PREMALIGNANT AND MALIGNANT TUMORS

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Dermatology Department
I have no conflict of interest to report
Objectives

- Present board fodder on malignant tumors
- Discuss selected areas of importance or new information
The keratoacanthoma variant characterized by sudden appearance during childhood of multiple eruptive KAs that slowly resolve and reappear later on is called?

a) Grybowski variant
b) Ferguson-Smith variant
c) Keratoacanthoma centrifugum marginatum
d) Giant keratoacanthoma
e) Common solitary keratoacanthoma
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Keratoacanthoma

- well-differentiated SCC
- **KA Variants**
  - KA centrifugum marginatum: up to 20 cm with raised border and central involution
  - Giant KA: up to 9 cm with local destruction
  - Ferguson-Smith (AD): eruptive KAs in *childhood* with slow resolution
  - Grzybowski: hundreds of 1-3 mm KAs in *adults*
  - KA associated with *Muir Torre Syndrome*
What is gene mutated in this syndrome?
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Gorlin Syndrome
PTCH1
Sonic Hedgehog Signaling Pathway

- Mutations in PTCH1 gene on chromosome 9q, codes for sonic hedgehog receptor
  - Gorlin Syndrome (Nevoid BCC Syndrome)
  - Sporadic BCC
Hedgehog Pathway Inhibitors

- **Erivedge (vismodegib)**
  - FDA approved in 2012
  - Smoothened inhibitor
  - Adverse side effects (>30% incidence)
    - Muscle spasms
    - Alopecia
    - Dysguesia
    - Weight loss
    - Fatigue

- **Odomzo (sonidegib)**
  - Newly FDA approved in 2015
  - Smoothened inhibitor
  - In trials, led to shrinkage or disappearance of tumors in 58% of patients who took it

  - **Black box warning:** can cause fetal death
    - No blood donations!
The following syndromes have been associated with increased BCCs, except:

a) Bazex-Dupre-Christol Syndrome
b) Gardner Syndrome
c) Xeroderma Pigmentosum
d) Brooke-Spiegler Syndrome
e) Rombo Syndrome
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Rombo Syndrome

- Basal cell carcinomas
- Atrophoderma vermiculatum
- Hypotrichosis
- Milia
- Acrocyanosis

Bazex Syndrome

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- Atrophoderma (follicular)
- Zero Hair
- Eccrine abnormalities - anhidrosis
- X-linked dominant > AD
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Not to be confused with acrokeratosis paraneoplastica, also called Bazex - violaceous psoriatic plaques associated with SCC of aerodigestive
Brooke-Spiegler

**CYLD** mutation
Trichoepitheliomas
Cylindromas
Spiradenomas
Basal cell carcinomas

Xeroderma Pigmentosum

Autosomal recessive
Defect of DNA repair
Early skin cancers
Associated neurological abnormalities
What are the most common benign and malignant neoplasms found with this lesion?
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Benign tumors: trichoblastoma, syringocystadenoma papilliferum
Malignant tumors: BCC
Which genetic bullous diseases predisposes patients to SCC?

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b) Junctional epidermolysis bullosa
c) Dowling-Meara type of epidermolysis bullosa
d) Dominant dystrophic epidermolysis bullosa
e) Recessive dystrophic epidermolysis bullosa
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Conditions Predisposing to SCC

- Conditions with chronic wounds / sinuses
- Oculocutaneous albinism
- Transplant patients
- Patients on long-term voriconizole
- Patients on BRAF inhibitors
- Previous radiation therapy (20 years)
- Tanning bed use
- Many more...
Organ Transplant Recipients

- **Substantial risk of NMSC**
  - BCC 5-10x
  - SCC 40-250x
- **Directly related to dose and length of immunosuppressive drug use**
- **Heart transplant, 27% died of skin cancer, most SCC** (study was in Australia)
- **Capcetabine or retinoids may decrease rate of NMSC in SOTR**
The following are true regarding verrucous carcinoma, **except**

a) A low grade variant of SCC  
b) Is successfully treated with radiation  
c) May show perineural or vascular invasion  
d) Located in the oral cavity, anogenital area or the sole of the foot  
e) Associated with HPV
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Verrucous Carcinoma

**Types**
- Oral florid papillomatosis: buccal mucosa
- Giant condyloma of Bushke-Lowenstein: (HPV 6,11)
- Epithelioma cuniculatum: plantar feet

**Deeply invasive but rarely metastasize**

**Becomes more aggressive after radiation**

**Treatment: excision (Mohs)**
SCC High Risk

- Size >2 cm
- Depth of invasion >6mm
- Anatomic location
  - Ear / lip / mucosae
- Immunosuppression
- Etiology
  - Chronic ulcer / sinus tract /
  - Radiation / scar
- Aggressive histologic subtype
What virus is found in 80% of these tumors?
Merkel Cell Carcinoma

- Cutaneous neuroendocrine tumor
- Solitary, pink to red nodule on head and neck of elderly
- Aggressive with high rates of recurrence and metastasis
- Polyomavirus associated (80%)
- Three histologic patterns
  - Stains: CK20, NSE, chromogranin A/B, synaptophysin
- Treatment
  - WLE with 2-3.0 cm margins or Mohs
  - +/- adjuvant therapy
References