Question 1

A 62-year-old man with a history of Crohn disease on Humira, presents for MMS for a nodular BCC on the left anti-helix. Please examine the 1st stage section (H&E stain).

Please select the best answer from the following:

A. The stage shows superficial and nodular BCC off of the yellow margin and micronodular BCC between blue and green margins. Take another stage.

B. The stage shows superficial and nodular BCC present off of the yellow margin. A melanocytic lesion is present at the between blue and green margin. Take another stage and consider confirming nature of the melanocytic lesion with permanent sections.

C. The stage shows a melanocytic lesion between the blue and green margins. Consider confirming nature of the melanocytic lesion with permanent sections. No further stages are needed.

D. This stage is clear, no further stages needed.

Discussion

Question 1

Correct Answer:

B. The stage shows superficial and nodular BCC present off of the yellow margin. A melanocytic lesion is present at the between blue and green margin. Take another stage and consider confirming nature of the melanocytic lesion with permanent sections.

Main Histologic Features:

- Rounded collections of basaloid keratinocytes with a peripheral palisade in the superficial dermis and budding off of the epidermis off of the yellow margin
- Myxoid stroma surrounding the collections of basaloid keratinocytes within the dermis off the yellow margin
- Multiple nests of melanocytes with round shape, vesicular nuclei and pale cytoplasm, without atypia or mitotic figures within the dermis between blue and green margins
- Melanocytes demonstrate maturation with progressive depth within the dermis

Differential Diagnosis:

- Micronodular BCC
- Intradermal melanocytic nevus
- Atypical melanocytic nevus or proliferation

Clinical Concerns:

- Melanocytic nevus cells are basophilic and may have a basaloid appearance similar to a BCC
- Unlike BCCs, melanocytic nests are typically rounded rather than angulated and lack peripheral palisading
- Melanocytic nests also lack myxoid stroma or clefting which is seen in BCC lesions (also demonstrated in this case)
- Failure to differentiate BCC from melanocytic nevus may lead to excessive stages for a benign entity
- Failure to identify atypia, mitoses or lack of normal maturation on Mohs frozen sections may lead to underdiagnosis and undertreatment of an atypical or malignant melanocytic lesion

References:

1. McKee Pathology of the Skin 4th Ed, J. Eduardo Calonje, Thomas Brenn, Alexander Lazar, and Phillip McKee, Elsevier 2011
2. Atlas of Practical Mohs Histopathology, Aasi S.Z., Leffell D.J., Lazova R.Z., Springer 2013
3. Franca K et al. Histopathologic pitfalls of Mohs micrographic surgery and a review of tumor histology. Wien Med Wochenschr. 2018 Jun;168(9-10):218-227
4. Shaver CM et al. Melanoma Within Basal Cell Carcinoma Nests Discovered During Mohs Micrographic Surgery. Dermatol Surg. 2019 Jan 11 Epub ahead of print

Question 2

A 70-year-old man received Mohs surgery for a post-auricular invasive cutaneous squamous cell carcinoma (cSCC) with features consistent with origin from an infundibular cyst, originally treated with a narrow margin excision with positive margins. Please review the 1st stage section (H&E stain).

Please select the best answer from the following:

A. Salivary gland with focal of reactive atypia present on the deep margin; no additional stage needed.

B. Foci of metastatic SCC within salivary gland; refer to head and neck surgery for parotid resection.

C. Basaloid squamous cell carcinoma is present on the deep margin; an additional stage needed.

D. cSCC present within subcutaneous fat; an additional stage needed.

Discussion

Question 2

Correct Answer:

A. Salivary gland with focal of reactive atypia present on the deep margin; no additional stage needed.

Main Histologic Features:

- Well demarcated basophilic nodule with lobular architecture within deep subcutis
- Organized glandular and ductal structures within
- Ducts often contain pink secretions within the lumen
- Focal reactive squamous metaplasia of ducts and acini without atypia, likely due to preceding excision
- Normal surrounding stroma
- No significant pleomorphism, apoptosis, or mitotic figures

Differential Diagnosis:

- cSCC with deep local extension into parotid gland
- Metastatic cSCC
- Basaloid squamous cell carcinoma
- Subcutaneous lymph node

Clinical Concerns:

- Tail of the parotid gland extends fairly superficially in the post-auricular area and may be seen on Mohs resections
- Focal reactive atypia may be seen in the parotid or salivary gland on Mohs sections, usually is attributed to inflammation due to prior biopsy or excision (in this case)
- cSCC with origin in an epidermoid (infundibular) cyst presents as a nodular lesion that can mimic a deeper process or a metastatic lesion clinically; however, exhibits marked cellular atypia, often with mitotic figures
- Failure to differentiate salivary gland with areas of reactive atypia from deep extension of cSCC or from metastatic SCC may result in excessive stages leading to clinical complications or referral for an unnecessary large resection with OHNS

References:

1. Lopez-Rios F et al. Squamous cell carcinoma arising in a cutaneous epidermal cyst: case report and literature review. Am J Dermatopathol. 1999 Apr;21(2):174-7.
2. Badlani J et al. Metastases to the parotid gland - A review of the clinicopathological evolution, molecular mechanisms and management. Surg Oncol. 2018 Mar;27(1):44-53
3. McKee Pathology of the Skin 4th Ed, J. Eduardo Calonje, Thomas Brenn, Alexander Lazar, and Phillip McKee, Elsevier 2011
4. Yu GY et al. A clinicopathologic study on basaloid squamous cell carcinoma in the oral and maxillofacial region. Int J Oral Maxillofac Surg. 2008 Nov;37(11):1003-8
5. Atlas of Practical Mohs Histopathology, Aasi S.Z., Leffell D.J., Lazova R.Z., Springer 2013

Question 3

This Mohs section is from the first stage excision of a tumor on the left cheek of a 67-year-old African American woman.

Which of the following is the best answer?

A. There is benign eccrine squamous syringometaplasia.

B. There is residual cystic basal cell carcinoma.

C. There is residual mucinous carcinoma.

D. There is residual aggressive papillary adenocarcinoma.

E. There is residual chondroid syringoma.

Discussion

Question 3

Correct Answer:

C. There is residual mucinous carcinoma.

Main Histologic Features

- Mucinous carcinoma is a dermal tumor composed of large pools of basophilic mucin divided by thin fibrous septa, creating a honeycomb pattern with “lakes of mucin” floating islands of neoplastic epithelial cells
- At the periphery a denser epithelial component may be seen. The neoplastic cells are described as cuboidal, round, or oval, with abundant cytoplasm, small regular nuclei, and rare mitotic figures. The epithelial mucin is positive for periodic acid–Schiff (PAS) stain, hyaluronidase and sialidase labile
- Mucinous carcinoma stains positive for low-molecular-weight cytokeratins, carcinogenic embryonic antigen, epithelial membrane antigen, gross cystic disease fluid protein, and salivary amylase. Variably stains with estrogen or progesterone receptors.
- Cytokeratin 20 is negative, allowing differentiation from metastatic mucinous gastrointestinal carcinoma.

Differential diagnosis

- Eccrine squamous syringometaplasia
- Cystic basal cell carcinoma
- Aggressive papillary adenocarcinoma
- Chondroid syringoma
- Malignant cylindroma, malignant spiradenoma
- Hidradenocarcinoma

Clinical Concerns

- Adnexal sweat gland neoplasm, likely apocrine in nature
- May have higher incidence in African Americans
- Presents as a small, solitary, asymptomatic, erythematous papule, cyst, ulcer, or nodule, frequently on the eyelid (44%), face (21%) or scalp (15%)
- Must be differentiated from extracutaneous metastatic mucinous adenocarcinoma – imaging, colonoscopy, up-to-date breast cancer screening
- Local recurrence rate after conventional surgery is 29%–34%; may be around 7% with Mohs surgery
- Metastatic potential is 3%-11% of cases

References

1. JAMA Dermatol. 2014;150(4):380-384.
2. Dermatol Surg. 2015;41:201–208.

Question 4

These Mohs sections are from the fourth stage excision of a squamous cell carcinoma on the scalp of a 68-year-old immunosuppressed male.

Which of the following is the best answer?

A. No residual malignancy, normal skin.

B. There is residual moderately differentiated squamous cell carcinoma.

C. There is residual moderately differentiated SCC, perineural invasion and lymphovascular invasion.

D. There is residual moderately differentiated SCC, perineural invasion but no lymphovascular invasion.

E. There is residual moderately differentiated SCC, lymphovascular invasion but no perineural invasion.

Discussion

Question 4

Correct Answer:

C. There is residual moderately differentiated SCC, perineural invasion and lymphovascular invasion.

Main Histologic Features

- Perineural invasion (PNI): Invasion of the nerve fiber or the presence of neoplastic cells within the perineural space, located between the perineurium and the nerve fiber
- Perineural lymphocytes are an important clue to the likely presence of perineural invasion in deeper sections
- Lymphovascular invasion (LVI): Presence of neoplastic cells within the lymphatic or vascular space, oftentimes with associated compression of the endothelial lining cells

Differential diagnosis

- Peritumoral fibrosis (PNI mimicker)
- Epithelial sheath neuroma (PNI mimicker)
- Perineural invasion (LVI mimicker)

Clinical Concerns

- Compared to large-caliber or named nerve involvement, SCC involving unnamed small nerves (< 0.1 mm in caliber) may have a low risk of poor outcomes in the absence of other risk factors
- Large-caliber nerve invasion is associated with an elevated risk of nodal metastasis (HR 5.6) and death (HR 4.5) compared to small nerve invasion
- Large caliber (versus small) perineural invasion is associated with vascular (p=0.01) and lymphatic (0.02) invasion
- Lymphovascular invasion associated with increased risk of death from SCC HR 15.3 (95% CI 3.7-62.8)

References

1. JAMA Dermatol. 2013;149(1):35-41.
2. J Cutan Pathol. 2009; 36: 937–942.

Question 5

An 81-year-old Caucasian male underwent Mohs micrographic surgery for a biopsy-proven nodular basal cell carcinoma on the left nasal ala. Infiltrative basal cell carcinoma was noted on stages 1 and 2. This slide is from the 3rd stage of Mohs surgery.

Please evaluate the slide and determine the next step:

A. Stop. The margin does not contain carcinoma.

B. Take another stage to clear the perineural basal cell carcinoma.

C. Take another stage to clear the peritumoral fibrosis.

D. Stop. The margin does not contain carcinoma. Re-excision perineural invasion is noted.

Discussion

Question 5

Correct Answer:

B. Take another stage to clear the perineural basal cell carcinoma.

Main Histologic Features of Perineural Basal Cell Carcinoma:

- Basaloid tumor cells immediately peripheral to the perineurium, or involving the epineurium and/or endoneurium, of cutaneous nerve tissue.[1]
- Once tumor has penetrated the nerve sheath, it spreads proximally toward nerve trunk.[1]
- Skip areas may represent artifact secondary to twisting or turning of specimen during processing which makes it impossible to visualize contiguous tumor spread in serial sections.[1]
- Perineural inflammation, peritumoral fibrosis, and skip areas may serve as indicators that there is proximal perineural tumor.[1]

Histologic Differential Diagnosis:

- Transected hair follicle: The tangential sections of hair bulbs and the hair papilla can resemble the cuffing of keratinocytic tumor around a nerve.[2]
- Peritumoral fibrosis: concentric layers of fibrous tissue surrounding and/or surrounded by tumor formations; Fibrosis will show spindled fibroblasts with tapered ends surrounding bundles of collagen rather than the wavy nuclei and plump cells characteristic of nerve fibers
- Perineural inflammation: Dense lymphocytic perineural inflammation. Lymphocytes are uniform in cell size and contain basophilic nuclei without atypia and scant cytoplasm; if inflammation involves non-neural structures too, it may be non-specific inflammation as opposed to indicator of tumor involvement[3]
- Re-excision perineural invasion or reactive neuroepithelial aggregates (RNEA): benign proliferation of perineural epithelial cells in previously biopsied areas due to aberrant reactive eccrine duct regeneration in the perineural space[4,5]
  - RE-PNI limited to scarred area
  - Benign appearing cells
  - Absence of residual epithelial tumor in vicinity of RE-PNI
  - Epithelial cells look distinct from original tumor
  - Similarly dystrophic eccrine ducts adjacent to RE-PNI
    - Studies show that most PNI in BCC is TRUE PNI and not RE-PNI
- Epithelial sheath neuroma – usually on the back - distinguish from PNI with the increased number and size of nerve fibers and lack of cytologic atypia of ensheathing squamous epithelium[6]
- Reparative perineural proliferation
  - Regenerating nerves in a healing surgical wound may reveal prominent proliferation of the perineurium → Concentric rings of bland spindle cells (EMA (+) like normal perineuriun; CK (-) and S100 (-))[3]

Clinical Concerns:

- PNI in BCC seen more commonly in infiltrative or micronodular BCC[7] but multiple histologies can be present within a single tumor so be vigilant even with nodular or superficial BCCs[8]
- PNI more likely to be present in large tumors, mid face location, high histologic grade or history of recurrence
- Peritumoral fibrosis is more sensitive marker for PNI than perineural inflammation[6]
- PNI confers increased risk of recurrence
- Concern for skip areas
- Consider radiation if large nerves involved >0.1mm or diffuse small nerve involvement[9]
  - Use PEAK Lupe 7x to measure nerve diameter intra-operatively; consider sending central debulk and marginal tissue for permanent section analysis to examine nerve diameter

References:

1. Ratner D et al. Perineural spread of basal cell carcinomas treated with Mohs micrographic surgery. Cancer, 2000. 88(7): p. 1605-13.
2. Shimizu, I. and V.D. Thomas, Evaluation of nerves in Mohs micrographic surgery: histologic mimickers of perineural invasion and nervous tissue on frozen section. Derm Surg, 2014. 40: 497-504.
3. Dunn M, Morgan M, et all. Histologic mimics of perineural invasion. Journal of Cutaneous Pathology, 2009; 36: 937-942.
4. Bechert, C.J. and J.B. Stern, Basal cell carcinoma with perineural invasion: reexcision perineural invasion? J Cutan Pathol, 2010. 37(3): p. 376-9.
5. Beer TW and Drury P. Perineural invasion in basal cell carcinomas is generally not re-exicison perineural invasion. JCP 2012; 39: 1047-48.
6. Hassanein, A.M., et al., Peritumoral fibrosis in basal cell and squamous cell carcinoma mimicking perineural invasion: potential pitfall in Mohs micrographic surgery. Dermatol Surg, 2005. 31(9): p. 1101-6.
7. Young L et al. Perineural invasion present exclusively in central tissue blocks of Mohs surgical excisions of basal cell carcinoma. Austral J Dermatol. 2018; 59: e62-e65.
8. Singh B et al. Detections of high-risk histologic features and tumor upstaging of non-melanoma skin cancers on debulk analysis. Dermatol Surg 2017; 43: 1003-11.
9. National Comprehensive Cancer Network. Basal cell carcinoma (Version 1.2016).

Question 6

A 71-year-old Caucasian male presents for treatment of a recurrent melanoma in situ on the left infra-auricular cheek. The site was previously treated with excision. Both H+E and MART-1 immunostains are performed during Mohs surgery. This slide is from the second stage of Mohs surgery.

What is your next step?

A. The peripheral margin contains melanoma in situ. Take an additional layer.

B. The peripheral margin is positive for melanoma in situ and the deep margin is positive for invasive melanoma. Take an additional layer including periphery and depth.

C. The peripheral margin contains melanoma in situ and the deep margin contains a nevus. Take an additional layer of the periphery only.

D. The peripheral margin contains melanoma in situ and the deep margin contains a nevus. Take an additional layer of the periphery and depth.

Discussion

Question 6

Correct Answer:

D. The peripheral margin contains melanoma in situ and the deep margin contains a nevus. Take an additional layer of the periphery and depth.

Histologic Criteria of Melanoma with MART-1 immunostains[1]:

- nests of at least 3 atypical melanocytes
- melanocytes above the dermoepidermal junction (pagetoid spread)
- confluence of more than 9 adjacent melanocytes
- "vertical stacking" of melanocytes
- melanocytic hyperplasia significantly different in one area as compared with the rest of the margin (can look for distinct border between normal and increased density)
- presence of nests of atypical cells in the dermis

Main Histologic Features of Intradermal nevi[2]:

- Well-formed nests of melanocytes and single melanocytes in the superficial dermis with decrease in size deeper in the dermis; Atypia and mitoses are typically not seen.
- Congenital nevi can extend to SQ fat and can surround and envelope adnexal structures.

Differential Diagnosis:

- Atypical melanocytic hyperplasia in sun damaged skin: Confluence of melanocytes (up to 9), focal pagetosis, superficial follicular extension (<1mm), and mild or moderate cytologic atypia can be observed in non-lesional sun damaged skin. MIS displays areas of confluence > 9 melanocytes as well as nesting and pagetoid spread.[3]
- Compound nevus: Junctional and dermal nests of melanocytes. Pagetoid spread usually not seen in benign nevi. Rare mitoses. Junctional nevus and the edge of a melanoma in situ have similar diagnostic criteria and are difficult to differentiate during Mohs. In contrast, incidental dermal and compound nevi can often be differentiated from melanoma.[4]
- Invasive melanoma: Asymmetrical proliferation of nested/sheets of melanocytes with poorly demarcated border; junctional nests are smaller than the dermal nests. Melanoma in situ is commonly present in the epidermis. ~5% LM become invasive[5]
  - Desmoplastic melanoma: proliferation of spindle cell melanocytes which can be mistaken for scar; overlying skin shows features of MIS/LM; dense stroma; S-100 (+); HMB-45 (-)
  - Elastic fibers present within a nevus and pushed to edges of a melanoma[6]
- Metastatic melanoma: Sheets of atypical melanocytes located in the dermis with rare junctional nests[4,5]
- Recurrent Nevus: irregular junctional activity overlying a zone of dermal fibrosis and chronic inflammation; dermal melanocytes can be seen underneath the scarring; pagetoid melanocytes do not extend beyond the scar[4]

Clinical Concerns

- It is reasonabe to remove incidental nevi as recurrent nevus may be difficult to differentiate from melanoma recurrence.
- Desmoplastic melanoma stains poorly with MART-1. Often melanoma in situ is seen overlying a deeper focus of spindle cell desmoplastic melanoma which is mistaken for scar. Be cautious when examining dermis in MIS patients and consider desmoplastic melanoma if you see a spindle cell proliferation

References

1. Valentin-Nogueras SM, Brodland DG, Zitelli JA, Gonzalez-Sepulveda L, Nazario CM. Mohs Micrographic Surgery Using MART-1 Immunostain in the Treatment of Invasive Melanoma and Melanoma In Situ. *Dermatol Surg.* 2016;42(6):733-744.
2. Calonje E, Brenn T, Lazar A. (2012) McKee's Pathology of the Skin. (4th Edition). China: Elsevier.
3. Hendi A, Brodland DG, Zitelli JA. Melanocytes in long-standing sun-exposed skin: quantitative analysis using the MART-1 immunostain. *Arch Dermatol.* 2006;142(7):871-876.
4. Rapini R. *Practical Dermatopathology*. 1st ed: Elsevier; 2005.
5. Guido Massi, Leboit PE. *Histological Diagnosis of Nevi and Melanoma.* 2nd ed: Springer; 2014.
6. Kamino et al. The use of elastin immunostain improves the evaluation of melanomas associated with nevi. Journal of Cutaneous Pathology. August 2009, Vol. 36 Issue 8, p845

Question 7

These Mohs sections (Slides 1 and 2) are from the first stage excision of a tumor on the nasal ala of a 65-year-old man.

Which of the following is the best answer?

A. There is residual tumor in each slide.

B. There is residual tumor in slide 1 only and benign folliculocentric basaloid proliferation in slide 2.

C. There is residual tumor in slide 2 only and benign folliculocentric basaloid proliferation in slide 1.

D. There is no residual tumor, but benign folliculocentric basaloid proliferation is present in both slides.

Discussion

Question 7

Correct Answer:

C. There is residual tumor in slide 2 only and benign folliculocentric basaloid proliferation in slide 1.

Main Histologic Features[1]:

- Major criteria:
  - Vertically oriented
  - Folliculocentric
  - Axial distribution
  - Prominent hyaline basement membranes, ribbonlike
  - Normal surrounding stroma
- Minor criteria:
  - Radial pinwheel, girondole, or floretlike configuration
  - Superficial, does not involve skeletal muscle or subcutaneous fat
  - No direct epidermal attachments
  - No keratin cysts
  - Uniform latticelike lobular epithelial aggregates
  - Small clefts between hyaline basement membrane and stroma
  - No single cell necrosis
  - No mitotic figures
  - No single-cell dyskeratosis
  - No melanin in basal cells

Differential Diagnosis:

- Tumors with basaloid proliferation and follicular differentiation
  - Basal cell carcinoma
  - Basaloid follicular hamartoma
  - Trichoepithelioma
  - Trichofolliculoma
  - Trichoblastic fibroma
  - Fibrofolliculma

Clinical Concerns:

- Basal cell carcinoma can cause changes to the epithelium of nearby uninvolved pilosebaceous structures, which is best appreciated in horizontal rather than vertical section slides.
- In the report by Leshin and White, folliculocentric basaloid proliferations were noted in 5.7% of nasal and peri-nasal Mohs stages for basal cell carcinoma, therefore recognition and accurate identification is important to avoid unnecessary stages.
- In contrast to other tumors with basaloid proliferation and follicular differentiation, there is no clinical lesion present.
- Histologically, this is most similar to a basaloid follicular hamartoma, particularly the generalized type. Folliculocentric basaloid proliferation is more likely to be vertically oriented, has less associations with the overlying epidermis, is associated with a mature follicle, and has no clinical correlate.

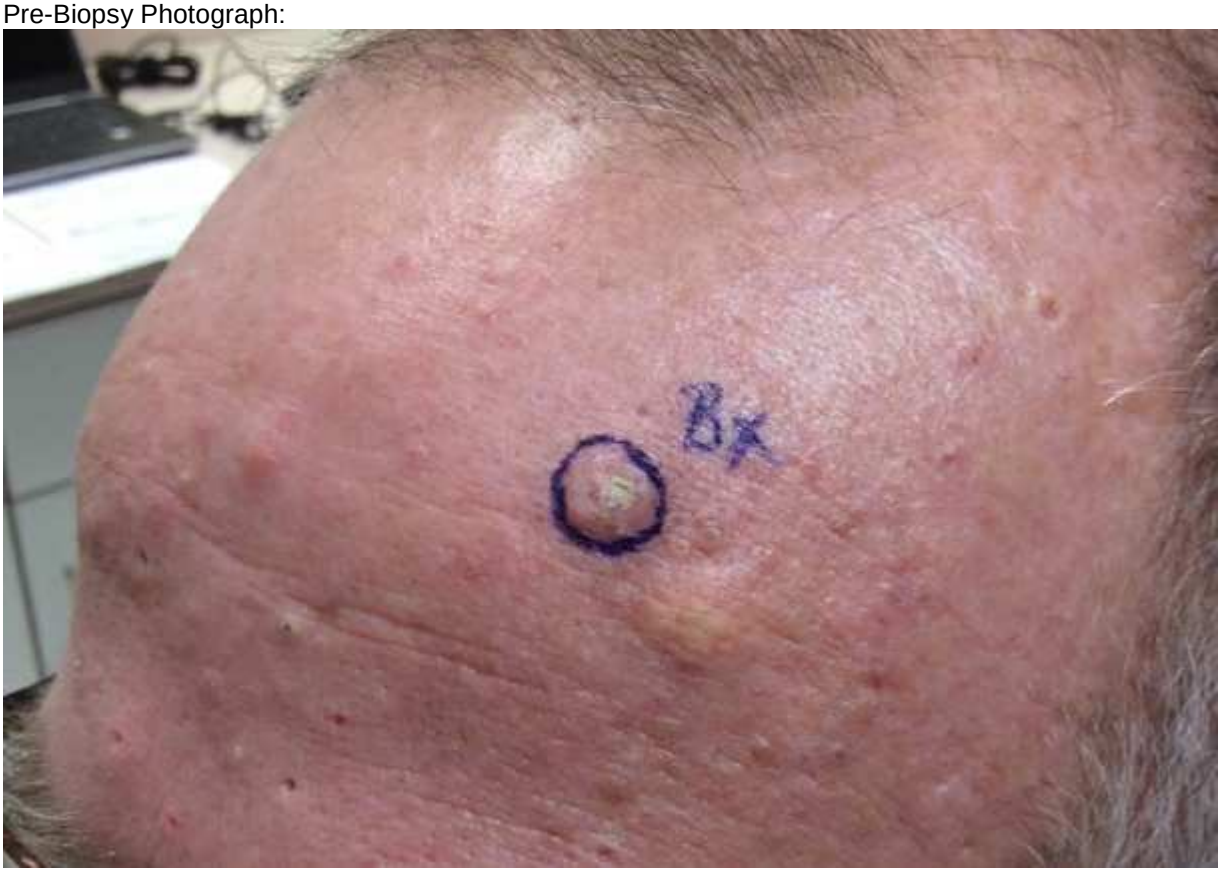
References:

1. Folliculocentric Basaloid Proliferation. The Bulge (der Wulst) Revisited. Leshin B and White WL. Arch Dermatol. Vol 126, July 1990. 900-906
2. Studies on the “Bulge” (Wulst) in superficial basal cell epitheliomas. Madsen A. Arch Dermatol. 1964; 89:698-708.

Question 8

These Mohs sections (Slides 1 and 2) are from the first stage excision of a squamous cell carcinoma on the forehead of a 43-year-old man.

Pre-Biopsy Photograph:



Which of the following is the best answer?

A. There is residual tumor in each slide.

B. There is no residual tumor in either slide, findings are consistent with Darier's disease.

C. There is invasive SCC in slide 1 and acantholytic actinic keratosis in slide 2.

D. No further stages needed, findings consistent with a warty dyskeratoma.

Discussion

Question 8

Correct Answer:

B. There is no residual tumor in either slide, findings are consistent with Darier's disease.

Main Histologic Features:

- Acantholytic dyskeratosis, suprabasal cleft formation and corps ronds and grains of Darier
- Corps ronds: large structures, often in the granular layer.
    - Consist of an irregular, eccentric nucleus with halo within a basophilic or eosinophilic "shell"
    - May have keratoyhalin granules
- Grains: located within the horny layer
    - Flattened oval cells with elongated nuclei and keratohyalin granules
- Hyperkeratosis, often parakeratosis
- Villus formation

Differential Diagnosis:

- Acantholytic squamous cell carcinoma
- Acantholytic actinic keratosis
- Warty dyskeratoma
- Hailey-Hailey disease
- Pemphigus
- Grover's disease

Clinical Concerns:

- Due to mutation in ATP2A2, a gene encoding type 2 sarcoendoplasmic reticulum CA 2+-ATPasd (SERCA2)
- Integrity of intercellular junctions is likely dependent on intracellular calcium, therefore mutations in one copy of the gene lead to cellular acantholysis and dyskeratosis
- Clinical Findings
    - Clinical lesions are hyperkeratotic yellow-brown papules and plaques
        - Common locations: scalp, forehead, ears, nasolabial folds, upper chest, back
    - Palms and soles may have pits and punctate keratoses
    - Nail changes
        - Longitudinal white or red streaks
        - Nicking of the free margin of the nail
        - Painful splitting
    - Oral lesions present in 50%
        - Small white papules on the hard palate
        - Nodular or verrucous plaques also possible

References:

1. McKee's Pathology of the Skin. 5th Ed. Acantholytic Disorders, Chapter 5. Calonje E, et al. 2020 Elsevier Limited.
2. Mimickers of classic acantholytic diseases. Ho J and Bhawan J. Journal of Dermatology 2017; 44:232-242

Question 9

This Mohs section is taken after a permanent section biopsy of a 1.2 cm nodule on the lower lip of a 55-year-old woman demonstrated well-differentiated squamous cell carcinoma.

Given this finding, which of the following is the best answer?

A. No tumor is present.

B. Incidental salivary gland adenocarcinoma is present.

C. Incidental sebaceous carcinoma is present.

D. Perineural invasion is noted, and tumor is upstaged according to both BWH and AJCC staging systems.

E. Residual tumor is noted, but original tumor stage remains unchanged.

Discussion

Question 9

Correct Answer:

D. Perineural invasion is noted, and tumor is upstaged according to both BWH and AJCC staging systems.

Main Histologic Findings:

- With perineural invasion of SCC, malignant keratinocytes are noted to invade the perineurium and track along nerve.
- Perineural fibrosis refers to the presence of concentric rings of fibrous tissue that when accompanied by tumor cells can mimic microscopic PNI.
- With re-excision perineural invasion, benign squamous epithelium is present in the perineural spaces of cutaneous nerves in re-excision specimens and may form a complete cuff around the nerve fascicle.
- Reparative perineural proliferation can be seen in healing surgical wounds and is characterized by concentric rings of spindle shaped cells enveloping a nerve adjacent to surgical scar.
- Epithelial sheath neuroma is characterized by nerve complexes enveloped by mature squamous epithelium with mucinous stroma.

Differential Diagnosis

- Perineural fibrosis
- Re-excision perineural invasion
- Reparative perineural proliferation
- Epithelial sheath neuroma

Clinical Concerns:

- Perineural invasion is estimated to be seen in 6% of cutaneous SCC.
- Presence of large caliber PNI (>0.1mm) is considered an adverse risk factor in both AJCC and BWH staging systems for cutaneous SCC, and when present may warrant a discussion of adjuvant treatment options (RT) to reduce the risk of recurrence of the primary tumor.
- In this case, tumor was upstaged intraoperatively according to both the AJCC (T1-->T3) and BWH (T1-->T2b) staging systems due to invasion into skeletal muscle and the presence of perineural invasion. BWH T2b tumors carry a significant risk of nodal metastasis, and nodal staging should be considered.

References:

1. Lever's Histopathology of the skin. 11th Ed. Edited by Elder DE, 2014; Wolters Kluwer.
2. Dunn M, Morgan M, et al. Histologic mimics of perineural invasion. J Cutan Pathol. 2009: 36: 937-942.
3. Fox MC, Brown M, et al. Nodal staging of high risk cutaneous squamous cell carcinoma. J Amer Acad Dermatol. 2018 Sep 15.

Question 10

This Mohs section is from the first stage excision of a tumor on the right pretibial lower leg of a 78-year-old man.

Which of the following is the best answer?

A. There is residual squamous cell carcinoma.

B. There is residual eccrine carcinoma.

C. As no tumor is identified.

D. Incidental Kaposi sarcoma is noted.

E. Incidental basal cell carcinoma is noted.

Discussion

Question 10

Correct Answer:

C. As no tumor is identified, discuss reconstruction versus healing by second intention, with plan to wrap the site with compression dressings during wound healing.

Main Histologic Features:

- With stasis dermatitis, epidermis may variably be hyperkeratotic with focal parakeratosis and underlying acanthosis and spongiosis.
- In the papillary and sometimes upper reticular dermis, lobular aggregates of capillary-sized blood vessels are seen, often surrounded by deposits of hemosiderin, extravasated RBC and lymphocytic infiltrate.
- At low power, angioplasia may mimic small epithelial nests, and when combined with a lymphocytic infiltrate, may be confused for superficially invasive squamous cell carcinoma.

Differential Diagnosis:

- Epithelial malignancy
- Actinic keratosis
- Eczema
- Kaposi sarcoma
- Eccrine hamartoma

Clinical Concerns:

- Cutaneous squamous cell carcinoma is commonly diagnosed on the lower legs, often arising in the clinical background of stasis dermatitis, which is also commonly seen with advancing age and results from venous hypertension related to retrograde flow due to obstruction or dysfunction of the venous system.
- It is important to differentiate nests of invasive squamous cell carcinoma from the cannonball vascular aggregates seen in stasis dermatitis, particularly when surrounding lymphocytic inflammation is present.
- Intradermal conservative thickness layers may be utilized as an effective technique to facilitate granulation following Mohs excision for tumors on the pretibial lower legs.
- Compression therapy is critical in correcting impaired venous return, thereby facilitating improved wound healing for lower leg defects.

References:

1. Lever's Histopathology of the skin. 11th Ed. Edited by Elder DE, 2014; Wolters Kluwer.
2. Sundaresen S, Migden MR, Silapunt S. Stasis dermatitis: pathophysiology, evaluation and management. Am J Clin Dermatol. 2017 Jun;18(3):383-390.
3. Tolkachjov S, Cappel J, et cal. Conservative thickness layers in Mohs micrographic surgery. Int J Dermatol. Int J Dermatol. 2018 Sep;57(9):1128-1134.
4. Alavi A, Sibbald RG, et al. What's new: management of venous leg ulcers: treating venous leg ulcers. J Amer Acad Dermatol. 2016 Apr;74(4):643-664.