useful. Nuclear expression of TTF-1 is a characteristic of both primary lung cancer and thyroid cancer.

We suggest that adenocarcinoma of the lung should be taken into consideration as a possible cause of inflammatory cutaneous metastasis.

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Generalized Idiopathic Benign Acanthosis Nigricans in Childhood

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Dear Editor:

Acanthosis nigricans (AN) is a velvety thickening of the epidermis that may signify internal diseases¹. During childhood, AN is obesity-associated amongst majority of cases, and it is considered an important cutaneous marker of insulin resistance (IR)¹. Axillae, posterior neck fold and flexor skin surfaces represent primarily affected areas.

However, although rarely, a generalized form of AN has been described²⁻⁵, which is not associated with IR or internal diseases. We present the case of a 2-year-old Caucasian girl that sought consultation to our clinic for the onset of skin roughness and darkening of the wrists. The mother reported that the skin roughness started a few months after birth, slightly extended to periflexural areas and was associated to a mild pruritus. The girl was born from non-consanguineous parents, with a normal pregnancy and delivery. Psychophysical development was normal. Weight, height and body-mass-index were normal according to age and sex. Skin examination revealed bilateral thickening, darkness, and rough plaques which affected the neck, main folds, navel, upper and lower limbs (Fig. 1). Mucosae, palms, soles, genitalia, hair and nails were not involved. A 3-mm-incisional-biopsy specimen obtained from the popliteal region showed papillomatosis, basket weave pattern hyperkeratosis, mild hyper-

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Fig. 1. A 2-year-old girl with benign, idiopathic generalized acanthosis nigricans. Clinical details of (A) neck; (B) popliteal folds; (C) right hand, right inguinal fold; and (D) feet, revealing thick, rough, plaques and darkening of the skin.

Fig. 2. A 3-mm-incisional-biopsy specimen obtained from the popliteal region showing epidermis with acanthosis and overlying hyperkeratosis, and focal upward projection of finger-like dermal papillae (H&E, $\times 10$).

granulosis and acanthosis with focal upward projections of finger-like dermal papillae. Superficial dermis indicated the presence of a slight perivascular lymphocytic infiltra-

tion (Fig. 2). Laboratory examinations, including routine blood cell counts, haemoglobin, platelets, glycemia, insulin, blood urea levels, creatinine, low density lipoprotein cholesterol, high density lipoprotein, triglycerides, hepatic transaminases, bilirubine, alkaline phosphatase, gamma-glutamyl-transpeptidase, lactate dehydrogenase, serum electrolytes, C-reactive protein, erythrocyte sedimentation velocity, serum protein electrophoresis, immunoglobulins, thyroid-stimulating hormone, thyroxine, anti-thyroperoxidase antibodies, anti-thyroglobulin antibodies were within the normal range in relation to age and sex. Chest X-ray was also normal. There was no history of drug intakes. There were no records of similar skin lesions from previous generations, nor history of maternal diabetes. Secondary causes of AN were excluded thus supporting the final diagnosis of generalized idiopathic benign AN. The patient was treated for 3 months with moisturizers and topical isotretinoin 0.05% gel being applied twice daily, and we repeated the treatment after further recurrences of the skin disease. The patient is currently under follow up, the skin lesions have improved significantly with the topical treatment.

Childhood AN is classified into 8 different clinical types: benign, obesity-associated, syndromic, malignant, acral, unilateral, drug-induced, mixed. Although the etiopathogenesis of AN remains unclear, proliferation of keratinocytes and dermal fibroblasts could be induced by IR and high levels of insulin binding capacity¹. Nevertheless, not all types of AN could be related to this mechanism, because hyperinsulinemia is not always present. In fact, in malignant AN, the inductor of keratinocytic growth could be a product of tumor tissue, tumor growth factor α , stimulating epidermal growth factor receptor and thus, inducing proliferation. Moreover, a familial series of non syndromic AN due to mutation of fibroblast growth factor receptor-3 has been recently reported⁶.

Benign AN has been considered a rare genodermatosis, inherited as an autosomal dominant trait with variable penetrance. Benign AN may rarely present a generalized involvement of the skin¹. We found that 8 of the cases of generalized benign AN had been previously reported in literature which showed similar clinical presentations to our case²⁻⁵, with generalized hyperpigmentation and velvety thickening of the skin, sometimes associated with pruritus in otherwise healthy children. However, only one⁴ had a familiarity for AN. On the basis of these data, we propose to distinguish this type of generalized benign AN from the benign form reported in literature. We propose to call it generalized, idiopathic, benign acanthosis nigricans (GIBAN). This could be considered a singular variant, probably related to a new mutation, occurring for

the first time in the family; thus, it is not possible to demonstrate autosomal transmission, due to the absence of familiarity and not being associated with IR or other internal diseases.

Larger case series and long-term follow-ups of these patients should exclude this scenario as the first cutaneous sign of IR only developed years after the clinical appearance of AN.

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