Brooke-Spiegler Syndrome

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History

- A 28 year-old female presented to the clinic with multiple facial papules that have been present since around the time of puberty.
- She had been previously diagnosed as having “milia”.
- There is no family history of similar skin lesions.
• She had recently become pregnant and thought that since becoming pregnant she was getting more spots.
• She wished to have them “extracted” like her previous dermatologist in North Carolina had done.
• On further examination she also had a few small scattered papules on her scalp
Differential Diagnosis

• Multiple facial papules
  • Brooke-Spiegler syndrome
  • Multiple familial trichoepitheliomas
  • Familial cylindromatosis
  • Cowden syndrome
  • Birt-Hogg-Dube
  • Tuberous sclerosis
  • Rombo syndrome
  • Bazex syndrome
  • Muir–Torre syndrome
Brooke-Spiegler Syndrome

- How did I get it? No one in my family has anything like this...
- Is it dangerous? Are these spots cancer, will they turn to cancer?
- Are other areas of my body going to be affected?
  - Other organs?
- How much worse are these going to get?
  - I googled Brooke Spiegler syndrome and the pictures I saw...is that going to be me?
- Is my unborn daughter going to get this?
  - What are the chances?
  - When will we know if she has it?
  - If she gets it, how bad will it be...like mine?
    - Like the pictures on google??
- I felt like these got worse during pregnancy, did I imagine that or do hormones influence these lesions?
- Most importantly...how do I get rid of these spots and stop new ones from growing? I HATE them!!!
Brooke-Spiegler Syndrome

- Features:
  - Trichoepithelioma
  - Cylindroma
  - Spiradenoma
- CYLD mutation on 16q12-q13
  - Familial Cylindromatosis
  - Multiple Familial Trichoepitheliomas
- Malignant counterparts
  - Cylindrocarcinoma
  - Spiradenocarcinoma
  - Basal cell carcinoma
- Rarely associated
  - Basal cell adenomas and adenocarcinomas of the parotid glands and minor salivary glands
Genetics

- Autosomal Dominant condition
- Women affected more severely than men
- Variable phenotypical expression
  - Drastically different presentations within the same family
- What causes the second hit that leads to loss of heterozygosity?
  - UV radiation
    - Cylindromas occur largely in sun exposed areas
  - Hormones
    - Androgen dependent areas of scalp / pubic area
    - Onset after adrenarche
    - Follicular neoplasms
    - One other case reported with worsening of lesions during pregnancy
CYLD

JNK

NF-κB
Cell survival through inhibition of apoptosis

Osteoclastogenesis and bone homeostasis.

Angiogenesis

Immune response and Inflammation

Spermatogenesis

Cell differentiation
Treatment

- Characteristic lesions of Brooke-Spiegler are considered benign, medical treatment is not necessary.
- Treatment for cosmetic reasons.
- Commonly reported treatments
  - Excision
  - Electrosurgery
  - Dermabrasion,
  - CO2 laser resurfacing,
  - Cryotherapy
  - Radiotherapy
- Potential for scarring/adverse side effects.
Future/Emerging Treatments

- NF-kB inhibitors
  - Nearly 800 compounds/drugs are inhibitors of NF-kB
  - ASA, TNF-alpha, cantharidin
  - Topical Salycylic Acid used on 17 cylindromas
    - Two showed complete remission

- JNK inhibitors
  - Tanzisertib (CC-930)
  - Bentamapimod
  - SP600125
References