WHAT ARE THESE STAINS?

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CONFLICTS

- No conflicts with the content of this lecture
TYPES OF STAINS

- Routine H&E
- Conventional special stains
- Immunohistochemical stains
- Immunofluorescent stains
ROUTINE STAINS

- H&E = Hematoxylin and Eosin
  - Hematoxylin stains cell nuclei blue
  - Eosin stains extracellular matrix and cytoplasm pink
ROUTINE STAINS

“Bug” Stains

- PAS: Periodic acid Schiff
- GMS: Grocott’s methanamine silver
- AFB: Ziehl-Neelsen stain, Wade-Fite
- Gram: Brown and Brenn
- Warthin-Starry
- Giemsa
ROUTINE STAINS

- PAS
- Giemsa
- Fontana-Masson
- Congo red
- Alcian Blue
IMMUNOHISTOCHEMICAL STAINS

• Antigen-Antibody reaction
• Different techniques
• Different chromogens
• Adjunct to H&E to confirm differentiation (not malignancy)
• Diagnostic
• Prognostic
IMMUNOHISTOCHEMICAL STAINS

• Panels or combinations of stains to determine differentiation
• Which lesions are positive with what stains?
• What stains are positive in which lesions?
• Specific situations: Histologic patterns
• Specific lesions: Melanoma and lymphoma
• Notable stains: CD vs CK
IMMUNOHISTOCHEMICAL STAINS
Specific Patterns

- Pagetoid pattern
- Clonal pattern
- Non atypical dermal spindle cell lesion
- Atypical dermal spindle cell lesion
- Small round blue cell tumor
- Large anaplastic epithelioid cell tumor
Atypical intraepidermal epithelioid cells involving upper and lower layers in small clusters of solitary cells.

Prototype: Paget’s disease

Paget’s disease, extramammary Paget’s disease, melanoma in-situ, pagetoid SCCIS, sebaceous carcinoma, pagetoid reticulosis, merkel cell carcinoma, some adnexal carcinomas metastatic to the skin.
IMMUNOHISTOCHEMICAL STAINS

Pagetoid Pattern

- Paget’s and extramammary Paget’s disease: CEA and CK7
- Melanoma in-situ: S100, Mart-1 (Melan A), MITF, SOX10
- Pagetoid SCCIS: Pan CK (not CK7)
- Sebaceous carcinoma: CEA, EMA (not CK7)
- Pagetoid reticulosis: CD3, CD4 or CD8 (not CD7)
- Merkel cell carcinoma: CK20 dot-like
IMMUNOHISTOCHEMICAL STAINS
Clonal Pattern

- Intraepidermal epithelioid cells involving upper and/or lower layers in variably-sized clusters of similar cells (clones).
- Borst-Jadassohn phenomenon
- Prototype: Hidroacanthoma simplex (poroma)
- Poroma, melanoma in-situ (nested), clonal SCCIS, clonal SK, superficial basal carcinoma, porocarcinoma
IMMUNOHISTOCHEMICAL STAINS
Clonal Pattern

- Hidroacanthoma simplex: CEA and Pan CK
- Clonal SK: Pan CK
- Clonal SCCIS: Pan CK
- Porocarcinoma: CEA and Pan Ck
- Superficial basal carcinoma: Ber-EP4
- Melanoma in-situ: S100, Mart-1, MITF, SOX10
IMMUNOHISTOCHEMICAL STAINS
Non Atypical Dermal Spindle Cell Lesion

- Uniform spindle-shaped cells involving the superficial and deep dermis (usually not the subcutis)
- Prototype: Fibrous histiocytoma (Dermatofibroma)
- Dermatofibroma, scar, leiomyoma, smooth muscle hamartoma, dermatomyofibroma, cellular blue nevus, and desmoplastic melanoma
IMMUNOHISTOCHEMICAL STAINS
Non Atypical Dermal Spindle Cell Lesion

- Dermatofibroma: Factor XIIa +, CD34 -, S100 -, Actin +/-
- Scar: Triple negative (Factor XIIa, CD34, S100) Actin +/-
- Leiomyoma/smooth muscle hamartoma: Actin +, Desmin +
- Dermatomyofibroma: Actin +, Factor XIIa -, CD34 -, S100 -
- Neurofibroma and cellular blue nevus: S100 +, SOX 10 +
- Desmoplastic melanoma: S100 +, SOX 10 +
IMMUNOHISTOCHEMICAL STAINS
Atypical Dermal Spindle Cell Lesion

- Non uniform (atypical) spindle-shaped cells involving the superficial and deep dermis (and frequently the subcutis)
- Prototype: Atypical fibroxanthoma
- AFX, poorly differentiated SCC, angiosarcoma, Kaposi’s sarcoma, leiomyosarcoma, DFSP, spindle cell melanoma
IMMUNOHISTOCHEMICAL STAINS
Atypical Dermal Spindle Cell Lesion

- AFX: CD10, CD68
- Poorly differentiated SCC: P63
- Angiosarcoma: CD31
- Kaposi’s Sarcoma: HHV-8
- Leiomyosarcoma: Desmin
- DFSP: CD34
- Spindle cell melanoma: S100, SOX10, Multiplex stains
IMMUNOHISTOCHEMICAL STAINS
Small Round Blue Cell Tumor

- Uniform “small” basophilic cells involving the superficial and deep dermis (usually no epidermal continuity)

- Prototype: Merkel cell carcinoma

- Merkel cell carcinoma, small cell carcinoma (metastatic), melanoma, lymphoma, basal bell carcinoma
IMMUNOHISTOCHEMICAL STAINS
Small Round Blue Cell Tumor

- Merkel Cell Carcinoma: CK20 dot-like
- Small Cell Carcinoma (metastatic): TTF-1
- Melanoma: SOX10
- Lymphoma: CD45
- Basal Cell Carcinoma: Pan CK, Ber-EP4
IMMUNOHISTOCHEMICAL STAINS
Large Anaplastic Epithelioid Cell Tumor

- Large non uniform epithelioid cells involving the superficial and deep dermis (usually no epidermal continuity)
- Prototype: Metastatic carcinoma
- Metastatic carcinoma, adnexal carcinoma, PD squamous cell carcinoma, anaplastic large cell lymphoma, melanoma
IMMUNOHISTOCHEMICAL STAINS
Large Anaplastic Epithelioid Cell Tumor

- Metastatic Carcinoma: P63 Negative
- Adnexal Carcinoma: P63 Positive
- Squamous Cell Carcinoma: CK5/6
- Anaplastic Large Cell Lymphoma: LCA (CD45) and Pan CK
- Melanoma - Nodular or Metastatic: S100, SOX10, etc
Use of p63 expression in distinguishing primary and metastatic cutaneous adnexal neoplasms from metastatic adenocarcinoma to skin.

Ivan D, Nash JW, Prieto VG, Calonje E, Lyle S, Diwan AH, Lazar AJ.
Department of Pathology, University of Texas - M.D. Anderson Cancer Center
IMMUNOHISTOCHEMICAL STAINS
Specific Lesions

- Malignant melanoma
- Cutaneous T-cell lymphoma
- Cutaneous B-cell lymphoma
IMMUNOHISTOCHEMICAL STAINS
Malignant Melanoma

- SSMM: Pagetoid or nested pigmented epithelioid cells
- LM: Confluent pigmented epithelioid or spindle cells
- ALM: Pigmented cells with thicker dendrites
- DMM: Inconspicuous dermal spindle cells +/- LM
- Metastatic MM: Large epithelioid cells in dermis only
IMMUNOHISTOCHEMICAL STAINS
Malignant Melanoma

- SSMM: Atypia: Upward spread: MART-1, S100, etc
- LM: Minimal atypia high density: MITF, SOX10 > MART-1
- ALM: Thickened dendrites: MART-1 (aka Melan-A)
- DMM: Frequently negative for stains except: S100, SOX10
- Metastatic MM: Lacks epidermal component: S100, SOX10
- Adjunctive/Prognostic: HMB-45, BAP-1, P16, Ki-67, BRAF
Diagnostic Utility and Comparative Immunohistochemical Analysis of MITF-1 and SOX10 to Distinguish Melanoma In Situ and Actinic Keratosis.

Buonaccorsi JD, Prieto VG, Torres-Cabala CA, Suster, S
Department of Pathology, University of Texas - M.D. Anderson Cancer Center
IMMUNOHISTOCHEMICAL STAINS
CTCL

- Top heavy (superficial)
- Intraepidermal lymphoid cells in basal layer or pagetoid
- Minimal epidermal spongiosis or interface alterations
- Dermal lymphoid cells and fibrosis
IMMUNOHISTOCHEMICAL STAINS
CTCL

- CD2, CD3, CD5, and CD7: Pan T-cell markers
- CD4: T-helper
- CD8: T-suppressor
- CD7: Expression is frequently lost in MF
IMMUNOHISTOCHEMICAL STAINS

B-cell Lymphoma

- Bottom heavy (deep)
- Monotonous dermal lymphoid cells with a Grenz zone
- Nodular, diffuse, or perivascular
- Lacks germinal centers
IMMUNOHISTOCHEMICAL STAINS

B-cell Lymphoma

- CD19, CD20, CD21, CD22, CD79: Pan B-cell markers
- BCL-6 and CD10: Follicular lymphoma
- CD5 and CD23: CLL/SLL and mantle cell lymphoma (bad)
- BCL2: Marginal zone lymphoma (good)
- CD30: Large cell lymphomas
- SOX11: Mantle cell lymphoma
IMMUNOHISTOCHEMICAL STAINS
Notable Stains

• P63
• SOX10
• CD7
• CK7
• CD20
• CK20
• Distinguishes primary skin cancers from metastatic cancers
• Distinguishes epithelial tumors from melanocytic lesions
• Distinguishes poorly differentiated SCC from AFX
SOX10

- Excellent melanocyte marker
- Nuclear stain similar to MITF
- Melan A frequently overemphasizes melanocyte density
- SOX10 and MITF very helpful in LM and unstable lentigo
• Pan T-cell marker

• Helpful in superficial dermal lymphoid infiltrates

• Distinguishes T cells from B cells

• Except expression is lost in MF
• Cytokeratin associated with breast cancer and Paget’s
• Extramammary Paget’s Disease (CK7 positive)
• Bowen’s disease and MIS (CK7 negative)
CD20

- Pan B-cell marker
- Helpful in deep dermal lymphoid infiltrates
- Distinguishes B cells from T cells
CK20

- Cytokeratin associated with GI malignancies
- Merkel cell carcinoma is dot-like CK20 positive
- Subset of extramammary Paget’s disease is CK20 positive
Summary

- Why do we do immunohistochemical stains?
  - Identify or confirm differentiation via antigen expression
  - Specific patterns
  - Specific lesions
  - Notable stains
    - P63
    - SOX10
    - CK vs CD
The doctor would like a stool sample, a urine sample, and a sperm sample.

What did she say?

They want your underwear.