

American College of Mohs Surgery
Diagnostic Quality Control Program 2011
(Review of Answers)

Question 1

A large ulcerated plaque overlying the right angle of the mandible of an otherwise healthy 59-year old female is referred for Mohs surgery.

The correct diagnosis is:

- a. Lymphoepithelioma-like carcinoma of the skin.
- b. Infiltrative basal cell carcinoma with reactive lymph node.
- c. Infiltrative carcinoma with lymph node metastasis.
- d. Infiltrative basal cell carcinoma with normal parotid tissue.

Discussion

Question 1

Correct Answer:

- b. Infiltrative basal cell carcinoma with reactive lymph node

Main Histologic Features:

- Superficially, the tumor is composed of small to medium-sized basaloid islands and cords with an infiltrating pattern
- Peripheral palisading and artifactual stromal retraction is noted
- In the deep soft tissues there is an organized nodular lymphoid infiltrate with germinal center formation
- No atypia of lymphocytes
- No evidence of lymph node involvement by the tumor

Differential Diagnosis:

- Metastatic disease to cutaneous lymph node
- Tumor surrounded by intense inflammation
- Secondary lymphoproliferative process
- Lymphadenoma

Clinical Concerns:

- Cutaneous and subcutaneous lymphadenoid inflammatory reactions are often noted at the edge of longstanding or large tumors
- Cutaneous lymph nodes can be mistaken as deeply-invasive carcinoma, particularly when treating squamous cell carcinomas with their characteristic inflammatory response
- If there is concern of tumor involvement, immunoperoxidase stains may be useful

References:

- Grosshans E, Juillard J, Schaeffle B, Ball C. Inflammatory lymphoid reactions around basocellular epitheliomas. *Am Dermatol Venereol.* 1984;111(5):447-59.
- Practical Dermatopathology. Edited by R. Rapini 2005 Elsevier Mosby.

Question 2

A flesh-colored papule on the left upper lip of an otherwise healthy 52-year old male is referred for Mohs surgery.

The correct diagnosis is:

- a. Keratotic basal cell carcinoma
- b. Trichoepithelioma
- c. Microcystic adnexal carcinoma
- d. Sebaceous carcinoma

Discussion

Question 2

Correct Answer:

- b. Trichoepithelioma

Main Histologic Features:

- Circumscribed basaloid tumor islands, often in a reticulated pattern or cribiform pattern
- Horn cysts common
- Peripheral palisading of nuclei is present, but no artifactual retraction between tumor and stroma
- Loose stroma with many fibroblasts surrounding basaloid islands
- Papillary mesenchymal bodies (clusters of fibroblasts adjacent to epithelial buds as in the germinal portion of the normal hair papilla)

Differential Diagnosis:

- Keratotic basal cell carcinoma
- Basal cell carcinoma with follicular differentiation
- Trichoblastoma
- Microcystic adnexal carcinoma (for desmoplastic trichoepithelioma)

Clinical Concerns:

- Common skin colored papule or nodule located on the central face
- Usually solitary, but multiple lesions with childhood onset may be inherited as an autosomal dominant condition
- It is a benign neoplasm, even though epithelioma usually means low grade carcinoma
- Can be difficult to distinguish from BCC.

References:

- Practical Dermatopathology. Edited by R. Rapini 2005 Elsevier Mosby.
- Skin Cancer. Edited by K. Nouri 2008 McGraw-Hill.

Question 3

The following Mohs section was taken from the right forehead of an otherwise healthy 78-year-old male.

The correct diagnosis is:

- a. Porocarcinoma
- b. Non-irritated seborrheic keratosis
- c. Seborrheic keratosis with foci of Bowenoid transformation
- d. Clear cell acanthoma

Discussion

Question 3

Correct Answer:

- c. Seborrheic keratosis with foci of Bowenoid transformation

Main Histologic Features:

- Epidermal proliferation with acanthosis and parakeratosis
- Horn pseudocysts are seen within the benign portion
- Mild to moderate atypia and squamous eddies suggest an irritated seborrheic keratosis
- Multiple foci of atypical keratinocytes with hyperchromatism and pleomorphism, multiple dyskeratotic keratinocytes and loss of orderly maturation.
- Numerous mitoses
- Perivascular and lichenoid lymphocytic infiltrate

Differential Diagnosis:

- Irritated/Inflamed seborrheic keratosis
- Actinic keratosis
- Viral verruca

Clinical Concerns:

- Malignant transformation is a rare event, usually occurs in long standing lesions with recent history of ulceration or increasing size
- Malignant change seems to occur in lesions located in the head and neck
- In addition to squamous cell carcinoma in-situ, invasive SCC and BCC have been reported
- Many of these cases are interpreted as in-situ carcinoma because the residual seborrheic keratosis may be difficult to detect

References:

- Sloan JB, Jaworsky C. Clinical misdiagnosis of squamous cell carcinoma in situ as seborrheic keratosis. A prospective study. *J Dermatol Surg Oncol* 1993;19:413-16.
- Sharma P, Sarma D, Adickes E. Seborrheic keratosis with in-situ squamous cell carcinoma changes. *Dermatol Online J* 2006;12 (7):19.

Question 4

The following Mohs section was taken from the right nasal ala of a 64-year-old female with a history of basal cell carcinoma.

The correct diagnosis is:

- a. Infundibulocytic basal cell carcinoma
- b. Fibrofolliculoma
- c. Basal cell carcinoma with follicular differentiation
- d. Folliculocentric basaloid proliferation

Discussion

Question 4

Correct Answer:

- d. Folliculocentric basaloid proliferation

Main Histologic Features:

- Vertically oriented, folliculocentric proliferations, with an axial distribution
- Prominent hyaline basement membranes, ribbon like
- Normal surrounding stroma, and absence of altered or myxoid stroma with artifactual retraction
- Superficial, does not involve subcutaneous fat, no direct epidermal attachment
- Radial pinwheel, girondele or floret-like configurations
- No single cell necrosis, mitoses, or dyskeratosis
- FBP differs from BFH by absence of keratin cysts and no direct epidermal attachments

Differential Diagnosis:

- Infundibulocystic basal cell carcinoma
- Trichoblastoma
- Trichoepithelioma
- Basaloid follicular hamartoma (BFH)

Clinical Concerns:

- Clinical features alone are not always helpful in distinguishing the various benign hair follicle tumors from BCC
- The discrimination of BCC from FPB on horizontal frozen sections can at times be difficult
- Failure to differentiate this entity from basal cell carcinomas could result in overly aggressive surgical excision of a benign adnexal tumor

References:

- Saxena A, Shapiro M, Kasper D, Fitzpatrick J, Mellette JR. Basaloid follicular hamartoma: A cautionary tale and review of the literature. *Dermatol Surg*, 2007;33:1130-1135.
- Leshin B, White W. Folliculocentric basaloid proliferation. *Arch Dermatol* 1990;126:900-906.

Question 5

This Mohs section is from the first stage of melanoma in-situ on the right nasal ala of a 78-year-old man.

Which of the following is true?

- a. Focal, residual melanoma in-situ is present; take a second stage.
- b. Atypical, sun-damaged melanocytes are present but no overt melanoma in-situ is seen.
- c. Evidence of trichoadenoma is present; take a second stage.
- d. Evidence of rhinophyma is present with melanoma in-situ; take a second stage.

Discussion

Question 5

Correct answer:

b. Atypical, sun-damaged melanocytes are present but no overt melanoma in-situ is seen

Main Histologic Features:

- Evaluation of melanocytic lesions in frozen sections can be challenging
- Normally, melanocytes are seen within the basal cell layer of the epidermis, hair bulbs and outer root sheath of hair follicles
- In sun damaged skin, melanocytes increase in number and in size. The most important point in differentiating positive from negative melanoma margins is the presence of confluence or nesting. Unfortunately, there is no immunohistochemical marker that helps in such differentiation. HMB-45 stains both normal and neoplastic epidermal melanocytes. Immunohistochemical staining for Melan-A or Mart-1 is sensitive and specific for melanocytes, but we found that a thin cut and properly stained Mohs section minimizes the need for immunohistochemical staining. The latter should be used in equivocal cases.
- Generally speaking, the histologic criteria for melanoma in-situ include: (1) confluence of atypical melanocytes along the dermo-epidermal junction with extension along adnexal structures with or without nesting. (2) extension of atypical melanocytes at the upper reaches of the epidermis (Pagetoid spread) and (3) presence of large starburst/giant melanocytes.

Differential diagnosis:

Melanoma in-situ should be differentiated from:

- Large atypical sun-damaged melanocytes
- Junctional and lentiginous nevi
- Some cases of Bowen's disease

References:

- Hendi A, Brodland DG, Zitelli JA. Melanocytes in long-standing sun-exposed skin: quantitative analysis using the MART-1 immunostain. *Arch Dermatol*. 2006 Jul; 142(7):871-6.
- Zitelli JA, Brown CD, Hanusa BH. Surgical margins for excision of primary cutaneous melanoma. *J Am Acad Dermatol*. 1997 Sep; 37(3 Pt 1):422-9.

Question 6

This specimen was shaved from the right leg of a 73 year-old man.

Which of the following is true?

- a. Focal, residual BCC with pseudoepitheliomatous hyperplasia present; margins are negative.
- b. Residual collision tumor (SCC and BCC); margins are negative.

Discussion

Question 6

Correct answer:

- a. Focal, residual BCC with pseudoepitheliomatous hyperplasia present; margins are negative

Main Histologic Features:

- A variable degree of keratinocytic atypia and rare normal mitotic figures in the basal cell layer can be seen in sun damaged skin.
- Pseudoepitheliomatous (pseudocarcinomatous) hyperplasia may create an indistinguishable picture from SCC for some Mohs surgeons.
- The most important and probably the only criteria for differentiating pseudoepitheliomatous hyperplasia from SCC are the lack of cytologic atypia and lack of atypical/bizarre mitoses that are seen in SCC. All other criteria of SCC can, unfortunately, be seen in pseudoepitheliomatous hyperplasia including irregular infiltration by variably sized groups of keratinocytes with mitosis and inflammatory reaction from the host.

Differential diagnosis:

- Squamous cell carcinoma.

Clinical Concerns:

- Misinterpreting pseudoepitheliomatous (pseudocarcinomatous) hyperplasia as SCC will result in a false positive margin and consequently a larger Mohs defect.

References:

- Tuttle MS, Rosenberg AS, Winfield HL, Somach SC. Pseudocarcinomatous hyperplasia with follicular differentiation overlying basal cell carcinoma. *Am J Dermatopathol.* 2009 Aug; 31(6):557-60.
- Zayour M, Lazova R. Pseudoepitheliomatous hyperplasia: a review. *Am J Dermatopathol.* 2011 Apr; 33(2):112-26.

Question 7

This biopsy specimen was taken from the forehead of a 72-year-old man.

The most likely diagnosis is:

- a. Adenoid basal cell carcinoma with amyloid deposits
- b. Microcystic adnexal carcinoma
- c. Metastatic duct carcinoma of the breast with collagenous spherulosis
- d. Metatypical basal cell carcinoma.

Discussion

Question 7

Correct answer:

- a. Adenoid basal cell carcinoma with amyloid deposits

Main Histologic Features:

- Adenoid basal cell carcinoma shows a reticulate pattern of basaloid cells or adenoid spaces within basaloid nodules often with mucinous collection mimicking glandular formation.
- Amyloid material is present in 66% to 77% of all subtypes of basal cell carcinomas. It is usually present at the advancing edge and is probably formed from keratin as a consequence of apoptosis.
- Amyloid deposits in basal cell carcinoma greatly resemble the phenomenon of collagenous spherulosis seen in breast pathology.

Differential diagnosis:

- Metastatic breast carcinoma with collagenous spherulosis.
- Microcystic adnexal carcinoma
- Metastatic mucinous carcinoma of the colon

References:

- Olsen K, Westermark P. Amyloid in basal cell carcinoma and seborrheic keratosis. *Acta Derm Venereol.* 1994;74:273-275.
- Looi LM. Localized amyloidosis in basal cell carcinoma. A pathological study. *Cancer.* 1983;52:1833-1836.

Question 8

This Mohs section was taken from the nasal dorsum of a 64 year-old female with a history of a nodular basal cell carcinoma.

Which of the following is true?

- a. There is a focus of dense inflammation that could be hiding a tumor; take a second stage.
- b. The findings are consistent with rosacea. A tumor free plane is reached.

Discussion

Question 8

Correct answer:

- b. The findings are consistent with rosacea. A tumor free plane is reached.

Main Histologic Features:

- Dense inflammatory infiltrate is said to be the pathologist's enemy.
- Higher power examination of dense inflammatory infiltrate is important to rule out any hidden individual cells, groups of tumor cells or perineural invasion. The latter can be hidden by dense perineural inflammation. Deeper/additional cuts may also be useful to determine if the inflammation is a response to the presence of tumor.
- On the other hand, dense inflammatory infiltrate can be reactive or represent a chronic skin disease. This is not uncommon in Mohs slides of facial tumors in anatomic sites that may show a variable degree of rosacea. The presence of multinucleated giant cells and/or granulomas within the lymphohistiocytic infiltrate is helpful in identifying rosacea. Granulomas are reported to be seen in only 10% of all cases of rosacea.
- If there is doubt interpreting dense inflammatory infiltrates, immunohistochemical stains would be greatly helpful i.e. AE1/3 for SCC and BER Ep-4 for BCC.

Differential diagnosis:

- Dense focal peritumoral inflammation
- Dense focal perineural inflammation with perineural invasion

References:

- Marks R., Harcourt-Webster JN. Histopathology of rosacea. *Arch Dermatol* 1969;100:683-689.
- Ioffreda M. Inflammatory diseases of hair follicles, sweat glands, and cartilage, in Lever's Histopathology of the Skin, Elder D (ed), pp463-464. Lippincott Williams & Wilkins, Philadelphia 2009.
- Katz KH, Helm KF, Billingsley EM, et al. Dense inflammation does not mask residual primary basal cell carcinoma during Mohs micrographic surgery. *J Am Acad Dermatol* 2001;45:231-238.

Question 9

An 80 year old man with a twice recurrent right lower eyelid sebaceous carcinoma has been referred to you for Mohs surgery. After 4 layers the tumor has tracked onto the bulbar conjunctiva. A portion of the bulbar conjunctiva is excised and shown on the submitted slide.

Which of the following of is the best answer? (Please examine all the sections to make your decision.)

- a. Sebaceous carcinoma is still present. Exenteration or topical chemotherapy should be discussed as options for the patient.
- b. A granuloma is present, the patient is now tumor free
- c. A careful family history regarding internal malignancies is not necessary in this situation
- d. Periocular sebaceous carcinomas are more likely to be associated with Muir-Torre syndrome than extra ocular sites.

Discussion

Question 9

Correct answer:

- a. Sebaceous carcinoma is still present. Exenteration or topical chemotherapy should be discussed as options for the patient.

Main Histologic Features:

- This specimen was obtained from bulbar conjunctiva, which is uncornified, stratified epithelium.
- Atypical cells with nuclear pleomorphism are present in both the epithelium as well as connective tissue layers indicating the persistence of marginal tumor despite stripping the bulbar conjunctiva.
- Granulomas do not exhibit cytologic atypia and this is also not an expected finding of sebaceous adenoma or epithelioma.
- SCC in-situ can be nearly impossible to differentiate with frozen sections from in-situ sebaceous carcinoma. Special stains can be performed, but are usually done on the biopsy rather than intraoperatively.
- Areas of normal appearing bulbar conjunctiva are also present.

Differential Diagnosis:

- Sebaceous adenoma
- Sebaceous epithelioma
- SCC in-situ
- Granuloma

Clinical Concerns:

- Sebaceous carcinoma is the second most common eyelid tumor, after basal cell carcinoma. Misdiagnosis is common, as distinguishing this tumor from chalazion can be quite difficult.
- These tumors have high rates of metastasis (approximately 25%) and recurrence (up to 50%) and may also be associated with the Muir-Torre tumor syndrome.
- Exenteration is advocated when the tumor can not be cleared or invades orbital fat by some authorities due to the aggressive nature of the tumor, but not everyone agrees with that approach.
- Mitomycin eye drops can be tried or depending on the patient's age they may choose to take their chances with the cancer rather than losing their eye.
- Data from these different approaches are sparse so universal recommendations regarding persistent bulbar tumor are inappropriate in my opinion and should be tailored to each individual case.
- See Clinical concerns for next question for further sebaceous carcinoma discussion.

Question 10

An 81-year-old man with a new sebaceous carcinoma on the left lower eyelid is sent for Mohs surgery of the lesion. The slide from the second layer is submitted.

Which of the following is the best answer? (Please examine all the sections to make your decision.)

- a. There is a moderate inflammatory process involving the palpebral conjunctiva resulting in pseudoepitheliomatous hyperplasia
- b. Electrosurgery artifact has resulted in disorganized, but normal appearing stratified squamous epithelium
- c. There is architectural and cellular atypia present in the epithelium consistent with persistent sebaceous carcinoma.
- d. There is architectural and cellular atypia, but these features are due to inflammation normally present within palpebral conjunctiva.

Discussion

Question 10

Correct answer:

- c. There is architectural and cellular atypia present in the epithelium consistent with persistent sebaceous carcinoma.

Main Histopathologic Features:

- There are areas of architectural disorder and nuclear pleomorphism present within the palpebral epithelium, a clear indication of tumor persistence.
- Though areas of cytoplasmic vacuolization, as is often seen with sebaceous carcinoma, are infrequent, with a prior biopsy confirmed diagnosis of sebaceous carcinoma the changes are consistent.
- As a practical matter it is very difficult to differentiate squamous cell carcinoma in-situ from in-situ sebaceous tumors with frozen sections. There is no indication of heavy electrosurgical artifact, which causes strung out spindly changes, often with separation at the dermal-epidermal junction.
- Regarding tumor histology for sebaceous carcinomas these lesions may be classified as well, moderately and poorly differentiated. In addition, four patterns are recognized by most authorities: lobular, comedocarcinoma, papillary, and mixed.
- Typical lesions have an irregular lobular pattern with sebaceous and undifferentiated cells. The tumor cells show a marked variation of nuclear shape and size, hyperchromatism, basaloid appearance, and high mitotic activity. The undifferentiated cells have eosinophilic cytoplasm with lipid granules that give them a frothy appearance.
- Atypical keratinizing cells may be present. The spread of tumor cells into the adjacent epithelium (Pagetoid spread) is also a known feature.
- The oil red O stain, Sudan IV stains, epithelial membrane antigen, and Leu-M1 immunostains may be helpful in discriminating sebaceous carcinomas from other tumors.

Differential Diagnosis:

- Sebaceous adenoma
- Sebaceous epithelioma
- SCC in-situ
- Granuloma

Question 10 cont'd

Clinical Concerns:

- Muir-Torre syndrome (MTS) is a phenotypic subset of the hereditary non polyposis cancer syndrome, also known as Lynch syndrome. It is autosomal dominant and affected individuals have high rates of colorectal cancer and other disorders of the urogenital and digestive tracts.
- Sebaceous neoplasms are rare and frequently associated with MTS (5-45% incidence). Therefore any patient with a sebaceous neoplasm, including sebaceous carcinoma, should be evaluated to exclude the syndrome.
- Extra ocular locations are more frequently associated with MTS than peri-ocular ones. A careful family history is helpful.
- If the family history is not suggestive additional testing (immunohistochemistry and microsatellite instability testing) can be performed on the tumor specimens to determine whether it is worthwhile proceed with genetic testing.
- Those identified with the syndrome should also consider screening additional family members. Evidence suggests affected individuals might benefit from intensive screening strategies, such as periodic colonoscopy, which could help detect tumors at earlier stages of development. A detailed discussion of suggested screening approaches was published in the JAAD in 2009.

References:

- Eisen DB, Michael DJ. Sebaceous lesions and their associated syndromes: part II. *J Am Acad Dermatol* 2009 Oct;61(4):563-578; quiz 579-580.
- Russell HC, Chadha V, Lockington D, Kemp EG. Topical mitomycin C chemotherapy in the management of ocular surface neoplasia: a 10-year review of treatment outcomes and complications. *Br J Ophthalmol*. 2010 Oct;94(10):1316-1321.
- Rudkin AK, Muecke JS. Mitomycin-C as adjuvant therapy in the treatment of sebaceous gland carcinoma in high-risk locations. *Clin Experiment Ophthalmol*. 2009 May;37(4):352-356.

Question 11

An 85-year-old woman is sent to you for Mohs surgery regarding a SCC.

Which of the following are the best answer regarding the submitted slide from her last layer? (Please examine all the sections to make your decision.)

- a. A follicular hamartoma is present at the deep margin. The patient is tumor free.
- b. There is a potential floater at the deep margin with obvious SCC present, as well as a follicular hamartoma. Another layer is necessary.
- c. There is a potential floater at the deep margin with obvious SCC present, as well as a SCC in the deep margin. Another layer is necessary.
- d. There is a potential floater at the deep margin with obvious SCC present, as well as a tangential section of a hair follicle in the deep dermis. Another layer is necessary.

Discussion

Question 11

Correct answer:

- c. There is a potential floater at the deep margin with obvious SCC present, as well as a SCC in the deep margin. Another layer is necessary.

Main Histologic Features:

- Next to the deep dermis there is an island of tissue (floater) with tumor cells exhibiting an infiltrative growth pattern. These cells have eosinophilic glassy cytoplasm and are present as small tumor strands and single cells.
- This pattern and morphology is compatible with SCC. Adjacent to this floater containing tumor there is a large follicular structure with attached sebaceous glands and keratin containing cysts.
- The lesion is larger than all other follicles on the slide and contains areas of acantholysis, a feature normally seen in SCC and some AK's. In addition cellular morphology at the periphery of this lesion resembles that of the tumor seen in the floater. Clearly another layer will be necessary

Differential Diagnosis:

- Tangential hair follicle
- SCC
- Hamartoma

Clinical Concerns:

- This question has two dilemmas: what to do with potential floaters, and how to distinguish tangential cuts from malignancy.
- The issue of floaters is a difficult one. In this case there is dye on floater, indicating it came from the bottom of this specimen. This supports the need for another layer, whether one has difficulty with the other tumor focus or not.

References:

- Kane CL, Keehn CA, Smithberger E, Glass LF. Histopathology of cutaneous squamous cell carcinoma and its variants. *Semin Cutan Med Surg.* 2004 Mar;23(1):54-61.

Question 12

A 67-year-old male is referred for Mohs surgery for a superficial BCC. The slide from his last layer is submitted.

Which of the following is the best answer?)Please examine all the sections to make your decision.)

- a. Superficial BCC is not present at the margin. There is an inflammatory focus involving a follicular bulb. No more layers are necessary.
- b. Superficial BCC is not present and sclerosing BCC is not a concern given the biopsy revealed the tumor to be superficial BCC. No more layers are necessary.
- c. Superficial BCC is present as well as infiltrative BCC. Another layer is required.
- d. No superficial BCC is present, an inflammatory focus containing sclerosing BCC is present, another layer should be performed.

Discussion

Question 12

Correct answer:

c. Superficial BCC is present as well as infiltrative BCC. Another layer is required.

Main Histologic Features:

- There are small foci of basaloid cells with surrounding metachromasia, peripheral palisading and retraction artifact. These changes are consistent with superficial BCC.
- There is an inflammatory focus in the mid to deep dermis surrounding a follicular bulb. Encompassed within this infiltrate are tumor islands with acute angles, indicative of infiltrative BCC. An inflammatory reaction is frequently encountered around cutaneous tumors. Though subtle, the tumor can clearly be seen in the deepest section of this specimen.
- In this situation another layer is advisable.

Differential Diagnosis:

- Infiltrative BCC
- Normal hair bulbs with dense inflammation
- Tangential vascular structures with dense inflammation

Clinical Concerns:

- Some surgeons believe the presence of dense inflammation is an indication for further excision, since obscured tumor cannot be ruled out.
- A small study has been performed on this topic by Katz et al.(10) They found no relationship between the presence of dense inflammation and hidden tumor. Of course we all have our own anecdotal experiences where deeper cuts into the block has shown persistent tumor, so as always, one has to weigh the clinical situation on how one proceeds with this dilemma.

References:

- Katz KH, Helm KF, Billingsley EM, Maloney ME. Dense inflammation does not mask residual primary basal cell carcinoma during Mohs micrographic surgery. *J Am Acad Dermatol.* 2001 Aug;45(2):231-238.