Unilateral nevoid acanthosis nigricans: Uncommon variant of a common disease

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ABSTRACT

Acanthosis nigricans (AN) is a fairly common dermatosis characterized by hyperpigmented velvety plaques, having a predilection for the intertriginous areas. We herein present a case of unilateral nevoid acanthosis nigricans over the left lateral chest, in an adult male. The rarity of documentation of this entity in the world literature prompted us to report the case.

Key words: Acanthosis nigricans, unilateral nevoid variant, rare presentation

INTRODUCTION

Unilateral nevoid acanthosis nigricans (UNAN) is a newly described entity characterized by lesions, morphologically similar to classical acanthosis nigricans (AN). The salient features of UNAN include localized distribution, benign course, lack of systemic and other tumor associations, and occurrence due to somatic mosaicism of postzygotic gene mutation.\(^1\)

CASE REPORT

A 25-year-old male presented with a localized area of non-itchy thickened and hyperpigmented skin on left side of the chest for 8 years. He was the second among four children born out of a non-consanguineous marriage, and there was no other family member with similar skin lesions. To start with, there was a small dark-colored asymptomatic papule over the left side of chest. It progressed over five years to attain the present status and remained inactive thereafter. There was no history of rubbing the area or any topical application. He did not give any history of consuming nicotinic acid derivatives, triazinate, and so on. Dermatological examination revealed multiple broad brown-black velvety plaques with soft ridges and ill-defined margins, measuring approximately 3 × 3 cm to 5 × 5 cm over the lateral aspect of the left side of chest [Figure 1]. The borders were irregular with a tendency of the affected skin to eventually merge inconspicuously with the surrounding normal skin, with a few hairs over the lesions. Otherwise, the skin was normal. The nape of neck, axillae, waist line, and buttocks were free from any skin lesions. Palms and soles, mucosae, genitals, hair, and nails were normal. The clinical differentials considered were linear epidermal nevus, linear acanthosis nigricans, and seborrhoeic keratosis.

The patient was non-obese, with a body mass index (BMI) of 21.2. Systemic examination was non-contributory. Complete blood count and routine urine analysis were normal. Serology for venereal disease research laboratory and human immunodeficiency virus was non-reactive. Fasting and postprandial blood sugar were 91 and 103 mg/dL, respectively. Fasting insulin level was 10.7 IU/mL. Hepatic

Figure 1: Multiple brown-black velvety plaques with soft ridges and ill-defined margins over the lateral aspect of the left side of chest

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profile, T3, T4, thyroid stimulating hormone, and growth hormone were normal as well. Radiological examination of the chest, skull, and hands were normal. In addition to this, abdominal ultrasonography was also found to be within normal limits. Biopsy of the skin showed hyperkeratosis, papillomatosis, hyperpigmentation of the basal layer, and mild acanthosis. The dermal papillae showed upward finger-like projections and the valleys between the papillae were filled with keratotic material [Figures 2 and 3]. Based on clinical and histopathological findings, a diagnosis of “unilateral nevoid acanthosis nigricans” was made. He has been prescribed topical retinoids, counselled regarding the benign nature of the disease and is under regular follow-up.

**DISCUSSION**

AN is a dermatosis characterized by velvety, papillomatous, brownish-black, hyperkeratotic plaques, typically of the intertriginous surfaces and neck. It may also affect eyelids, lips, vulva, mucosal surfaces, dorsal hands, and flexural areas in the groin, knees, and elbows.[2]

A number of observations suggest that insulin-dependent activation of IGF-1Rs can promote cellular proliferation and

![Figure 2: Photomicrograph showing hyperkeratosis, papillomatosis, hyperpigmentation of the basal layer and mild acanthosis. (H and E, ×10)](image)

![Figure 3: Photomicrograph showing upward finger-like projections of dermal papillae and the valleys between the papillae filled with keratotic material. (H and E, ×40)](image)

| Table 1: Differences between acanthosis nigricans and confluent and reticulate papillomatosis of gougerot and cartaud |
|---------------------------------------------------------------|
| **Salient points** | **Acanthosis nigricans** | **Confluent and reticulated papillomatosis** |
| **Background** | 80% idiopathic or benign conditions. Malignancy-associated disease is rare | Represents an endocrine disturbance, a disorder of keratinization, an abnormal host reaction to fungi or bacteria, a hereditary disorder, or a variant of amyloidosis |
| **Pathophysiology** | Caused by factors that stimulate epidermal keratinocyte and dermal fibroblast proliferation. (insulinlike growth factor, epidermal growth factor receptor or fibroblast growth factor receptor) | Abnormal keratinocyte differentiation and maturation. Increased melanosomes in the stratum corneum account for the observed pigmentary changes |
| **Epidemiology** | No sex predilection. More common in adult population | Common in females. Mean patient age at onset varies from 18.5-21 years |
| **Clinical features** | Symmetrical, hyperpigmented, velvety plaques most commonly appear on intertriginous areas of axilla, groin, and posterior neck. The reticulation is homogeneous | Asymptomatic oval macules usually beginning on the skin of the intermammary or epigastric region, spreading over a period of weeks or months to the breasts, the lower abdomen, the flanks, and the pubic area. The reticulation is heterogeneous |
| **Causes** | Obesity, diabetes, malignancy, drug-induced | Endocrine disturbance, keratinization disorder, abnormal host reaction to pityrosporum organisms or bacteria |
| **Histopathology** | Hyperkeratosis and papillomatosis but only slight, irregular acanthosis and usually no hyperpigmentation. Dermal papillae project upward as fingerlike projections and the valleys between the papillae are filled with keratotic material | Mild hyperkeratosis, papillomatosis, focal acanthosis, limited largely to the valleys between elongated papillae. Changes are similar to but milder than those of acanthosis nigricans |
Table 2: Differential diagnoses for linear lesions

| Determinant of pattern | Example                                      |
|------------------------|----------------------------------------------|
| Blood vessel           | Thrombophlebitis                             |
|                        | Varicose vein                                |
|                        | Temporal arteritis                           |
| Lymphatics             | Lymphangitis                                  |
|                        | Sporotrichosis                               |
|                        | Fish tank granuloma                          |
| Dermatomal             | Herpes zoster                                |
|                        | Zosteriform nevus                            |
|                        | Zosteriform Darier’s disease                 |
| Nerve trunks           | Leprosy (thickened nerve)                    |
| Developmental and Blaschko’s lines | Pigmentary demarcation lines           |
|                        | Epidermal naevi                              |
|                        | Incontinentia pigmentii                      |
|                        | Linear psoriasis                             |
|                        | Linear lichen planus                         |
|                        | Lichen striatus                              |
| Miscellaneous          | Striae distensae                             |
|                        | Burrow in scabies                            |
|                        | Larva migrans                                |
|                        | Phytophotodermatitis                         |
|                        | Caustics                                     |
|                        | Burns                                        |
|                        | Keloid scar, dermatitis artefacta            |
|                        | Purpura (cryoglobulinemia, amyloidosis)      |
|                        | Blister (Epidermolysis bullosa, porphyria)    |
|                        | Inoculation (wart, molluscum contagiosum)     |
|                        | Koebner (psoriasis, lichen planus, vitiligo)  |
|                        | Others (scar sarcoid)                        |
|                        | Linear scleroderma                           |
| Infestation            | Burrow in scabies                            |
|                        | Larva migrans                                |
| External injury        | Phytophotodermatitis                         |
| Plants                 | Elastopast, waistband                        |
| Allergens              | Caustics                                     |
| Chemical               | Burns                                        |
| Physical               | Keloid scar, dermatitis artefacta            |
| To normal skin         | Purpura (cryoglobulinemia, amyloidosis)      |
| To abnormal skin       | Blister (epidermolysis bullosa, porphyria)    |
|                        | Inoculation (wart, molluscum contagiosum)     |
|                        | Koebner (psoriasis, lichen planus, vitiligo)  |
|                        | Others (scar sarcoid)                        |

facilitate the development of AN and the severity of AN in obesity correlates positively with the fasting insulin concentration. Classification of acanthosis nigricans, as proposed by Schwartz, categorizes the entity into the following eight types: Benign, malignant, associated with obesity, syndromic, unilateral, drug induced, mixed and acral. UNAN has a morphology similar to classical AN, but the distribution is unilateral or localized and is manifested during childhood or later. It is inherited as an irregularly autosomal dominant trait. The natural history of the disease is a short period of activity for 4-5 years at the outset, following which stability without any tendency to resolution is the rule. There is no systemic, endocrine or syndromic association. Familial involvement in UNAN is not present, as found on extensive literature search. The first description was given by Krishnaram in 1991 and following that report, very few cases have been reported. Schwartz was the first to include this entity in the classification of AN in 1994. Classical AN is normally present over the flexures but UNAN does not have a predilection for intertriginous areas, consistent with our case and other reports as well. Most of the cases respected the midline with the distribution being essentially unilateral. According to a recent classification in a textbook, UNAN has been grouped together with “syndromic AN” and “acral acanthotic anomaly” under the heading “other” causes of AN. Clinical differentials include ichthyosis hystrix, confluent and reticulate papillomatosis, linear epidermal nevus and hyperkeratotic type of seborrhoeic keratosis. Petit et al. reported three cases of a rash with mixed clinical features of both epidermal nevus and acanthosis nigricans but, since the pathophysiology of this rash was unclear, they proposed to name it “RAVEN”, for “rounded and velvety epidermal nevus” In our case, late age of onset and presence of minimal acanthosis excluded epidermal nevus. Absence of horn cysts and basaloid cells ruled out seborrhoeic keratosis. In addition, other close mimickers were excluded due to the absence of their characteristic findings. The points of difference acanthosis nigricans and confluent and reticulate papillomatosis of Gougerot and Carteaud have been listed [Table 1].

The course of the disease is typically benign and improvement of the skin lesions is often the patient’s primary concern. No randomized, controlled trials exist for any treatment of AN. Multiple case reports suggest that acanthosis nigricans improves with treatment of its underlying condition. Various modalities reported to be successful include retinoids (topical and systemic), calcipotriol, fish oil, and long pulsed (5 msec) alexandrite laser treatment.

To conclude, linearity of a lesion can spark the synaptic flashpoint for diagnosis and a compact list of unilateral linear lesions has been provided [Table 2].

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