Pathogenesis and treatment of papillomas in Costello Syndrome

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BACKGROUND

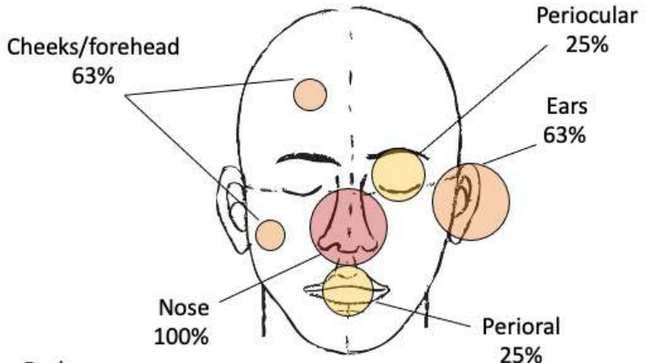
- Costello syndrome (CS) is caused by a mutation in the regulatory HRAS gene, leading to constitutive activation of the RAS/Mitogen-Activated Protein Kinase (MAPK) pathway.
- Skin findings include cutaneous papillomas, particularly around the nares and alar rim, palmoplantar keratoderma, acanthosis nigricans, and generalized hyperpigmentation.
- High papilloma burden can be irritating and/or stigmatizing for patients. Papillomas are often refractory to topical treatments and may require removal with snip excision, cryotherapy, or cautery.
- It remains unknown whether these lesions are due to human papillomavirus (HPV) infection or constitutive activation of the MAPK pathway in keratinocytes.

METHODS

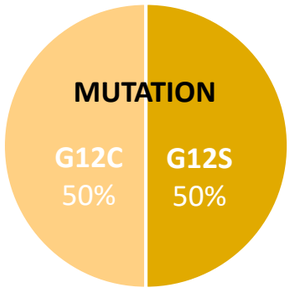
- Patients were recruited through the Costello Syndrome Family Network or physician recall
- 8 patients were identified who have CS confirmed by genetic testing and cutaneous papillomas requiring treatment
- Data was collected regarding skin findings, number and location of papillomas, treatments, and pathology results, if available
- For patients with banked tissue specimens, whole exome sequencing was performed to compare levels of HRAS activation in germline and papilloma tissue(s)

RESULTS

PAPILLOMA DISTRIBUTION



Body:
- Extremities: 25%
- Perianal: 25%
- Abdomen 13%

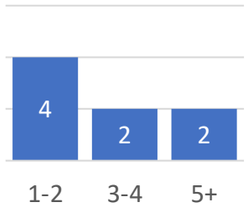


0%

HPV POSITIVE

(for 4 patients who had tissue tested at time of removal)

No. OF TREATMENTS



TREATMENT TYPES

Topical	Procedural
Fluorouracil 0.5% (38%)	Snip excision (88%)
Salicylic acid 10-40% (28%)	Cryotherapy (25%)
Sirolimus 0.5-1% (38%)	Candida injections (13%)
Tretinoin 0.025-0.05% (25%)	Pulsed dye laser (13%)

Results of genetic testing are pending

DISCUSSION

- Preliminary results support the theory that papillomas in CS may be caused by mosaic second hit mutations, rather than viral infection.
- Improved understanding of the pathogenesis of CS-associated papillomas will lead to targeted and improved treatment options for patients.

REFERENCES

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