Case Report
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A case report of squamous cell carcinoma in ichthyosis hystrix Curth-Macklin

İktiyozis histriks Curth-Macklin'de skuamöz hücreli karsinom olgusu

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Abstract

The Curth-Macklin type of ichthyosis hystrix is an extremely rare genodermatosis presenting as generalized or nevoid forms. Clinical expression varies in the time of onset and morphology, even within families, from painful palmoplantar keratoderma to a severe, generalized involvement with hyperkeratotic and papillomatous coalescent papules distributed extensively and bilaterally in whorled arrays of thickened, darkened, hystrix-like velvety lesions anywhere on the skin surface. There are few case reports of patients with ichthyosis hystrix who developed malignancies. We report a sporadic case of a 73-year-old man who presented with an unusual manifestation of ichthyosis hystrix and developed squamous cell carcinoma. Ichthyosis hystrix Curth-Macklin is a rare congenital ichthyosis that has developed multiple keratoses and malignancies over a long time. Therefore, early diagnosis, treatment, and regular follow-up are required in these patients.
Keywords: Ichthyosis hystrix, hyperkeratosis, malignancy

Öz

İktiyozis histriks Curth-Macklin, generalize veya nevoid formlarda ortaya çıkan konjenital iktiyozun oldukça nadir görülen bir genodermatozudur. Klinik ifade, aile içinde bile başlangıç zamanı ve morfoloji açısından değişiklik gösterir; ağrılı palmoplantar keratodermadan, deri yüzeyinin herhangi bir yerinde kalınlaşmış, koyulaşmış, histriks benzeri kadifemsi lezyonlardan oluşan sarmal diziler halinde yaygın ve iki taraflı olarak dağılmış hiperkeratotik ve papillomatöz birleşen papüllerle şiddetli, genel bir tutuluma kadardır. Malignite gelişen iktiyoz histriks hastalarına ilişkin çok az sayıda olgu raporu bulunmaktadır. Alışılmadık iktiyoz histriks belirtileriyle başvuran ve skuamöz hücreli karsinom gelişen 73 yaşında bir erkek hastayı rapor ediyoruz. İktiyozis histriks Curth-Macklin uzun süre içerisinde multipl keratoz ve malignite gelişimi gösteren nadir bir genodermatozdur. Bu nedenle bu hastalarda erken tanı, tedavi ve düzenli takip gereklidir.
Anahtar Kelimeler: İktiyoz histriks, hiperkeratoz, malignite

Introduction

Ichthyosis hystrix Curth-Macklin (IHCM) is a rare genodermatosis of keratinization disorder. It is an autosomal dominant disorder characterized clinically by the presence of dark, spiny hyperkeratotic plaques on the joints, sometimes on the entire body, severe palmoplantar keratoderma, and histopathologically, by epidermolytic hyperkeratosis. Ichthyosis hystrix is itself a rare disorder, and its association with malignancy is even rarer. Very few cases have been reported in the literature about the association between ichthyosis hystrix and malignancy. We report a sporadic case of a 73-year-old man who presented with an unusual manifestation of ichthyosis hystrix and developed squamous cell carcinoma.

Case Report

A 73-year-old male patient was referred from the surgery department to us with skin lesions since birth. He had

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developed multiple swellings over those lesions on the trunk and neck for one year. The swellings had an insidious onset and gradually increased in size and number. One of the swellings was associated with occasional pain for the last 6 months. He was the first child of non-consanguineous parents. His sisters and other family members were reported as not having similar complaints. There was no history of blistering or hearing loss. He had no skeletal or neurological symptoms. He was a farmer by occupation with a history of long-term sun exposure. On examination, he had dark, well-defined hyperkeratotic, velvety, shiny plaques encircling the right side of the abdomen, lower back, chest, and face in the whorled pattern (Figure 1). On the right side of the face, the lesion occupied the temporal region, around the eye and nose; the retro-auricular area was involved, sparing the ear. On the left side, it had affected the anterolateral aspect of the neck, left ear, and left side of the occipital, temporal region of the scalp. Over these lesions at various sites, multiple light-colored, verrucous, exophytic nodules of varying sizes were embedded; some were sessile, and others were pedunculated. One of the swellings was the largest, 5x5 cm, flesh-colored, multi-lobulated, verrucous-surfaced, pedunculated, and seen on the anterior aspect of the lower neck (Figure 2, 3). Nails and mucosa were normal in this patient. Laboratory investigations such as complete hemogram, urine analysis, and liver and renal function tests were within normal range.

A biopsy was done at the two sites: One from congenital verrucous plaque and the other from pedunculated growth. Histopathological examination of the congenital verrucous plaque revealed church-spire hyperkeratosis, acanthosis, and papillomatosis in the epidermis (Figure 4). Focal hypergranulosis, vacuolar degeneration of keratinocytes, and increased melanin pigmentation are also seen in a few areas. A few binucleate keratinocytes are present in the suprabasal layer of the epidermis (Figure 5). There is no evidence of acantholysis. Histopathological study of pedunculated growth showed features suggestive of well-defined squamous cell carcinoma (Figure 6). Electron microscopy and genetic analysis could not be performed due to lack of facilities. Informed consent was obtained.

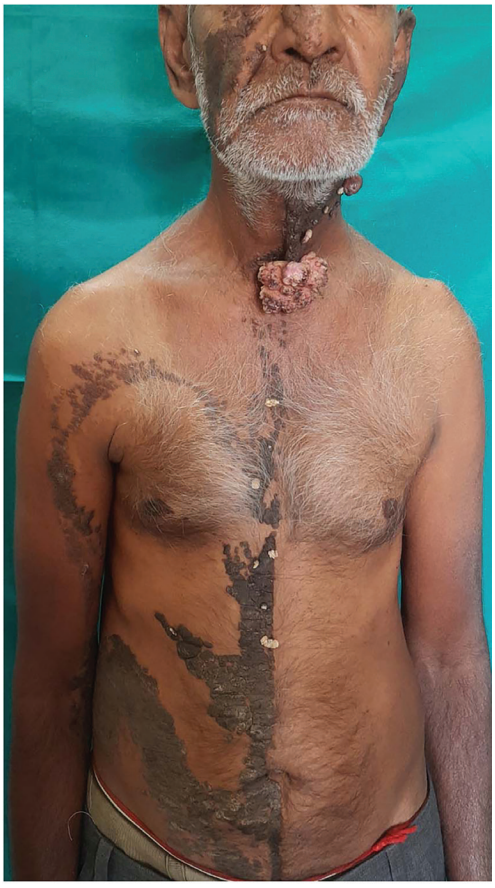

Figure 1. Hyperpigmented, hyperkeratotic plaques encircling the right side of the abdomen, chest, arm, forearm, and left side of the neck

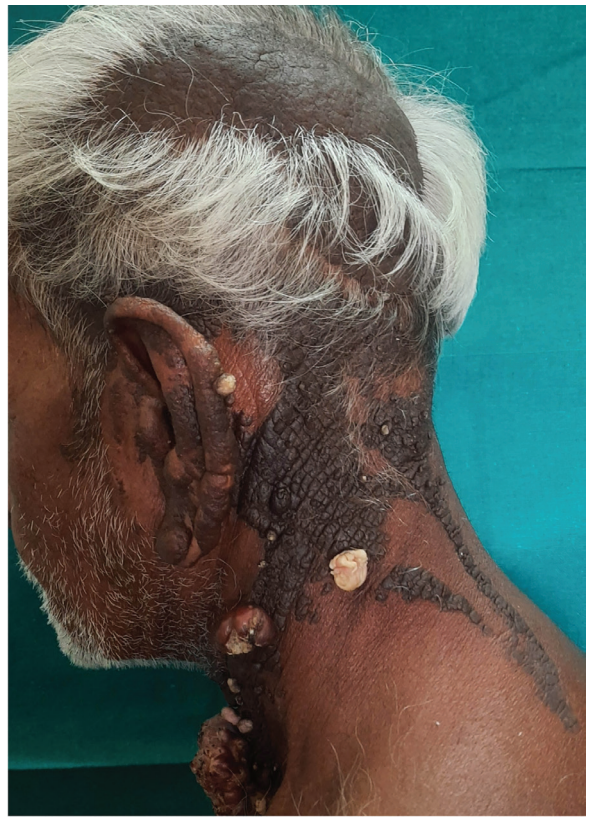

Figure 2. Well-defined, hyperkeratotic, velvety, shiny plaques with cobblestoned papules and multiple keratoses seen on the left side and nape of the neck

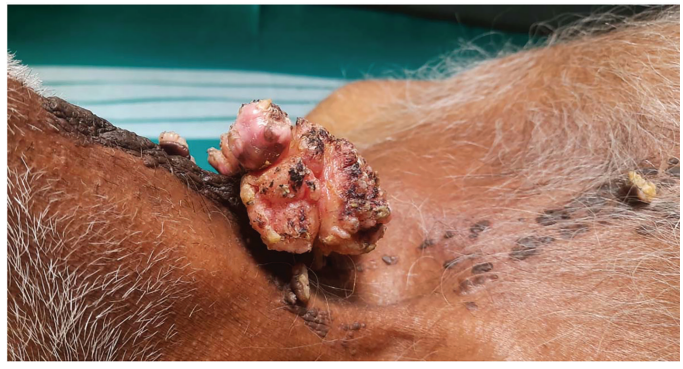

Figure 3. Flesh-colored, multi-lobulated, verrucous surfaced, pedunculated growth on the neck

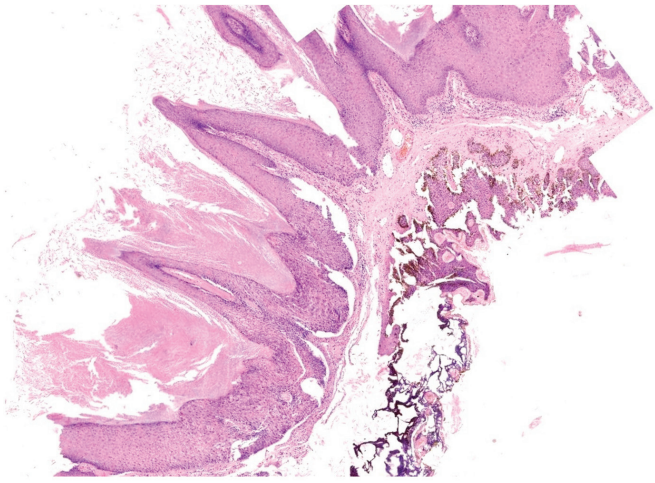

Figure 4. Histopathological findings: Church-spire hyperkeratosis, acanthosis, and papillomatosis in the epidermis (haematoxylin and eosin stain, original magnification, x10)

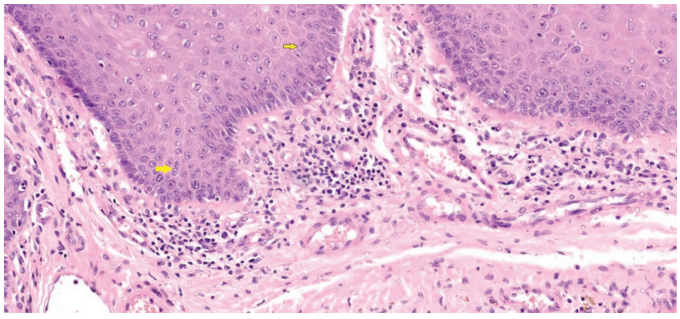

Figure 5. Histopathological picture showing binucleate keratinocytes in the suprabasal layer (haematoxylin and eosin stain, original magnification, x40)

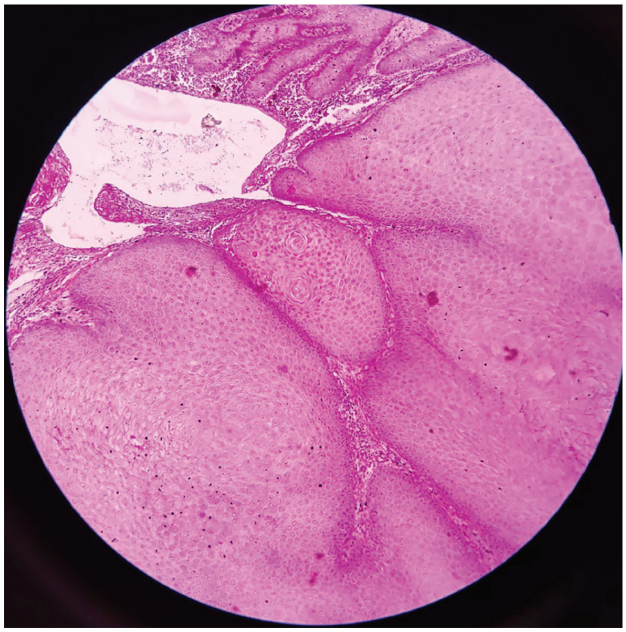

Figure 6. Histopathological findings of well-differentiated squamous cell carcinoma (haematoxylin and eosin stain, original magnification, x40)

Discussion

Ichthyosis hystrix is a rare congenital ichthyosis presenting as generalized or nevoid forms[1]. The word "hystrix" means the porcupine's spines; the family members affected by Lambert type of ichthyosis hystrix were well-known in England as porcupine men[2]. Five different clinical variants have been described in ichthyosis hystrix: Brocq type, Lambert type, Curth-Macklin type, Rheydt type, and Bäfverstedt type. Erythroderma and blistering are the features of Brocq type with less nevoid forms. In Lambert type, spines cover all over the body, sparing face, genitalia, palms, and soles. IHCM type presents as thick, verrucous spiny scales affecting various body parts and palmoplantar keratoderma. The hystrix-like hyperkeratosis, ichthyosiform erythroderma, mild-palmolantar keratoderma and sensorineural deafness characterize rheydt type. Later, it was considered under the term "HID", the acronym for hystrix-like ichthyosis and deafness. Bafverstedt type is characterized by nevoid, extensive ichthyosis hystrix with striking follicular hyperkeratosis[3].

IHCM is an autosomal dominant condition first reported in 1954 by Curth and Macklin[4]. To date, three families and a few sporadic cases, around ten, have been reported worldwide. There is no evidence of a greater likelihood of occurrence of IHCM in any specific ethnic group or gender.

IHCM is a scarce type characterized by extensive, spiny, verrucous or velvety, ridged or cobblestoned hyperkeratotic papules and plaques over the large joints, extremities, and trunk along with severe, painful palmoplantar keratoderma. IHCM is also described as an organized epidermal nevus composed of hyperkeratotic papules and plaques with bilateral distribution. The onset of clinical features could be at birth or a few weeks after birth. Though the lesions of IHCM are usually symmetrical, our patient presented with an asymmetrical distribution of the lesions bilaterally. The presentation in a few patients might be restricted only to the palms and soles as severe transgradient palmoplantar keratoderma with cobblestoned papules or starfish-like hyperkeratosis or knuckle pad, nail dystrophy. Development of constriction bands (pseudoainhum) in these patients may cause auto-amputation, leading to functional impairment.

IHCM is a member of keratinopathic ichthyosis caused by frameshift mutation in the keratin gene (*KRT1*), which encodes proteins with disrupted keratin filament network[5]. Light microscopy shows orthokeratotic hyperkeratosis, hypergranulosis, acanthosis, papillomatosis, perinuclear vacuolization, and binucleated cells[5]. In contrast to epidermolytic hyperkeratosis, epidermolysis is typically absent. The ultrastructural feature of this condition is peculiar with the presence of keratin intermediate filaments aggregated into continuous, peripheral shells in binucleated suprabasal keratinocytes. Other features include a perinuclear compartment filled with ribosomes and other organelles, coated vesicles with a surrounding tonofibril shell, normal-appearing tonofilaments, and keratoyalin granules of variable size and shape[6].

Ichthyosis may be a marker for immune deficiency and cancer-prone conditions. Though there are a few case reports in the literature about the association of congenital ichthyosis with malignancies, it is still unclear whether there is an increased risk of developing malignancies in congenital ichthyosis[7-9]. In a few reported cases of ichthyosis hystrix, multiple keratoses and squamous cell carcinomas developed; however, one case was attributed to the prior carcinogenic treatment

received[3,10]. Our patient represents such a rare occurrence of well-defined squamous cell carcinoma with multiple keratoses in IHCM. Whether it is a co-incidental finding or is there a role of this genetic condition "ichthyosis hystrix" in the development of malignancy yet to be elucidated. In contrast to this, many cases have been reported for the development of skin and oral cancers in KID syndrome[11-13]. IHCM can be easily differentiated from epidermolytic ichthyosis and epidermolytic palmoplantar keratoderma by the absence of blistering and skin fragility. It is considered to be a type of epidermal nevus with bilateral presentation[14]. Therefore, histopathological characteristics such as hyperkeratosis, acanthosis, and papillomatosis may be observed. The presence of binucleate keratinocytes in IHCM helps differentiate it from epidermal nevus. Systemic retinoids, topical keratolytics, and emollients are the available treatment modalities with promising results for IHCM. The efficacy of systemic retinoids in tumor prevention is unknown, and their poor response may reflect the slow epidermal turnover rate in ichthyosis hystrix[3].

IHCM is a rare genodermatosis with varied clinical manifestations ranging from mere palmoplantar keratoderma to severe erythroderma. Multiple keratoses and the development of malignancies in IHCM over time have been reported, which might need early chemotherapeutic/surgical intervention. However, in this patient, the occurrence of SCC as a separate entity following long-term sun exposure in old age or as an association with ichthyosis hystrix cannot be elucidated. Therefore, early diagnosis, treatment, and regular follow-up are necessary in these patients.

Ethics

Informed Consent: It was obtained.

Footnotes

Authorship Contributions

Concept: V.S.P., Design: R.R.Y., Data Collection or Processing: V.S.P., R.R.Y., Analysis or Interpretation: V.S.P., Literature Search: R.R.Y., Writing: V.S.P., R.R.Y.

Conflict of Interest: No conflict of interest was declared by the authors.

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