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Case Presentation

Axillary basal cell carcinoma in patients with Goltz-Gorlin syndrome: report of basal cell carcinoma in both axilla of a woman with basal cell nevus syndrome and literature review

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Abstract

Background: Basal cell carcinoma of the axilla, an area that is not usually exposed to the sun, is rare. Individuals with basal cell nevus syndrome, a disorder associated with a mutation in the patch 1 (PTCH1) gene, develop numerous basal cell carcinomas.

Purpose: To describe a woman with basal cell nevus syndrome who developed a pigmented basal cell carcinoma in each of her axilla and to review the features of axillary basal cell carcinoma patients with Goltz-Gorlin syndrome.

Methods: Pubmed was used to search the following terms: axillary basal cell carcinoma and basal cell nevus syndrome. The papers and their citations were evaluated.

Results: Basal cell nevus syndrome patients with basal cell carcinoma of the axilla were observed in two women; this represents 2.5% (2 of 79) of the patients with axillary basal cell carcinoma. Both women had pigmented tumors that were histologically nonaggressive. The cancers did not recur after curettage or excision.

Conclusions: Basal cell carcinoma of the axilla has only been described in 79 individuals; two of the patients were women with pigmented tumors who had basal cell nevus syndrome. Similar to other patients with axillary basal cell carcinoma, the tumors were histologically nonaggressive and did not recur following treatment. Whether PTCH1 gene mutation predisposes basal cell nevus patients to develop axillary basal cell carcinomas remains to be determined.

Key Words: axilla, axillary, basal, carcinoma, cell, nevus, syndrome

Introduction

Basal cell carcinomas usually occur on sun-exposed sites [1,2]. Basal cell nevus syndrome is an autosomal dominantly inherited disorder typically associated with a mutation in the patch 1 (PTCH1) gene in which the affected individuals develop numerous basal cell carcinomas [3]. A woman with basal cell nevus syndrome who developed multiple axillary basal cell carcinomas is described and the literature regarding basal cell carcinoma in the axilla of basal cell nevus syndrome patients is reviewed.

Case report

A 48-year-old woman with an established diagnosis of basal cell nevus syndrome presented with a tender right axillary mass and an asymptomatic left axillary nodule. Both lesions had been present for more than one year; the right axilla had recently become symptomatic. She also had several pigmented basal cell carcinomas that had been excised.

Cutaneous examination showed a 4 x 2 cm linear brown nodule situated parallel to her skin folds in the right axilla (Figure 1). The lesion was firm, yet tender to palpation. A bacterial culture grew Staphylococcus aureus, Proteus mirabilis, and Morganella morganii. The infection resolved following treatment with oral antibiotics to which the bacteria were susceptible.

A 10 x 8 mm sharply demarcated brown nodule was observed in the inferior aspect of her left axilla (Figure 2). The ventral palms and lateral hands had numerous pits (Figure 3). Similar pits were observed on the ventral and lateral surfaces of her feet (Figure 4).

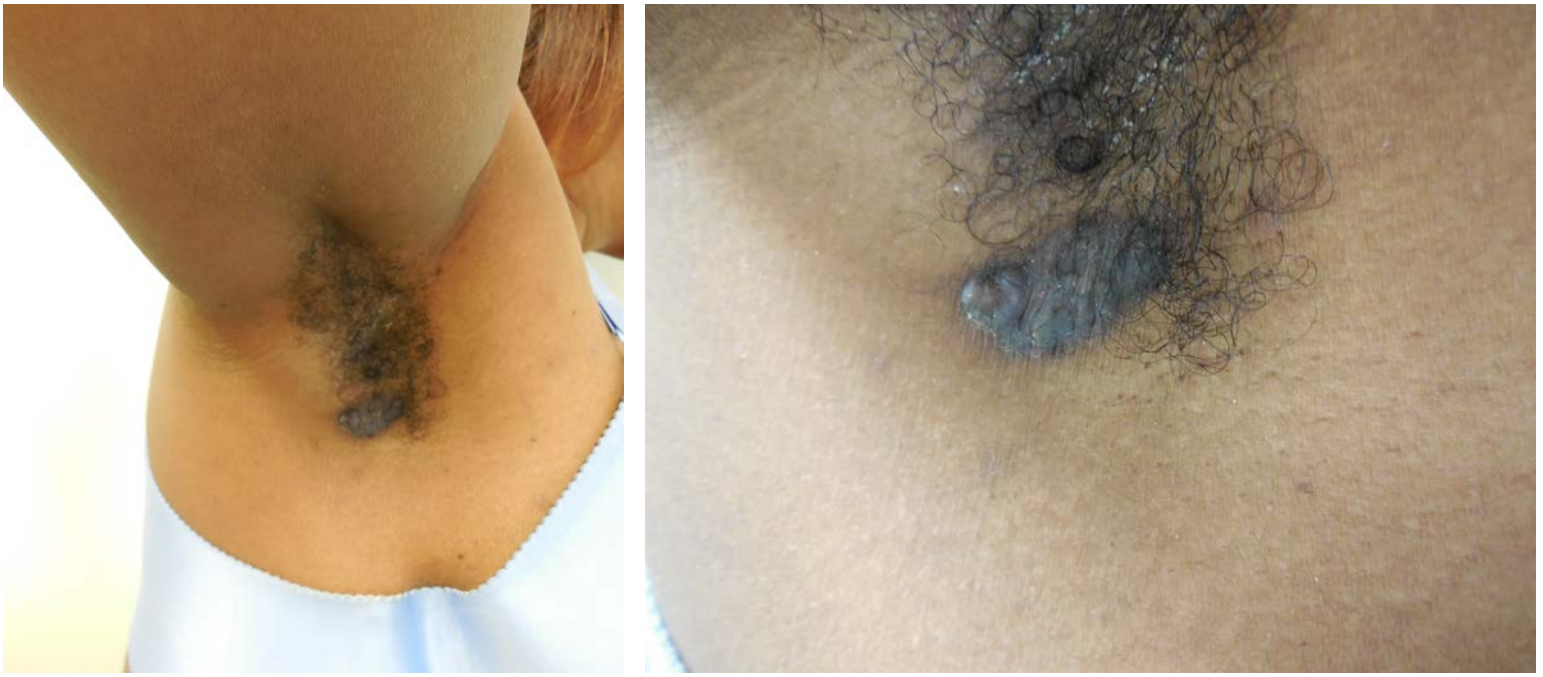


Figure 1 (a and b). Distant (a) and closer (b) views of the right axilla show a pigmented nodular basal cell carcinoma in a woman with basal cell nevus syndrome that appears as a brown linear 4 x 2 cm nodule.

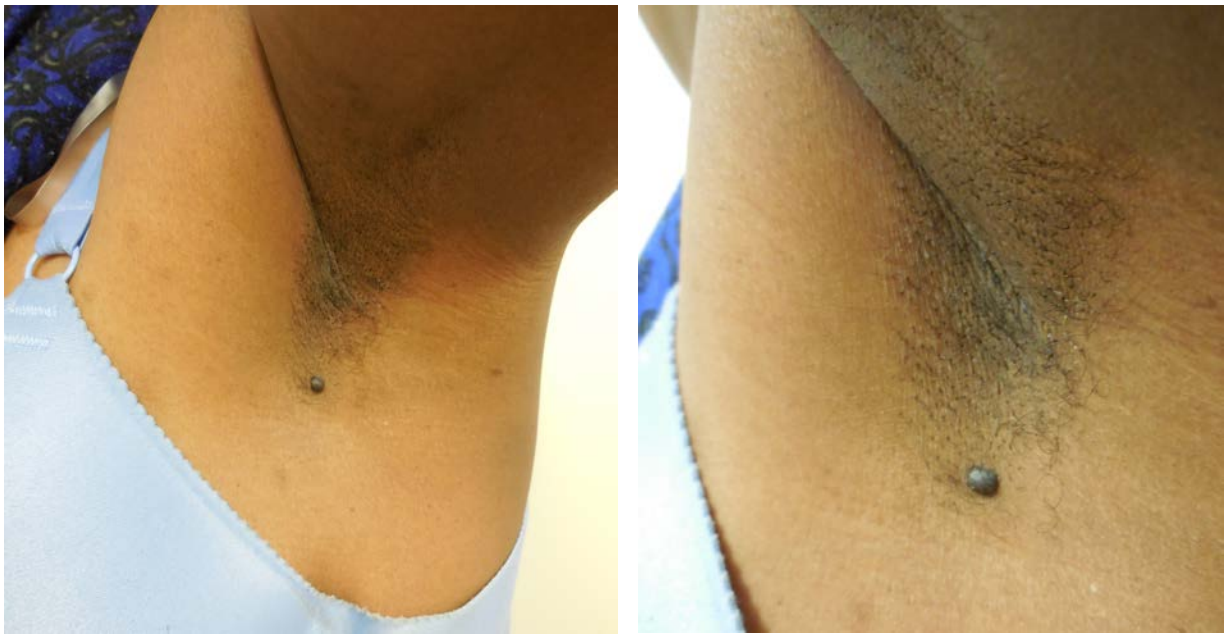
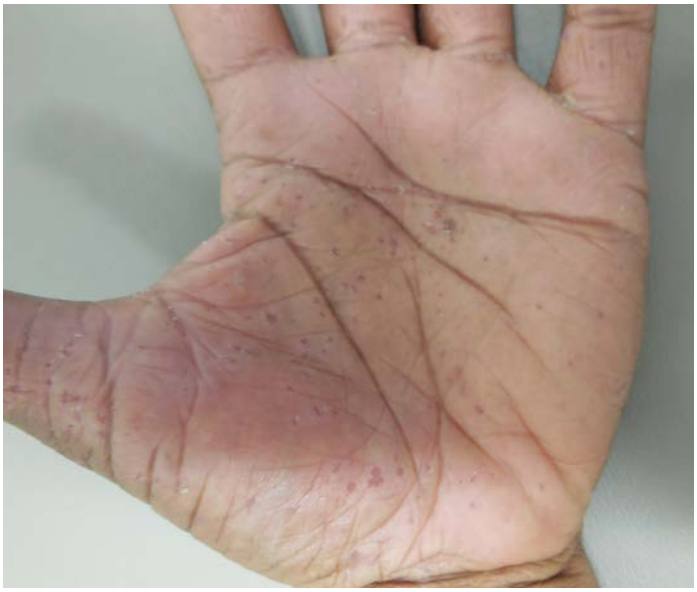


Figure 2 (a and b). Distant (a) and closer (b) views of the left axilla show a pigmented nodular basal cell carcinoma in the same woman with basal cell nevus syndrome that appears as a 10 x 8 mm sharply demarcated brown nodule.



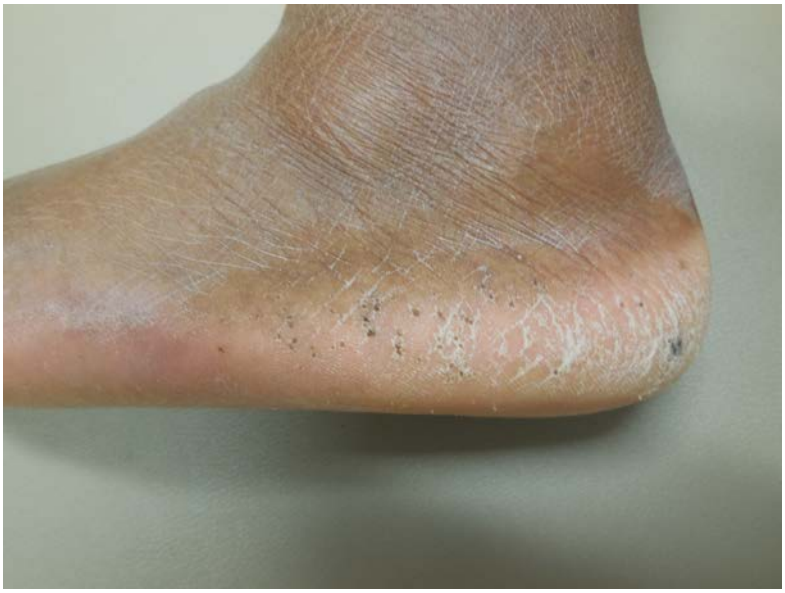


Figure 3. Basal cell nevus syndrome-associated palmar pits on the ventral surface of the left hand **Figure 4.** Basal cell nevus syndrome-associated plantar pits on the lateral surface of the left foot

Microscopic examination of both axillary lesions showed similar pathologic changes. Nodular aggregates of basaloid cells are present in the dermis. Pigment is found both within the tumor cells and in melanophages in the associated dermal fibrocellular stroma.

Correlation of the clinical presentation and the pathology establish the diagnosis of pigmented nodular basal cell carcinomas in each axilla. Each of the tumors was excised. The surgical defect was repaired with a layered closure. There has been no evidence of tumor recurrence at follow up examinations.

Discussion

Basal cell carcinoma is the most common neoplasm in humans [4]. Albeit less commonly, basal cell carcinoma can occur in unusual sites and areas not exposed to the sun [5-9]. Basal cell carcinoma of the axilla is rare; including the woman reported herein, only 81 tumors have been reported in 79 patients [10-15].

Risk factors for basal cell carcinoma includes environmental exposures, immunosuppressed individuals, physical phenotypic characteristics, and certain inherited syndromes (Table 1) [11,16-19]. However, with the exception of basal cell carcinoma syndrome, axillary basal cell carcinoma has not been observed in patients with any of the other genodermatoses that predispose individuals to this neoplasm. Whether this observation is coincidental or related to the PTCH1 gene mutation in basal cell nevus syndrome patients remains to be determined.

Drs. Gorlin and Goltz originally described basal cell nevus syndrome in 1960. They reported a family with multiple basal cell carcinomas, odontogenic keratocysts of the jaws, and bifid ribs [20]. Major criteria for the syndrome include lamellar calcification of the flax, jaw keratocysts, palmar and plantar pits, multiple (greater than five) basal cell carcinomas or a basal cell carcinoma before the age of 30 years, and a first degree relative with the syndrome. Minor criteria include lymphomesenteric or pleural cysts, macrocephaly, cleft lip and/or cleft palate, vertebral or rib abnormalities (such as bifid or splayed or extra ribs and bifid vertebrae), polydactyly (prexial or postaxial), ocular anomalies (cataracts, developmental defects, and retinal epithelium pigmentary changes), childhood medulloblastoma, and fibromas (cardiac or ovarian). The presence of either two major and one minor or one major and three minor criteria establish the diagnosis of basal cell nevus syndrome [3,21-23].

Basal cell carcinoma of the axilla has only been described in two women with basal cell nevus syndrome (Table 2) [15]. One woman was 27-years-old and the other was 48-years-old. Both women had a history of prior basal cell carcinomas. Indeed, the 27-year-old woman also had another basal cell carcinoma in a sun-protected site—her inguinal region. Neither woman was receiving immunosuppressants nor had other cancers. In contrast to the younger woman who did not have a family history of basal cell nevus syndrome or basal cell carcinomas, the older patient's mother also had basal cell nevus syndrome.

Both of the women with basal cell nevus syndrome and axillary basal cell carcinoma had non-aggressive histologic subtypes of the tumor: micronodular and nodular. The current patient was African American and had a pigmented basal cell carcinoma; the

other woman, whose race was not stated, also had pigmented tumors. The tumors were successfully treated with either curettage or excision.

The reported woman had a basal cell carcinoma in each of her axilla. The location of the axillary tumors in the second woman was not stated. Whether axillary basal cell carcinomas indeed occur more commonly in patients with basal cell nevus syndrome remains to be evaluated.

Conclusion

Basal cell carcinoma of the axilla is rare. The site is an unusual location for this tumor since the axilla typically receives little or no sun exposure. Two of the 79 patients with axillary basal cell carcinoma (2.5 %) were women who had basal cell nevus syndrome. They had several additional basal cell carcinomas besides those that occurred in their axilla. Similar to other patients with axillary basal cell carcinoma, the tumors were histologically non aggressive and did not recur after curettage or excision. Whether basal cell carcinoma of the axilla is more prevalent in patients with basal cell nevus syndrome remains to be determined.

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Table 1. Basal cell carcinoma: risk factors

- Genodermatoses
  - Basal cell nevus syndrome [a]
  - Bazex syndrome [b]
  - Epidermolysis bullosa simplex-Dowling Meara subtype [c]
  - Oculocutaneous albinism [d]
  - Rombo syndrome [e]
  - Xeroderma pigmentosum [f]
- Environmental exposures
  - Radiation
    - Ionizing
    - Tanning bed
    - Ultraviolet
      - Sun exposure
      - Ultraviolet A
      - Ultraviolet B
  - Toxins
    - Arsenic (pesticides)
    - Coal tar (hydrocarbons)
    - Paraffin
- Immunosuppression
  - Human immunodeficiency virus seropositive
  - Solid-organ transplant recipient
- Physical phenotype
  - Burn/tan: always/never
  - Eyes: blue or green
  - Freckles: present
  - Hair: blond or red
  - Skin color: fair or light

[a] Also referred to as: Gorlin syndrome, Gorlin-Goltz syndrome, Nevoid basal cell carcinoma syndrome; an autosomal dominant condition: basal cell carcinomas, bifid ribs, central nervous system defects, frontal bossing, odontogenic keratocysts, and palmoplantar pits are some of the features.

[b] Also referred to as: Bazex-Dupre-Chistol syndrome; an X-linked dominant comdition: anhidrosis (localized), atrophoderma (follicular), basal cell carcinomas, and hypotrichosis are some of the features.

[c] An autosomal dominant condition with mutations of K5 or K14; perhaps the most severe form of epidermolysis bullosa simplex. Blisters at birth; blisters can affect oral cavity, gastrointestinal tract, and rarely upper respiratory tract. Eventually, confluent keratoderma of hands and feet. Heat exacerbates blistering; milia after blisters heal. The nails are thick and discolored.

[d] An autosomal recessive condition characterized by a disruption of melanin synthesis and affecting the eyes (vision problems), skin (fair colored and having an increased risk of skin cancer, including basal cell carcinoma), and hair (white or light colored).

[e] An autosomal dominant condition: atrophoderma vermiculata, basal cell carcinomas, hypotrichosis, milia, peripheral vasodilatation, and trichoepithelioma are some of the features.

[f] An autosomal recessive condition in which the ability to repair ultraviolet light-associated DNA damage is deficient; patients develop multiple basal cell carcinomas in addition to melanomas and squamous cell carcinomas at a young age.

Table 2. Characteristics of women who have basal cell nevus syndrome and axillary BCC

C	A(y) R	Dur	Side	Size (mm)	PSC (#)	BCC at other SPS	Histology	Treatment	Ref
1	27 NS	NS	NS	3x3	BCC (13)	Inguinal	MNod Pigmented	Curettage	14

		NS	NS	3x3			MNod Pigmented	Curettage	
2	48 AA	>1y	Left	10x8	BCC (>12)	None	Nodular Pigmented	Excision	CR
		>1y	Right	40x20			Nodular Pigmented	Excision	

Abbreviations: A, age; AA, African American; BCC, basal cell carcinoma; C, case; Dur, duration of BCC prior to diagnosis; CR, current report; mm, millimeter; MNod, micronodular; NS, not stated; PSC, previous skin cancer; R, race; Ref, referenece; Side, side of body affected by BCC; SPS, sun-protected site; y, year; >, greater than; #, number