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Case Report

Keratinocytic epidermal nevus with ipsilateral breast hypoplasia☆,☆☆

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ABSTRACT

Breast hypoplasia has been reported in some epidermal nevus syndromes, but not with a keratinocytic epidermal nevus. Herein, we describe the first case of breast hypoplasia associated with a keratinocytic epidermal nevus. Keratinocytic epidermal nevi have been shown to be associated with somatic mutations in *FGFR3*, *PIK3CA*, and *HRAS*. We hypothesize that hypoplasia may be due to a local mutation in the *FGFR3* gene or increased androgen receptors in affected breast tissue. The patient was treated with CO_2 laser with good cosmetic outcome.

Introduction

Epidermal nevi are common benign cutaneous hamartomas that can be congenital or acquired. Epidermal nevus syndromes encompass a group of rare disorders characterized by the presence of an epidermal nevus with associated extracutaneous manifestations. Breast hypoplasia has been previously described in epidermal nevus syndromes (particularly in Becker's nevus syndrome) in which breast hypoplasia is the most common associated anomaly (Danarti et al., 2004).

To the best of our knowledge, breast hypoplasia has never been reported in association with a keratinocytic epidermal nevus (KEN).

Case report

A healthy 22-year-old female patient with no significant medical history presented for evaluation of an asymptomatic lesion that had been present since birth. She had not had any prior treatment to the area. On examination, there were multiple hyperpigmented papules coalescing into a linear, verrucous plaque along the left flank (Fig. 1). The ipsilateral breast was noted to be 4 cup sizes smaller than the contralateral breast (Fig. 2). Upon further questioning, the patient had no family history of abnormal breast development. She subsequently had normal endocrine test results with her obstetrician-gynecologist, and was told this was likely an unexplained normal variant. A shave biopsy was performed, and the histopathology test results showed a KEN without epidermolytic hyperkeratosis. No genotyping was performed. The patient decided to have the KEN treated with CO_2 laser with good cosmetic outcome after one treatment (Fig. 3).

Discussion

The association of breast hypoplasia with a KEN has not been previously reported, and there is no established mechanism for this phenotype. We suggest two hypotheses. The first hypothesis is that the mechanism is similar to that seen in Becker's nevus syndrome. Although the pathophysiology is not fully understood, breast hypoplasia is thought to be secondary to increased androgen receptors in the affected tissue (Grande Sarpa et al., 2008). Mammary cell proliferation is regulated by the balance between estrogens and androgens, which stimulate and inhibit proliferation, respectively (Labrie, 2006). With an increased number of androgen receptors on the ipsilateral breast tissue, a perceived imbalance in favor of androgens could lead to breast hypoplasia. A similar hormonal milieu in this patient may account for these findings.

Another possible explanation for this patient's unique presentation is a common mosaic genetic mutation. KENs have been shown to be associated with somatic mutations in *FGFR3*, *PIK3CA*, and *HRAS*, all of which are involved in cellular signaling and growth regulation (Miranda et al., 2013). Activating mutations in these genes are more commonly associated with tissue hyperplasia (including CLOVE syndrome, macrocephaly-capillary malformation syndrome, and KENs). However, tissue hypoplasia, particularly of the bone and

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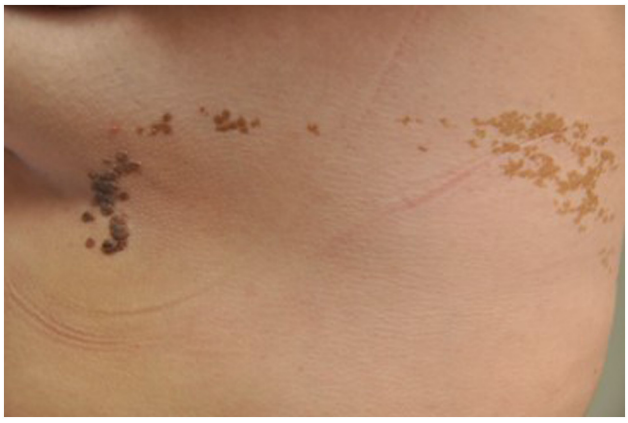

Fig. 1. Posterolateral view of keratinocytic epidermal nevus along the left flank.

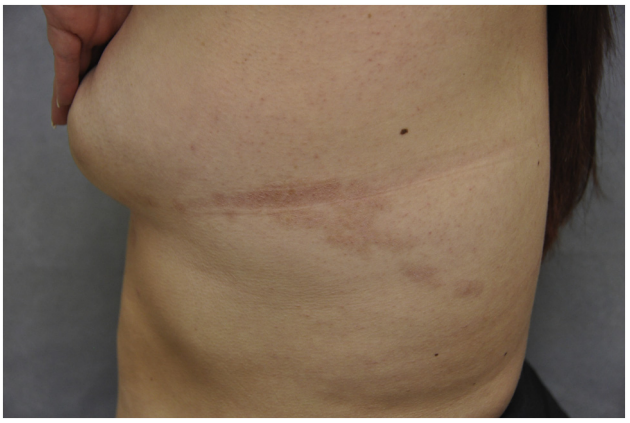

Fig. 3. Keratinocytic epidermal nevus after cosmetic treatment with CO_2 laser.

cartilage, has been observed in several disorders caused by germline *FGFR3* mutations.

FGFR3 has also been shown to be related to lacrimo-auriculo-dento-digital syndrome, which is a rare condition with symptoms that include hypoplasia of both the lacrimal and salivary glands and ducts (Rohmann et al., 2006). A similar mutation in the *FGFR3* gene may be responsible for the hypoplasia of this patient's mammary tissue, as well as the dysregulation of growth in the keratinocytes in her KEN. These hypotheses are meant to be thought provoking, but it cannot be scientifically proven that this case does not represent idiopathic breast hypoplasia with a coexistent epidermal nevus.

Future studies will need to further examine the molecular mechanisms that contribute to the development of epidermal nevi and their associated features.

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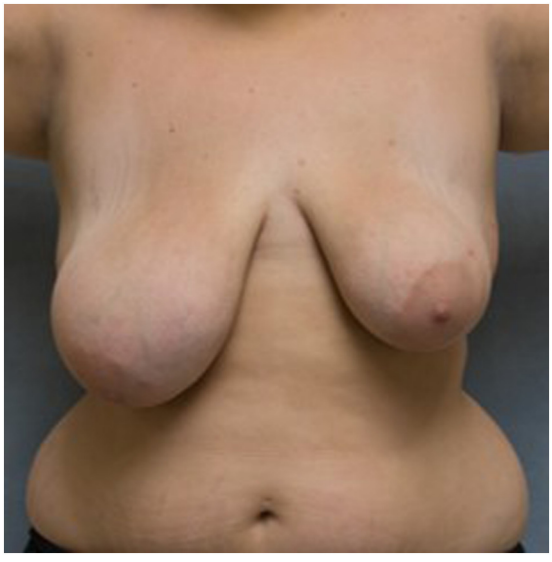

Fig. 2. Asymmetric breasts with ipsilateral mammary hypoplasia.