Introduction to Dermatopathology – Part 1

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Skin - Constituents

• Keratinocytes - The main constituents of the epidermis

• Melanocytes - Pigment producing cells

• Langerhans cells - Antigen-processing cells.

• Merkel cells - Neuroendocrine cells in the basal layer of the epidermis that have neuroendocrine granules
• Mild melanocytic hyperplasia
Terms

• **Hyperkeratosis**
  - Thickening of the stratum corneum
  - Often occurs secondary to irritation eg chronic eczema, lichen planus, etc but also occurs in pre-neoplastic and neoplastic lesions.
  - Clinically appears as thickened scaly skin
Terms

• **Parakeratosis**
  – Thickening of the stratum corneum; similar to hyperkeratosis but nuclei are retained within keratinocytes
  – Is associated with rapid turnover of keratinocytes in the epidermis. Can occur in inflammatory conditions (e.g., psoriasis) and in pre-neoplastic and neoplastic lesions.
Terms

• **Acanthosis**
  – Thickening of the viable portions of the epidermis.
  – Can also occur in a variety of conditions, including simple irritation and pre-neoplastic and neoplastic conditions.
Terms

• **Acantholysis**
  - Loss of intercellular bridges between keratinocytes in the epidermis.
  - Can occur in a variety of settings including neoplastic and pre-neoplastic conditions as well as inflammatory diseases
Terms

• **Spongiosis**
  – Intra-epidermal oedema
Neoplasia and Pre-neoplasia
Solar keratosis

- Pre-neoplastic lesion which is considered to be an indicator of cumulative UV exposure.
- Up to 95% of SCCs are thought to arise in AKs (If you suspect an SCC but you receive a report of solar keratosis on a biopsy make sure that the pathologist has cut adequate levels).
- Estimated to evolve into SCC at the rate of 0.2-10% per year.
- SCCs arising in AKs at most body sites rarely metastasize (<1% rate of metastasis).
- Histo: Partial thickness keratinocytic atypia
Bowenoid solar keratosis

- Pre-neoplastic lesion
- Considered to be a step further along the spectrum to SCC
- Histo: Focal full-thickness keratinocytic atypia that does not involve hair follicles.
Neoplastic keratinocytic lesions
Keratoacanthoma

- Rapidly growing crateriform lesion
  - usually on the face or upper extremity
  - More common in men over 50yrs
- Eventually regress and involute with scarring
- Commonly confused with a well-differentiated squamous cell carcinoma
- Clinical: dome shaped nodules with central crater containing keratin
- Histo: Crateriform keratinocytic lesion containing squamous cells with abundant glassy eosinophilic cytoplasms
Keratoacanthoma (KA)

- Differentiating KAs from well diff SCCs can be difficult to impossible in superficial biopsies.
- In order to differentiate them we need to be able to see the base of the lesion; KAs are well circumscribed whereas SCCs are infiltrative.
Squamous cell carcinoma

- Malignant neoplasm of keratinocytes.
- May be in situ ("Bowens Disease") or invasive.
- Occurs in a variety of subtype which vary in terms of their clinical behaviour.
SCCs can be keratinizing or non-keratinizing.
SCC - Subtypes
Trichilemmal like carcinoma
Spindle cell SCC
Lymphoepithelioma like Carcinoma
Desmoplastic SCC
Subtypes of SCC

SCC can be divided into low, intermediate and high risk based upon rates of recurrence and metastasis.

<table>
<thead>
<tr>
<th>Low (&lt;3%)</th>
<th>Intermediate (3-10%)</th>
<th>High (&gt;10%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCC arising in AK, HPV-related SCC, TLC, spindle cell CA</td>
<td>Acantholytic SCC, LELCS, invasive IEE</td>
<td>Desmoplastic SCC, Invasive Bowen’s, Adenosquamous CA, de novo SCC, radx &amp; scar-assoc</td>
</tr>
</tbody>
</table>

TLC – Trichilemmal-like carcinoma. LELC- Lymphoepithelioma like carcinoma, IEE – Invasive intraepithelioma (Jadassohn tumour) with invasion.

From Casarina et al Cutaneous clinicopathologic classification J. Cutan. Pathol 2006 Part 1;33:191-206
## SCC – Prognostic factors

<table>
<thead>
<tr>
<th>Prognostic risk factors in primary cutaneous squamous cell carcinoma.</th>
<th>Tumour diameter</th>
<th>Location</th>
<th>Depth/level of invasion</th>
<th>Histologic features</th>
<th>Surgical margins</th>
<th>Immune status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk</td>
<td>Less than 2 cm</td>
<td>Sun exposed sites (except ear/lip)</td>
<td>Less than 6 mm/invasion above subcutaneous fat</td>
<td>Well-differentiated Common variant or verrucous</td>
<td>Clear</td>
<td>Immuno-competent</td>
</tr>
<tr>
<td>High risk</td>
<td>More than 2 cm</td>
<td>Ear/lip</td>
<td>More than 6 mm/invasion beyond subcutaneous fat</td>
<td>Moderately, or poorly differentiated grade Acantholytic, spindle, or desmoplastic subtype</td>
<td>Incomplete excision</td>
<td>Immunosuppressed (organ transplant recipients, chronic immunosuppressive disease or treatment)</td>
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<tr>
<td></td>
<td></td>
<td>Non-sun exposed sites (sole of foot) SCC arising in radiation sites, scars, burns or chronic inflammatory conditions</td>
<td>Recurrent SCCs</td>
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</table>

Stratigos A. et al., Diagnosis and treatment of invasive squamous cell carcinoma of the skin: European consensus-based interdisciplinary guideline, Eur J Cancer (2015), http://dx.doi.org/10.1016/j.ejca.2015.06.110
Basal Cell Carcinoma

- The most common type of skin cancer; 8 out of 10 skin cancers are BCCs.
- Approx. 85% of BCCs occur on the face, head, and neck.
BCC histology

Histologic features:
- Peripheral palisading
- Fibromyxoid stroma
- Retraction artefact
## BCC subtypes

<table>
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<th>Less Aggressive subtypes</th>
<th>More Aggressive subtypes</th>
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</thead>
<tbody>
<tr>
<td>• Superficial &amp; multifocal</td>
<td>• Micronodular</td>
</tr>
<tr>
<td>• Nodular</td>
<td>• Infiltrating</td>
</tr>
<tr>
<td>• Fibroepithelioma of Pinkus</td>
<td>• Metatypical</td>
</tr>
<tr>
<td>• Infundibulocystic</td>
<td>• Basosquamous</td>
</tr>
<tr>
<td>• Organoid</td>
<td>• Sclerosing /morphoeic/ morphoeaform</td>
</tr>
<tr>
<td>• Adenoid</td>
<td></td>
</tr>
<tr>
<td>• Pigmented</td>
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Clinically important features

1. Superficial & multifocal
2. Nodular - deep (Important for treatment - Imiquimod or other topical therapy)
3. Infiltrative/ Sclerosing / morphoeic / morpheaform
   - May have an “iceberg” underneath
4. Pigmented
Superficial BCC histology
Nodular BCC histology
Aggressive BCCs subtypes

Infiltrative BCC

Morpheaform BCC

Micronodular
Aggressive BCCs subtypes - Metatypical
Margins

Terminology used for describing margins – narrowly excised, approximating/abutting, etc

Fully excised (margins free of tumour)

Tumor involving lateral/transverse margin and base/deep margin
Margins

Tumor abutting margin

Margins in S&M BCCs are problematic
Perineural invasion

- Rare for BCC (<1% of cases)
- Usually occurs in infiltrative subtypes
Lymphovascular invasion and metastasis

- Only a few reported cases of BCCs with lymphovascular invasion.
- Approximately 300 reported cases of metastatic BCC
- Risk factors for BCC metastasis include:
  - Tumours of the head and neck
  - Large or long-standing lesions
  - Significant tumor depth
  - Middle age
  - Immune compromise
- Most commonly metastasis occurs in regional lymph nodes and then in lungs, bones, and skin.