SQUAMOUS CELL CARCINOMAS IN A GIRL WITH ICHTHYOSIS AND SEVERE MALNUTRITION

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Case report. A 9-year-old girl was admitted with diffusely dry, scaly, pruritic, and exfoliating skin present for six years. The condition was intermittent and worsened in cold and dry environments. Four months prior to admission, two crusted lesions appeared on her back and nose. These lesions progressively enlarged and were characterized by easy bleeding, foul odor, and pain. One month before admission, the patient became progressively debilitated and bedridden. She was born at 7 months of gestation and had no history of congenital erythroderma or collodion membrane at birth. There was no history of systemic illness, no known family history of ichthyosis or cutaneous malignancy, and she had never undergone genetic evaluation. Psychosocial history was notable for delayed medical care due to reliance on traditional healers and limited parental awareness of disease severity. She was brought to the hospital for generalized weakness and inability to tolerate oral intake.

On admission, the patient appeared ill and febrile, with a temperature of 39.6°C, heart rate of 94 beats/min, respiratory rate of 48 breaths/min, and body weight of 18 kg, consistent with severe malnutrition. Skin examination revealed diffuse hyperkeratotic macules and plaques covered with adherent scales, associated with marked hyperkeratosis and fissuring. Several fissures were extensive and bleeding, particularly in pressure areas such as the knees, wrists, and ankles, while flexural regions were relatively spared (Fig. 1).

Dermatologic examination revealed two tumoral lesions. In the nasal region, there was a hard, verrucous, ulcerated mass measuring approximately 2 × 1 × 1 cm with poorly defined margins (Fig. 1). On the back, a larger exophytic tumor measured approximately 14 × 5 × 3 cm. This lesion was irregular, ulcerated, indurated, and friable, with crusts and areas of bleeding (Fig. 2). The clinical morphology of both lesions was highly suggestive of squamous cell carcinoma.

Initial laboratory evaluation demonstrated severe microcytic hypochromic anemia (hemoglobin 3.7 g/dL, reference range 11.5-15.5 g/dL), leukocytosis with neutrophilic predominance, C-reactive protein 311.1 mg/L (reference <0.5 mg/L), albuminemia 2.3 g/dL (reference 3.8-6.4 g/dL), iron deficiency, electrolyte imbalance, and findings consistent with systemic inflammation and severe malnutrition. Following transfusion, hemoglobin improved to 9.0 g/dL. Urinalysis showed cloudy urine with increased renal tubular epithelial cells and a mild increase in hyaline casts. Serologic tests for hepatitis B and HIV were non-reactive. Fine-needle aspiration cytology revealed malignant epithelial cells with spindle morphology, nuclear pleomorphism, coarse chromatin, and eosinophilic cytoplasm, consistent with squamous cell carcinoma.

Given the patient's severely compromised clinical status, the pediatric oncology consultant determined that chemoradiotherapy was not feasible, and palliative care was planned. The patient was discharged against medical advice at the parents' request. Two days after discharge, she passed away at home.

Fig. 1

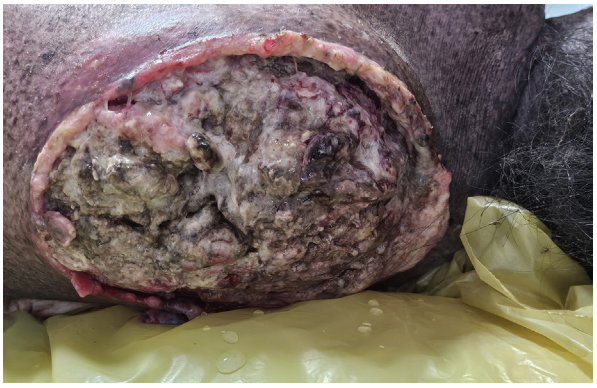

Fig. 2

Fig. 1, 2: Squamous cell carcinomas of the nose and back in a girl with ichthyosis and severe malnutrition.

Discussion. Inherited ichthyoses represent a heterogeneous group of disorders of keratinization characterized by abnormal cornification and impaired epidermal barrier function, with wide variability in clinical severity and systemic involvement (1). In many resource-limited settings, diagnosis remains primarily clinical, as molecular testing and specialized investigations are not always available. In our patient, cutaneous manifestations began around three years of age in a girl born prematurely at seven months of gestation, with no history of congenital erythroderma or collodion membrane at birth. Scaling predominantly affected extensor surfaces with relative sparing of flexural areas and no marked inflammatory background, suggesting ichthyosis vulgaris.

Cutaneous malignancies, particularly squamous cell carcinoma, have been reported in association with some severe congenital ichthyoses, presumably related to chronic barrier dysfunction, persistent inflammation, and impaired cutaneous immune surveillance (2). Therefore, Netherton syndrome was carefully considered in the differential diagnosis. This condition typically presents with congenital erythroderma, early growth retardation, and characteristic hair shaft abnormalities, particularly trichorrhexis invaginata (3, 4). In our case, there was no history of neonatal erythroderma or systemic involvement during early childhood. Dermoscopic evaluation of the scalp and hair did not reveal features suggestive of trichorrhexis invaginata, and there were no clinical signs of hair fragility. Unfortunately, ultrastructural hair shaft examination and genetic testing were not available, representing a significant limitation.

Xeroderma pigmentosum was also considered due to the early onset of squamous cell carcinomas; however, the absence of marked photosensitivity, recurrent severe sunburns, early lentigines in sun-exposed areas, or poikiloderma made this diagnosis unlikely (5).

The development of squamous cell carcinoma in childhood in the context of inherited ichthyosis is extremely rare. Cutaneous malignancies have been more frequently reported in severe congenital ichthyoses, likely related to chronic barrier dysfunction, persistent inflammation, oxidative stress, and impaired immune surveillance (6). Chronic epidermal barrier dysfunction may play a central role in cutaneous carcinogenesis. Persistent transepidermal water loss, recurrent fissures, and microtrauma can lead to sustained keratinocyte activation and a pro-inflammatory cytokine microenvironment, with increased expression of interleukin-1 and tumor necrosis factor-alpha. This state of chronic low-grade inflammation can promote oxidative stress, DNA damage, and dysregulated cellular proliferation. In the absence of an intact skin barrier, repeated environmental insults and secondary infections can further amplify this inflammatory cascade (7).

In the present case, systemic deterioration became evident several months prior to admission, characterized by progressive malnutrition and rapid enlargement of the tumoral lesions. Severe malnutri-

tion in this patient may have acted not only as a comorbidity but also as a biological cofactor facilitating carcinogenesis. Protein-energy malnutrition is known to impair cell-mediated immunity, reduce Langerhans cell density and antigen-presenting capacity, and weaken antitumor immune surveillance. Additionally, deficiencies in essential micronutrients and antioxidants can increase oxidative stress and compromise DNA repair mechanisms. In chronically inflamed and fissured ichthyotic skin, this immunocompromised state may create a permissive microenvironment for malignant transformation (8). Therefore, the convergence of prolonged barrier dysfunction, persistent inflammation, and systemic nutritional compromise may have synergistically contributed to the unusually early and aggressive development of squamous cell carcinoma in this girl (9).

Conclusion. Squamous cell carcinoma arising in the context of ichthyosis is extremely rare, particularly in pediatric patients. This case highlights how chronic epidermal barrier dysfunction, persistent inflammation, and systemic malnutrition can collectively contribute to early malignant transformation in vulnerable skin.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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