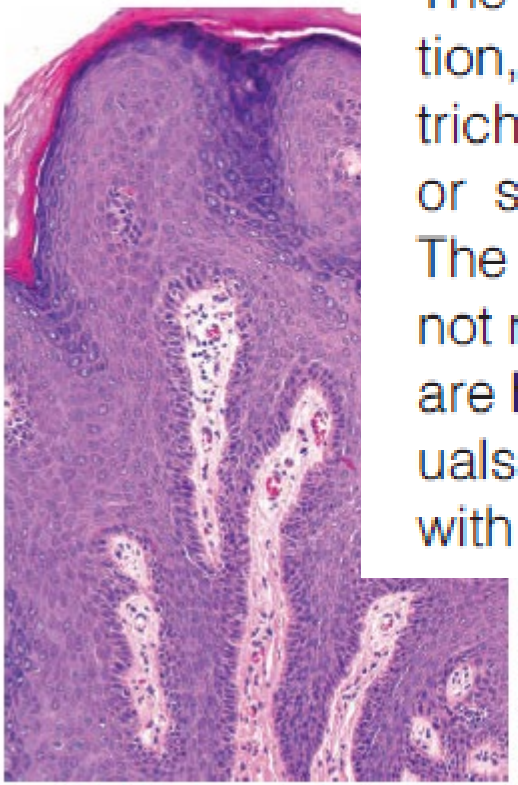


Fig. 9.08 Condyloma acuminatum. Acanthosis and papillomatosis with only focal viral cytopathic effect (centre right near the surface).

with HSIL (VIN 2/3) {1159}.

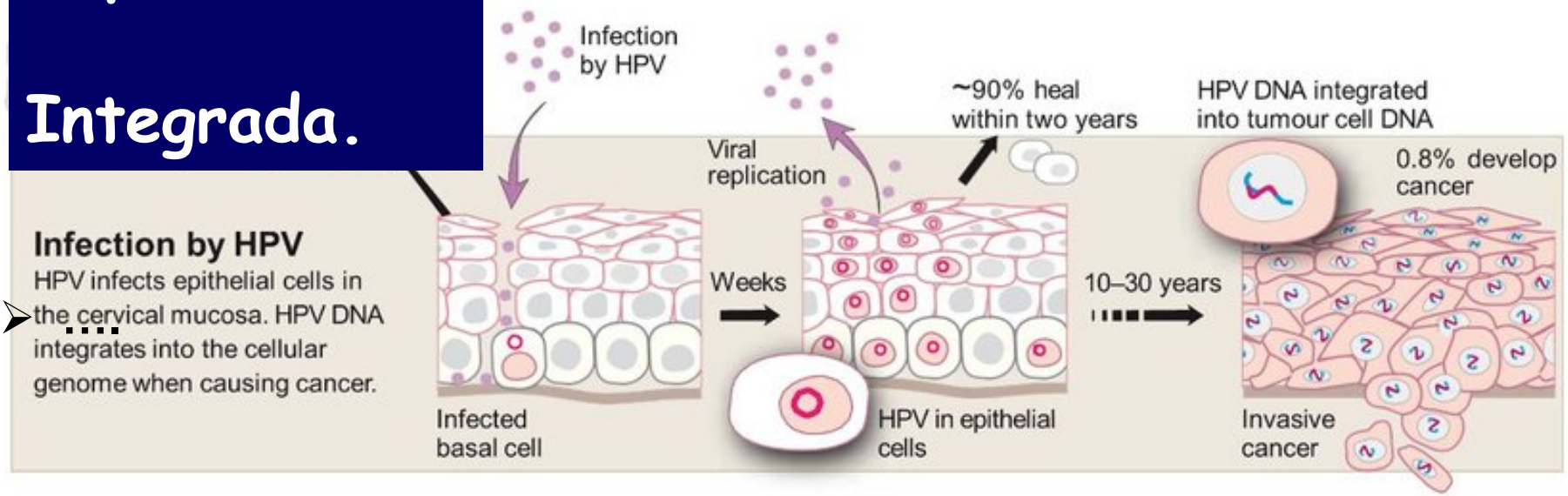
Vestibular papilloma

Definition
A benign epithelial excrescence with a squamous epithelial mucosal surface that overlies a delicate fibrovascular stalk.

Episonal.

Replicativa.

Integrada.



International Journal of Gynecological Pathology
00:1–5, Lippincott Williams & Wilkins, Baltimore

Original Article

HPV 6-associated HSIL/Squamous Carcinoma in the Anogenital Tract

Martina Z. Liu, M.D., Yin P. Hung, M.D., Ph.D., Eric C. Huang, M.D., Ph.D., Brooke E. Howitt, M.D., Marisa R. Nucci, M.D., and Christopher P. Crum, M.D.

Despite the dual biologies attributed to high-risk and low-risk HPV types, exceptions have been reported, with occasional squamous cell carcinomas arising in association with low-risk HPV types (4). In several reports the tumors associated with HPV types 6 or 11 have been well differentiated verruciform carcinomas (5–8). including so-called giant condylomas of Buschke Lowenstein. Rare cases of malignant transformation in HPV6-associated or HPV11-associated laryngeal papillomas have been described (9–11).

1.- COINFECCIÓN
2.- MUTACIÓN DE p53

Sheela na Gigs

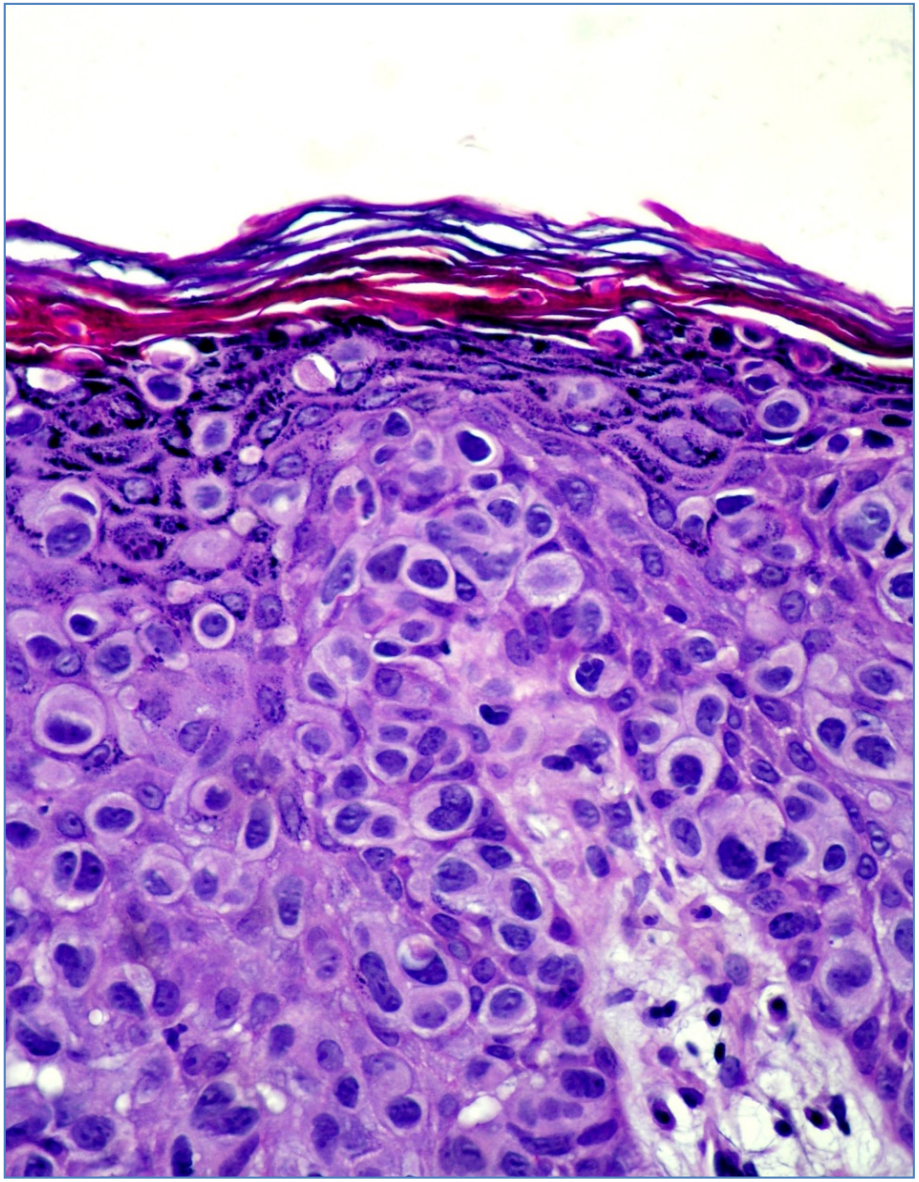
- Los condilomas pueden asociarse a HSIL.
- Hay que analizar al menos las muestras más representativas.
- P16 no es útil en lesiones de bajo riesgo ni en vulva.

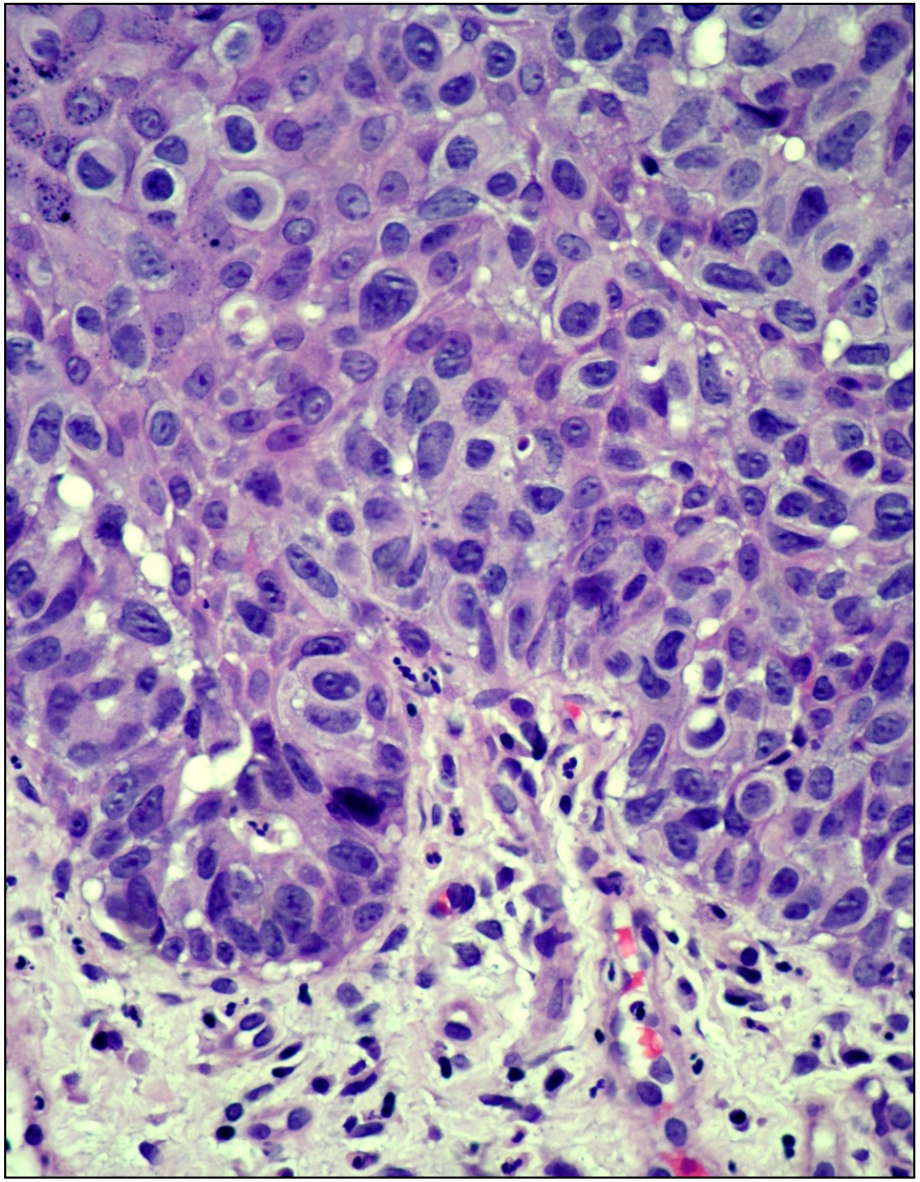
ADENOCARCINOMAS DE VULVA CON EXTENSIÓN PAGETOIDE.

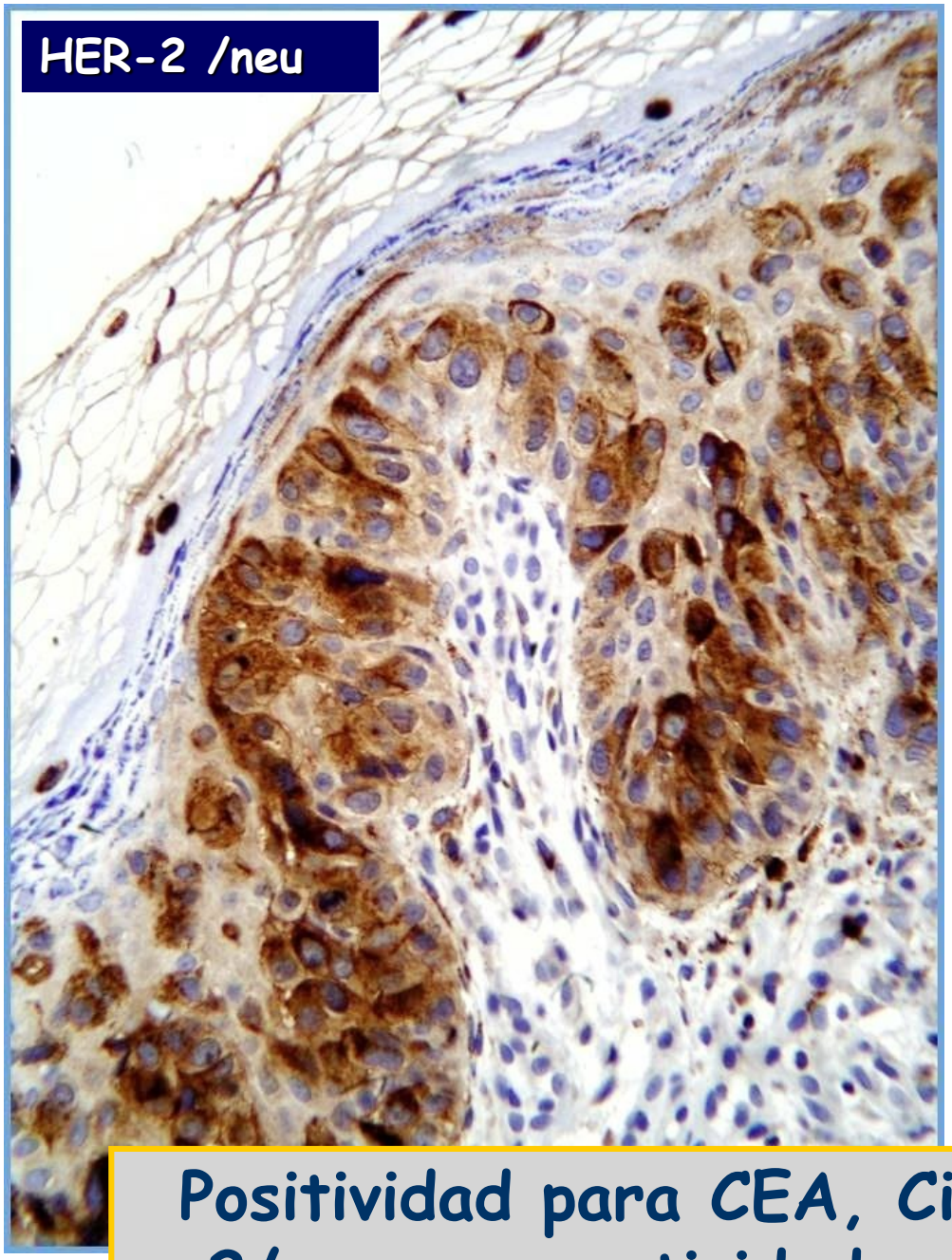
Enfermedad de Paget vulvar cutánea, no invasiva.

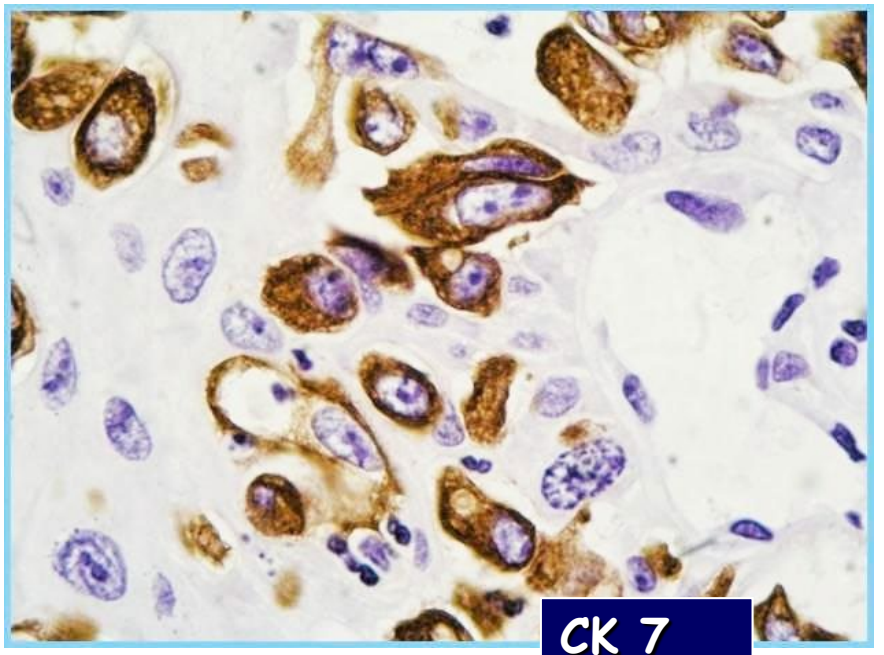
Paget de vulva

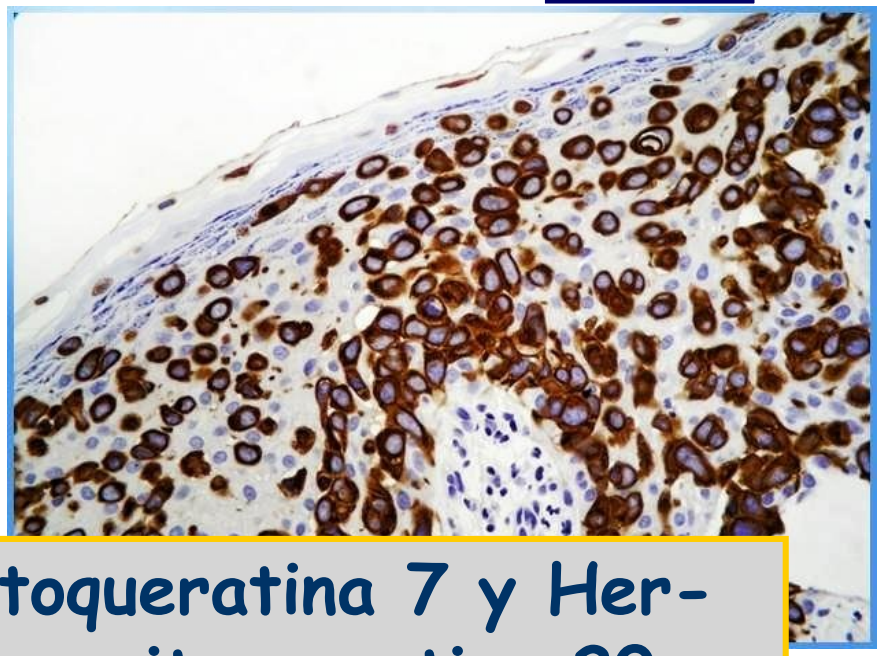
Paciente de 65 años, asintomática, que presenta lesión vulvar bien delimitada de 4 x 3 cm, discretamente sobreelevada, blanquecina y exudativa.











Positividad para CEA, Citoqueratina 7 y Her-2/neu; y negatividad para citoqueratina 20.

La enfermedad de Paget es una neoplasia epitelial.
Derivada de las células madre pluripotenciales, situadas en la epidermis interfolicular y en la unidad folículosebáceo apocrina.
También puede derivarse de adenocarcinoma situado en los anejos cutáneos o estructuras adyacentes (carcinoma anorectal, urotelial, genital…)

CLASIFICACIÓN DE LA ENFERMEDAD DE PAGET EXTRAMAMARIA:

Primarios:

1- Tumor intraepitelial.
2- Tumor intraepitelial con invasión.
3- Tumor proveniente de adenocarcinomas de anejos cutáneos glándula de Bartholino.

Secundarios:

1- Adenocarcinomas de colon-recto.
2- Tumores uroteliales.
3- Adenocarcinomas de otras localizaciones.

Contents lists available at ScienceDirect

Critical Reviews in Oncology/Hematology

journal homepage: www.elsevier.com/locate/critrevonc

Paget disease of the vulva

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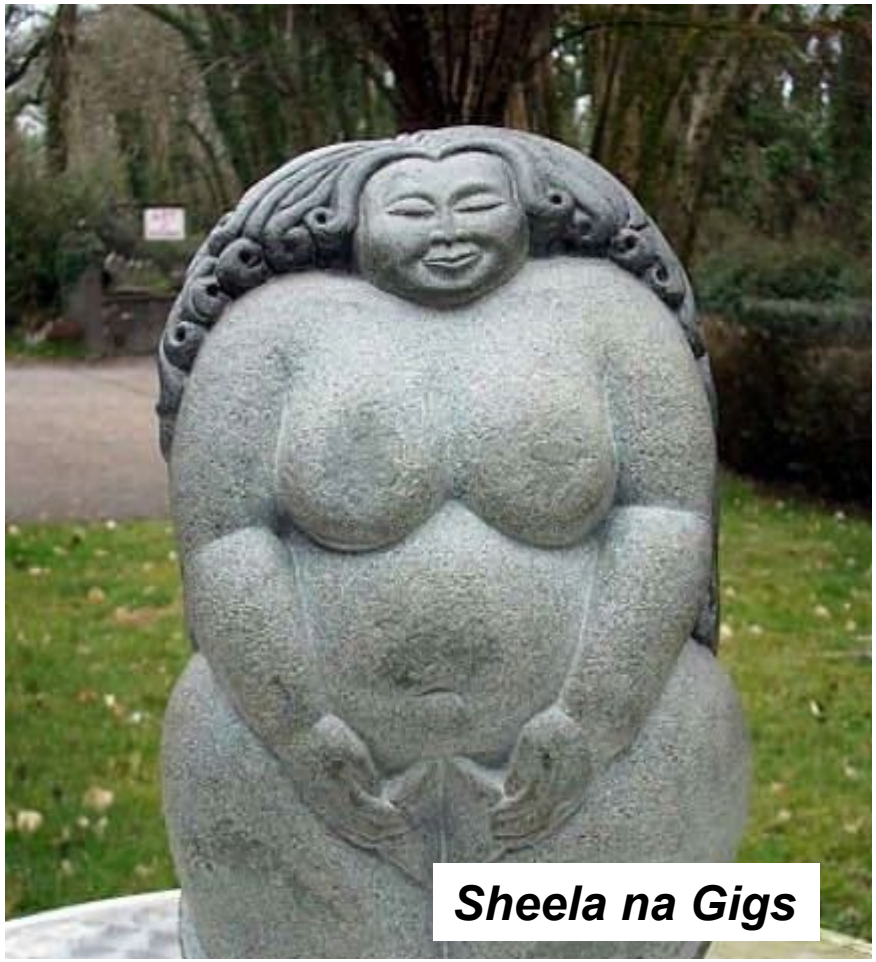
Classification of vulvar Paget disease by Wilkinson (Delport, 2013; Crum et al., 2014).

Primary VPD (cutaneous)	Type 1a	Cutaneous vulvar non-invasive Paget's disease
	Type 1b	Cutaneous vulvar invasive disease: dermal invasion of Paget cells
	Type 1c	Cutaneous vulvar disease as a manifestation of an underlying vulvar adenocarcinoma
Secondary VPD (non-cutaneous)	Type 2	VPD originates from rectal or anal adenocarcinoma
	Type 3	VPD originates from urogenital neoplasia



Sheela na Gigs

- Paget: casi siempre adenocarcinoma intraepitelial. Primario o secundario.
- Compleja clasificación histopatológica
- La inmunohistoquímica es útil en caso de Paget no cutáneo.

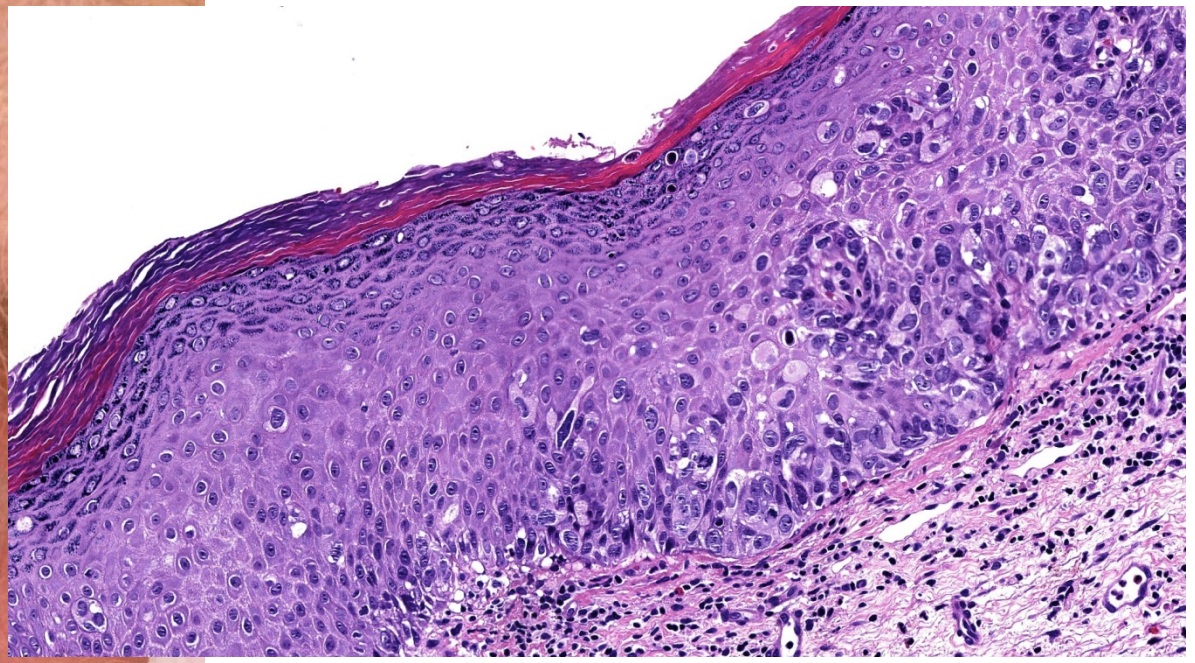
ADENOCARCINOMAS DE VULVA CON EXTENSIÓN PAGETOIDE.

Enfermedad de Paget vulvar cutánea, asociada a adenocarcinoma vulvar:

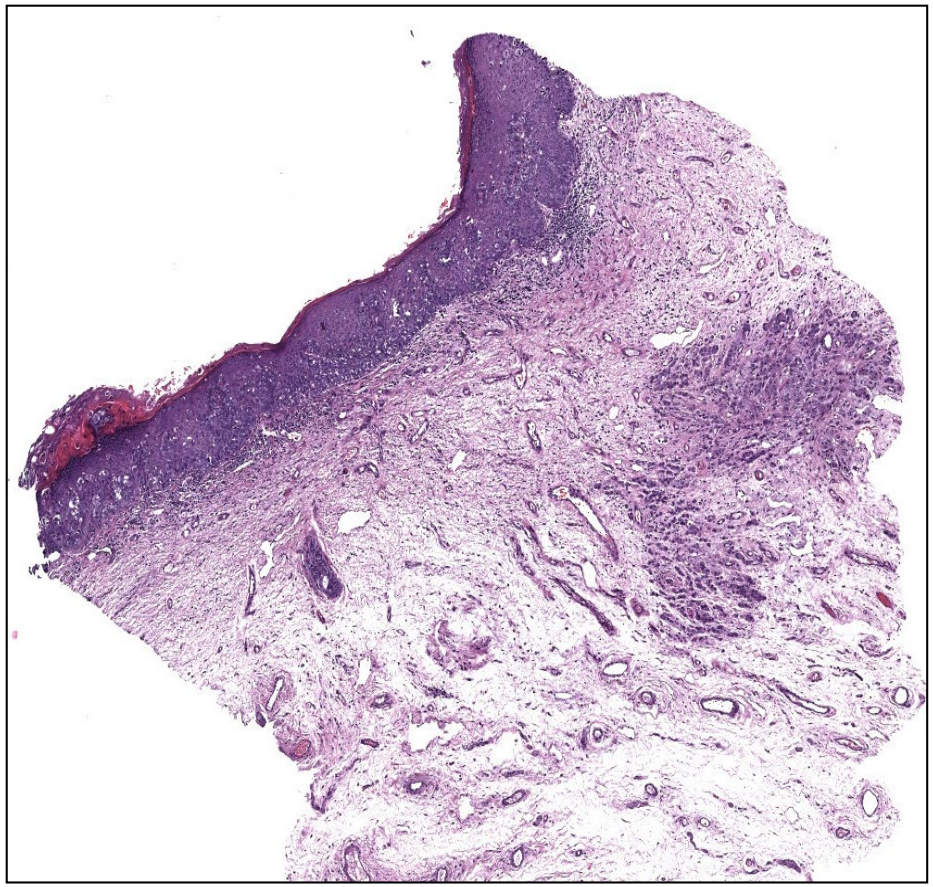
1.- Adenocarcinoma apocrino.

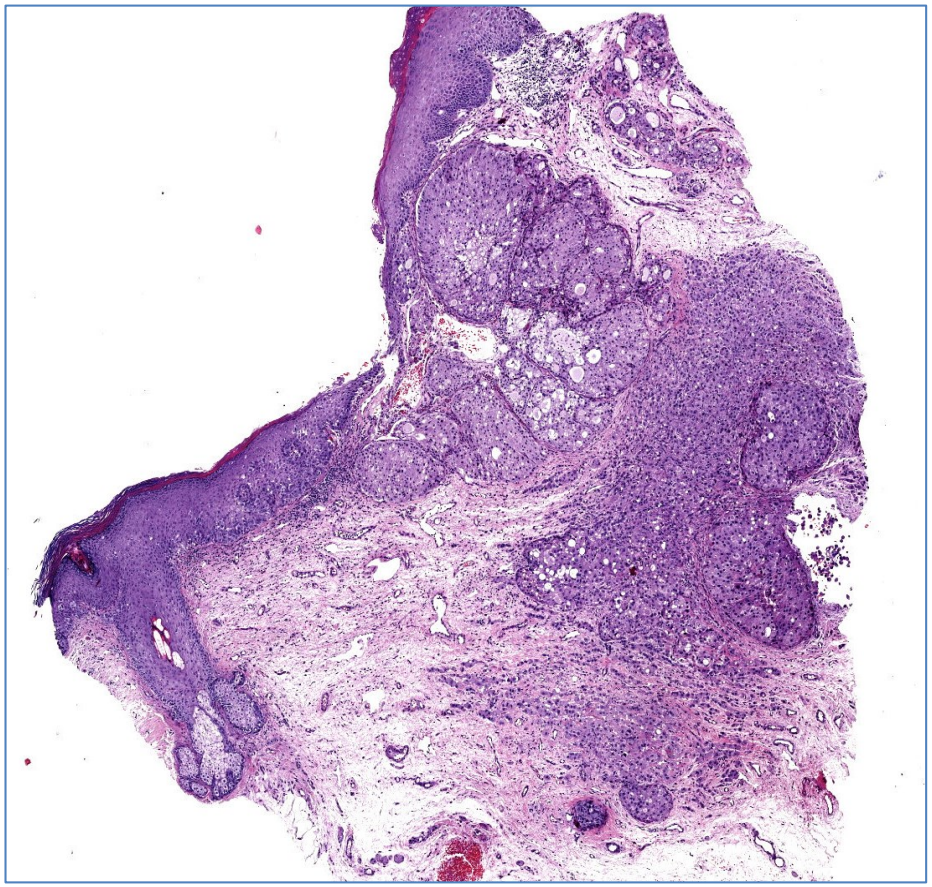
2.- Adenocarcinoma mama-like

Adenocarcinoma apocrino con extensión pagetoide

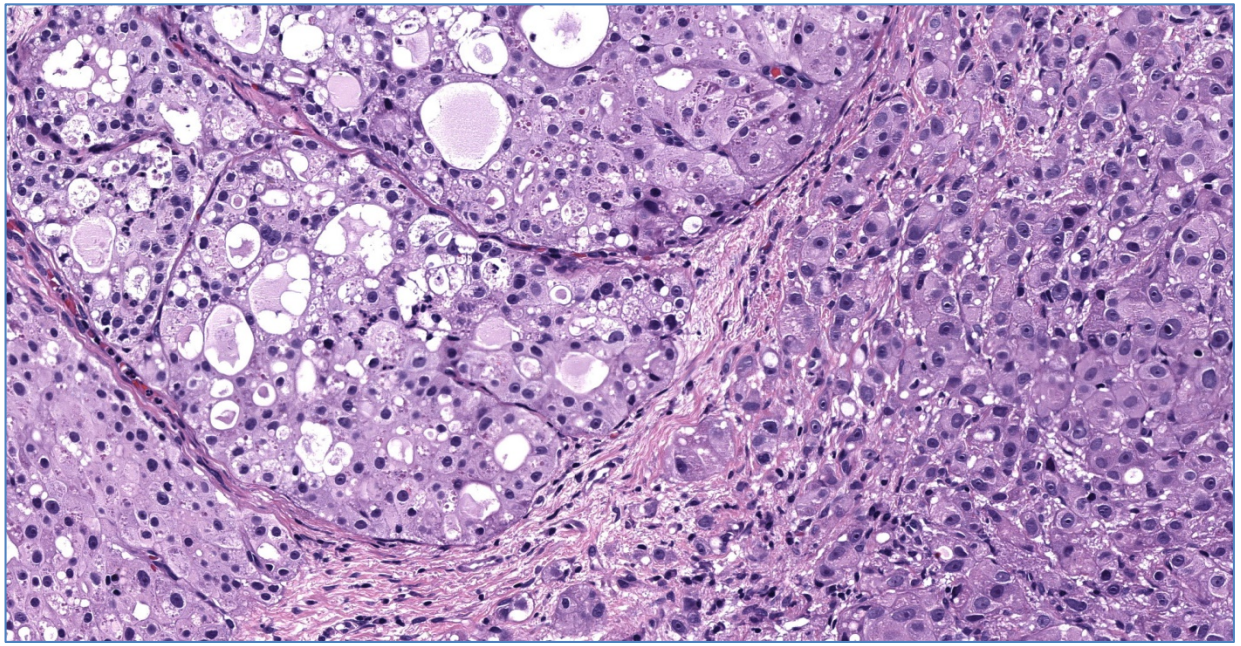


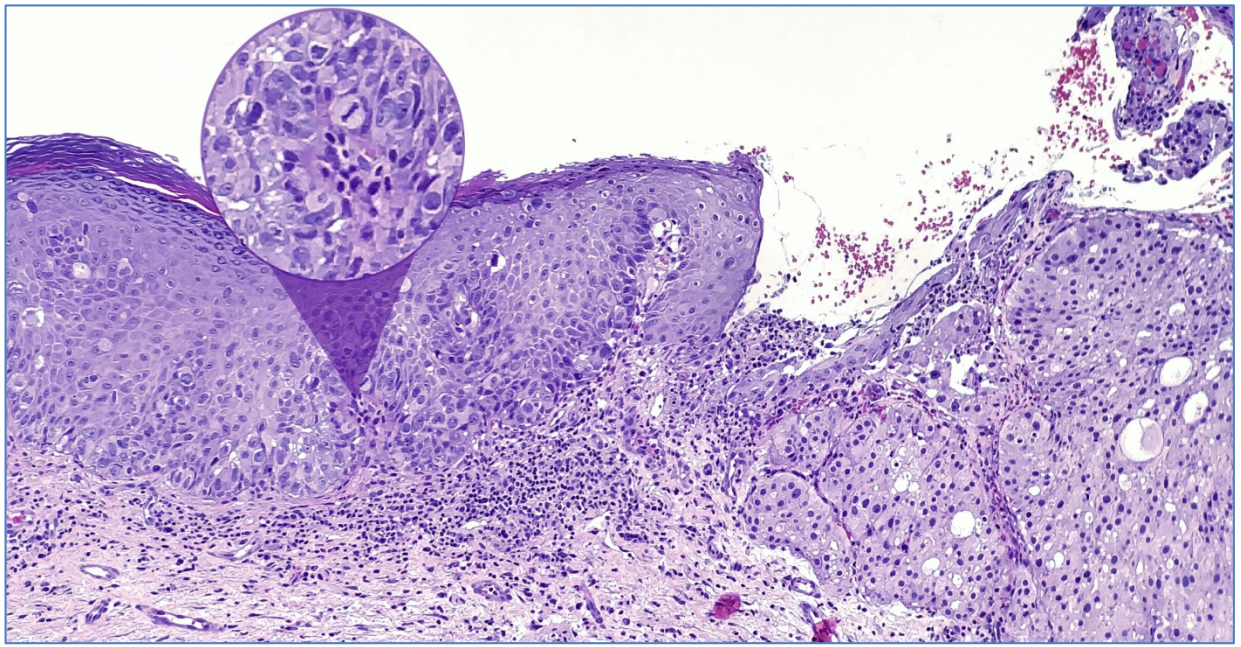
Adenocarcinoma apocrino con extensión pagetoide





Adenocarcinoma apocrino con extensión pagetoide





Adenocarcinoma apocrino con extensión pagetoide

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Case Report

Apocrine Adenocarcinoma of the Vulva: A Case Report and Review of the Literature

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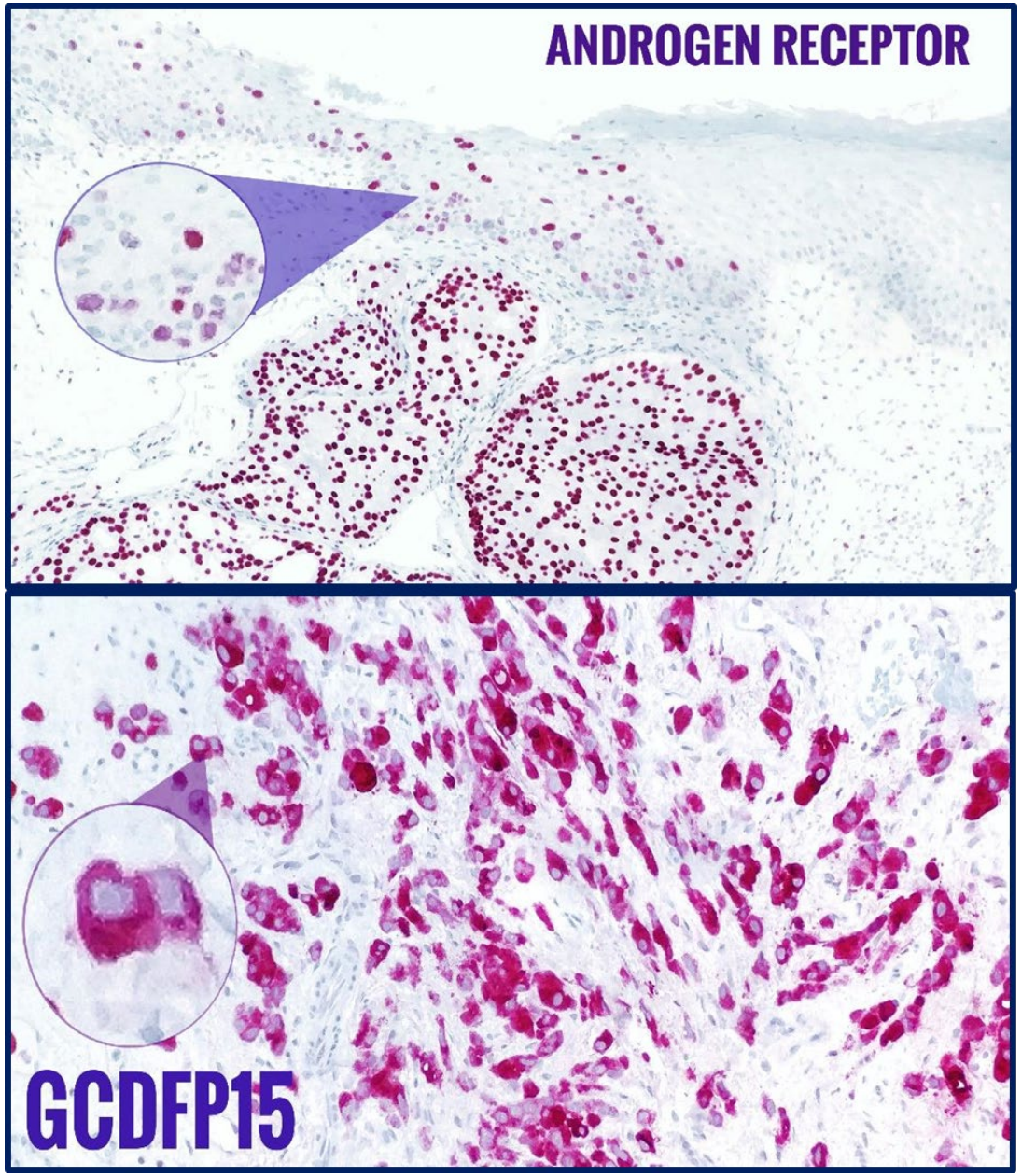
mor, pagetoid spread of neoplastic cells was limitedly present (Figure 2(d)). In immunohistochemical findings, the tumor cells were positive for pan-cytokeratin, cytokeratin 7, epithelial membrane antigen, gross cystic disease fluid protein-15 (Figure 3(a)), and androgen receptor (AR) (Figure 3(b)), confirming the apocrine origin of the tumor. Staining for cytokeratin 20, carcinoembryonic antigen, and

Adenocarcinoma apocrino con extensión pagetoide



ADENOCARCINOMAS PRIMARIOS DE VULVA CON EXTENSIÓN PAGETOIDE.

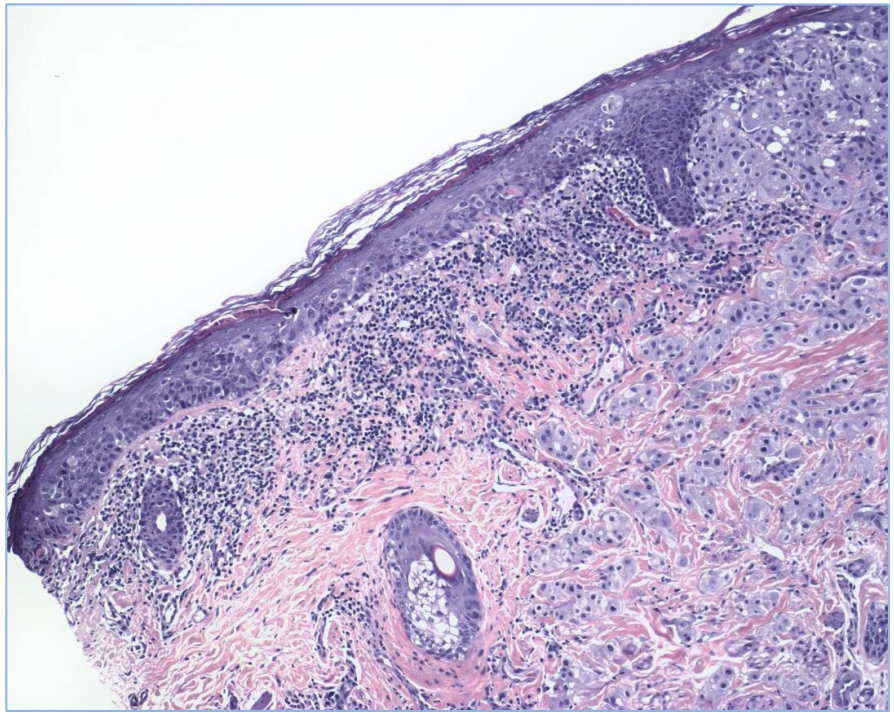
Enfermedad de Paget vulvar cutánea, asociada a adenocarcinoma vulvar:

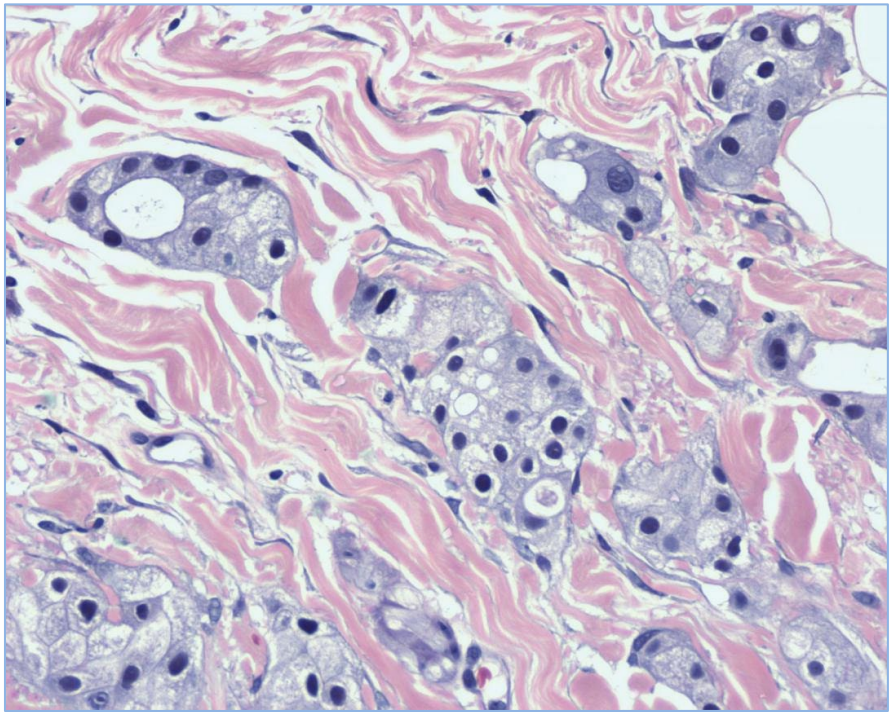
1.- Adenocarcinoma apocrino.

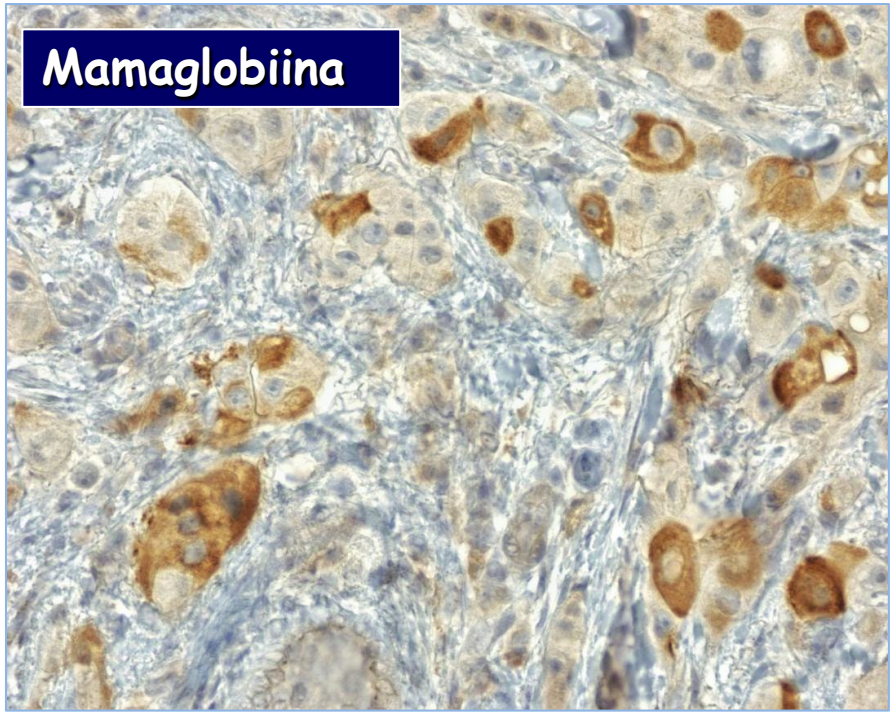
2.- Adenocarcinoma mama-like

Adenocarcinoma mama-like

Mujer de 60 años que consulta por lesión ulcerosa en vulva de más de 1 mes de evolución.
Menopausia a los 52 años. Portadora del gen BRCA2. Mastectomía subcutánea bilateral y doble anexectomía realizadas de manera profiláctica en 2009 y 2011 respectivamente. El resultado anatomopatológico de la doble anexectomía realizada informó de displasia intraepitelial de alto grado de la trompa de Falopio derecha, con controles posteriores normales.
A la exploración vulvar, presentaba borramiento de labios menores con enterramiento de clítoris y lesión ulcerada de aproximadamente 5mm, en labio mayor izquierdo, no indurada ni sobreelevada.



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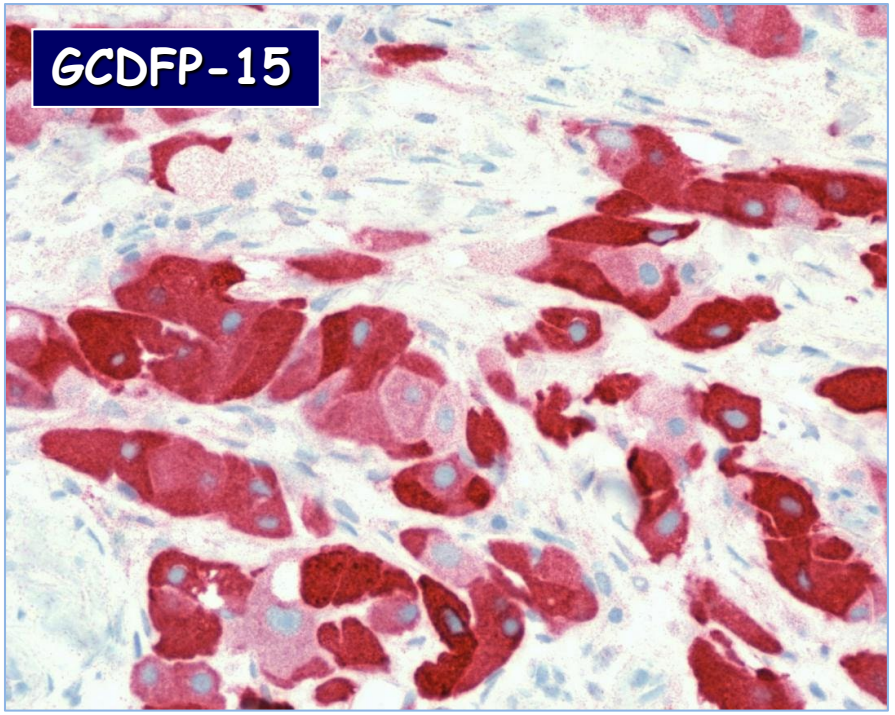
GCDFP-15

La *Leçon de Claude Bernard* (1889), de Léon Lhermitte.

La mejor técnica en dermatopatología es cortar de nuevo.

Gracias