

Updates on Gorlin Syndrome: Physician and Patient Perspectives

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Disclosure

Clinical Research

Sol Gel Technologies

Pellepharm

Palvella Therapeutics

Consulting

Inhibitor Therapeutics

Gorlin Syndrome (Basal cell nevus syndrome)

FACTS



- Existed since Dynastic Egyptian times – 3000 BCE
- 1960 –Gorlin (oral pathologist) and Goltz (dermatologist)
described classic triad -multiple BCC, jaw keratocysts, bifid ribs
- Autosomal dominant – high penetrance, variable expression
- De novo (sporadic) mutations – 20-30% cases

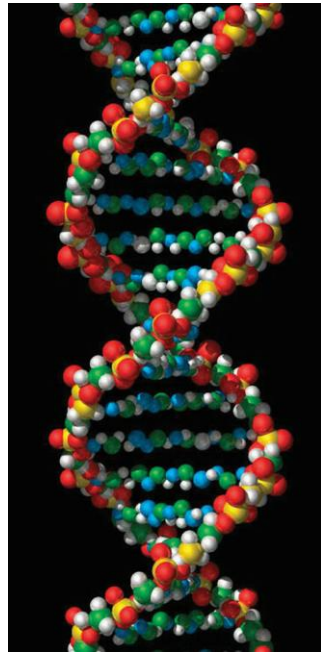
Gorlin Syndrome

- Tumor predisposing disorder
- Estimated 1:30,000
- Approx 11,000 in US
- Orphan disease
- Systemic manifestations
- **Lifelong challenge**



Gorlin Syndrome- what is it?

- Germline pathogenic genetic mutation affecting the Sonic Hedgehog signaling (SHH) pathway
- PTCH-1 gene – tumor suppressor gene
- PTCH-2 and SUFU mutations



Diagnosis of Gorlin Syndrome



2 major criteria

1 major and 2 minor criteria

1 major and genetic confirmation

Major Criteria

1 BCC before age 20 or multiple BCC

Odontogenic keratocysts

2 or more palmar pits

Intracranial calcification

First degree relative with BCNS

Minor criteria

Macrocephaly

Congenital facial malformation

Polydactyly

Rib abnormalities

Ovarian or cardiac fibroma

Medulloblastoma

Eye abnormalities

Gorlin Syndrome

- Bcc can appear as early as 3-4 years of age
- Average age is 25
- Can look like skin tags
- Palmar pits – 30-65% have by age 10
80% by age 15

More on palms than soles

- 30% have milia around the eyes or on forehead/cheeks
- 75-90% have jaw keratocysts, occur at a young age
- 10% do not develop basal cell carcinoma







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Characteristic facies

frontal bossing, macrocephaly, hypertelorism, high arched eyebrows, widened nasal bridge





Chiritescu E, Maloney M. Acrochordons as a presenting sign of nevoid basal cell carcinoma syndrome J Am Acad Derm 2001;44:789-94



Patient_ID: 767610



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Gorlin Syndrome: management of BCC and support of the patient

**Prevention – sun protection
avoid radiation**

Combination multiple therapeutic approaches

Counseling – genetic, emotional support



Treatment – Basal Cell Carcinoma

Multiple modalities

- Cycle through different approaches as tolerated
- Breaks may be needed to help with compliance and avoid treatment fatigue



How do we decide?

Partnership

- Individualized approach
- Number, size, location of bcc
- Primary vs recurrent
- Distance and ability to travel



Management concepts

- Goal may not be complete eradication of all BCC
- Treatment may be tailored per each patient goal
- Most threatening tumors – location, size, recurrence
- Most symptomatic tumors – bleeding, cosmesis
- Most bothersome to patient for any reason

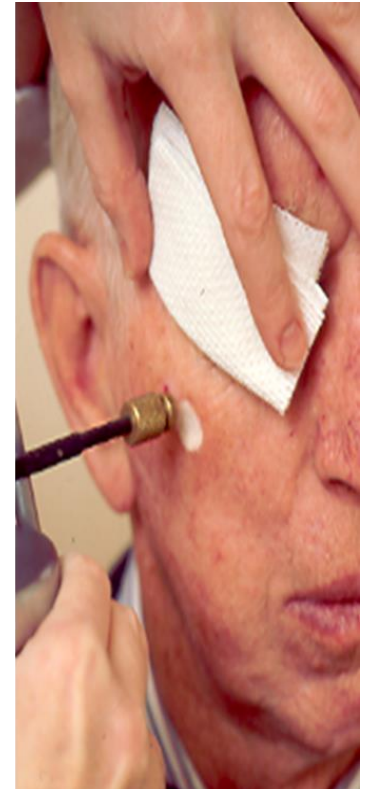
Non- surgical treatment - BCC

- Cryotherapy
- 5-fluorouracil
- Imiquimod
- PDT

Some success with MAL-PDT

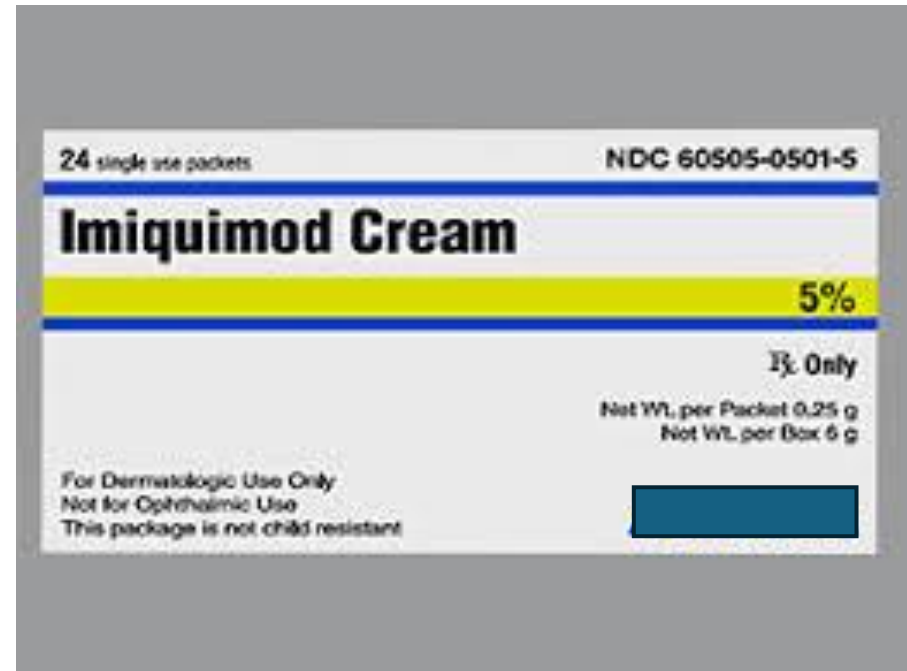
Red light and blue light

Best for superficial BCC



Topical Therapeutic Agents

- Imiquimod
- 5-Fluorouracil



Day 4



Day 7



Day 13



Day 33



Laser treatment

Ablative - ultrapulse CO2

Nonablative – 755 nm alexandrite, 595 nm pulsed dye



Hedgehog inhibitors

Vismodegib 150 mg daily

Sonidegib 200 mg daily



Hedgehog inhibitors



- Approved for locally advanced and metastatic basal cell carcinoma
- Various dosing regimens for patients with Gorlin syndrome
- Side effects can be problematic
 - Muscle cramps
 - Taste disturbance
 - Hair loss
 - Fatigue

for some individuals –can be life changing

When to consider oral HHI

- Surgically challenging – disfiguring outcomes
- Metastatic or inoperable
- Poor surgical candidates – age, other comorbidities
- Numerous smaller lesions in patients with surgical fatigue





Strategies for oral hedgehog inhibitors

- Individualized dosing approach– pulse/adjust to tolerate side effects
- Breaks – may increase compliance while decreasing tumor burden
- Cost/ help from pharmaceutical company



Surgical approaches

- Scissor tags
- Curettage
- Excision
- Mohs



When do we choose Mohs?



- Recurrent tumors
- Certain histologic types
- Location of tumor - Need to preserve normal skin – eyelid, lip, ear
- **Balance between preserving tissue, higher cure rate, and surgical fatigue**

Clinical trials (clinicaltrials.gov)

Patidegib topical gel 2%

Sirolimus 3.9% topical gel

Dosing regimens for vismodegib

PDT

SUBA- Itraconazole 150 mg po BID

many others

Trials currently enrolling



Gorlin Syndrome Alliance

Gorlinsyndrome.org



- Information for patients, families, medical professionals
- Chat groups
- Support meetings /Town Halls
- Clinical trial notifications
- FDA advocacy

Guidelines for the Management of BCC in Gorlin Syndrome

- 2023 – goal to develop guidelines for approaching management of Gorlin patients – taking into account all dimensions of care
- 130 individuals – dermatologists, mohs surgeons, oral surgeons, patients, family members, counselors
- scoping review of the available evidence, an expert evidence survey consisting of over 280 questions, detailed one-on-one qualitative patient interviews, multiple meetings and delphi analysis

Will be published 2024

Summary

- Patient – doctor relationship is critical
- Challenging lifelong condition
- Respect the emotional component
- Multiple treatment options, mix them up!
- Individualized approaches – different goals, tolerance
- There is hope!

