

Site-Specific Inheritance of Basal Cell Carcinoma

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We report a 21-year-old white woman who developed a large basal cell carcinoma (BCC) on her left upper vermilion border. Her mother and maternal grandmother both had a history of BCCs occurring in the same location. No documented BCC-related genetic disorder was suspected. Our case supports a theory of site-specific inheritance of nonmelanoma skin cancer, which should be further explored.

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Case Report

A 21-year-old white woman presented in Florida for an evaluation of a biopsy-proven nodular basal cell carcinoma (BCC) on her left upper vermilion border (Figure, A). Clinical examination revealed a 1-cm pearly papule. She had no history of skin cancer and her skin was free of congenital skin lesions. She reported that she had used indoor tanning beds since she was a teenager. She underwent 4 stages of Mohs micrographic surgery with a defect size of 2.1×1.4 cm (Figure, B). The defect was closed with a star-shaped advancement flap (Figure, C), and she was clinically without recurrence or new malignancy at 3-year follow-up.

A family history taken on presentation revealed that both her mother and maternal grandmother were seen at the same facility for evaluation of BCCs on their upper lips. After reviewing their medical records and photographs, the information provided through the family history was confirmed. The patient's mother had been diagnosed at the age of 52 years with a recurrent BCC on her left upper lip. Mohs micrographic surgery was advised and treatment was obtained elsewhere. The patient's grandmother had been diagnosed at the age of 70 years with an

ulcerated BCC on her upper lip, 3 years prior to our patient's presentation. The grandmother's tumor cleared with 3 stages of Mohs micrographic surgery with a defect size of 1.9×1.3 cm.

All 3 patients were confirmed to be biologically related. They were fair skinned with either hazel or blue eyes and red or blond hair; they were considered to have Fitzpatrick skin type II. After reviewing each patient's history, there were no findings suggestive of basal cell nevus syndrome. None of the patients were immunosuppressed. According to their patient histories, they had not smoked or received radiation therapy for the treatment of acne. The family grew up in the South with an abundant amount of sun exposure throughout their lives.

Comment

Basal cell carcinoma is the most common form of skin cancer, affecting approximately 2.8 million individuals annually in the United States.¹ Basal cell carcinoma mainly affects white individuals, particularly those with Fitzpatrick skin types I or II (fair skin; light hair; blue, green, or gray eyes).²⁻⁴ The most important risk factor for the development of BCC is long-term sun exposure, which can lead to gene mutations that cause cancer.³⁻⁵ Other factors that increase one's risk for BCC include immunosuppression, a family history of skin cancer, and a prior diagnosis of BCC.^{3,4} The mean age of BCC development is 55 years, and the male to female ratio is 2.1 to 1.³ The age of onset has decreased over time, with increased exposure to UV and artificial UV cited as the primary cause.¹⁻³

Basal cell carcinoma usually is caused by an interaction between genetic factors and environmental factors.^{3,4} Although family members inherit similar traits that can increase their risk for BCC (ie, fair skin), mutated genes that predispose BCC from one generation to the next only occur in rare genetic disorders such as basal cell nevus syndrome, xeroderma pigmentosum, and Bazex syndrome. These disorders account for a small number of cases of BCC.⁶ Moreover, other abnormalities are present in these

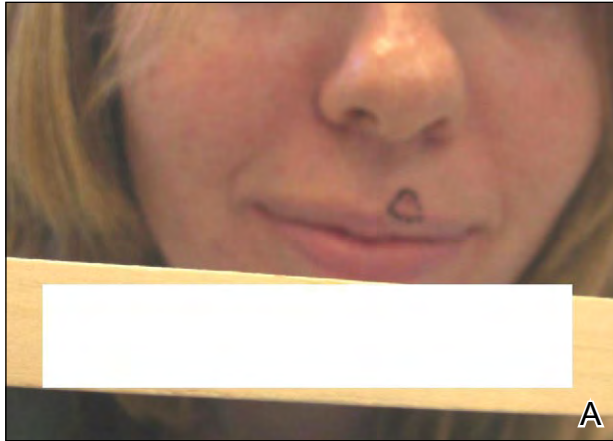
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disorders, and BCCs are developed at an earlier age and in larger numbers.^{7,8}

Basal cell nevus syndrome has been well-documented.⁷⁻⁹ Also referred to as Gorlin syndrome, it is a rare autosomal-dominant disorder characterized



Nodular basal cell carcinoma on the left upper vermilion border before treatment (A). Following 4 stages of Mohs micrographic surgery the defect was 2.1×1.4 cm (B). The defect was closed with a star-shaped advancement flap (C).

by multiple BCCs; palmar and plantar pits; odontogenic keratocysts; and osseous anomalies of the ribs, spine, and skull.⁷⁻⁹ Basal cell nevus syndrome most often is caused by mutations in the hedgehog pathway of the tumor suppressor gene patched 1, *PTCH1*.⁶⁻¹¹ Sporadic BCCs also can be caused by a mutation in this gene.^{10,11} However, for sporadic BCCs to develop, mutations to both alleles of *PTCH* must be inactivated by postnatal insults (ie, UV irradiation).¹¹ Basal cell carcinomas associated with basal cell nevus syndrome do not require as much influence from environmental factors. Because one allele is already mutated through inheritance, postnatal influences only need to inactivate the remaining allele for BCCs to develop.¹¹

Basal cell carcinoma most commonly presents on areas of long-term sun exposure. Approximately 70% of all BCCs occur on the head and neck, with the nose being the most commonly affected site.^{2-4,12} Although there is a correlation between the site of sun exposure and the site of BCC development, site-specific cumulative UV exposure alone has not been shown to be an adequate predictor of BCC frequency.¹² Heckmann et al¹² suggested that certain anatomic sites have specific textural changes, such as reduced tension and dermal thickness, that decrease the ability to resist or repair DNA damage from UV light. Development of a BCC on the upper lip, though not unusual, is not especially common. This site does not appear to be a prevalent site of BCC development; however, our case would support a theory of site-specific inheritance of nonmelanoma skin cancer.

Conclusion

We present BCC developing on the upper lip in 3 successive generations in a family with no known history of a BCC-related genetic disorder such as basal cell nevus syndrome. Additional studies are needed to further clarify the relationship between environmental factors and genetics involved in the development of BCCs.

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