Short Report

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Autosomal Recessive Lamellar Ichthyosis and Acute Lymphoblastic Leukemia

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Key Words
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Abstract
Autosomal recessive lamellar ichthyosis (ARLI) is a congenital disorder of keratinization, the gene of which has been mapped to chromosome 14q11. This band is also the breakpoint in various chromosomal rearrangements in T cell acute lymphoblastic leukemia (ALL). We describe a patient with ARLI who developed ALL at the age of 2.5 years. High resolution banding showed no abnormality or rearrangement involving chromosome 14. To our knowledge, this is the first description of the occurrence of the two conditions in one patient.

Introduction

Autosomal recessive lamellar ichthyosis (ARLI) is a congenital disorder of keratinization (Mendelian Inheritance in Man 242100, MIM, estimated incidence 1:250,000) [1]. The gene for this disease has been mapped to chromosome 14q11 by linkage analysis [2]. Mutations in the keratinocyte transglutaminase gene (TGK) have been identified in families with this disease [3, 4]. Since the TGK gene maps to chromosome 14q11 [5], it is assumed that it is the disease gene in ARLI. The same band, 14q11, is the breakpoint in various chromosomal rearrangements in T cell acute lymphoblastic leukemia (ALL) and the locus for alpha and delta T cell receptor genes [6]. X-linked ichthyosis and ALL have been reported before in one patient [7]. We describe here a patient with ARLI who developed ALL, which to our knowledge has not been reported before. We also discuss the genetic relations of these two conditions and leukemogenesis.

Case Report

A 2.5-year-old female patient was admitted to the Princess Badi'a Teaching Hospital with a 3-day history of right upper quadrant and periumbilical abdominal pain and loss of appetite. There was a prolonged history of difficulty in swallowing. She was born with mild erythroderma and generalized dryness of the skin, which improved with time. She is the second child of distantly related normal parents. Her younger sister aged 1.5 years is healthy, but her 4-year-old sister has a similar skin condition.

On physical examination she had stable vital signs and generalized fine scaling of the skin most pronounced on the trunk. The flexures and face were involved but the palms and soles were spared. She had mild ectropion, slight crumpling of the ears and sparsity of scalp hair. Her teeth and nails were normal. She had obvious abdominal distension with gross hepatosplenomegaly and generalized lymphadenopathy. A chest x-ray did not show any mediastinal mass. Laboratory studies showed Hb: 10 g/dl, ESR 60 mm/h, platelet count: 19 × 10^9/l, WBC: 6.4 × 10^9/l with 91% lymphocytes and 9% neutrophils. Bone marrow examination confirmed the diagnosis of ALL (L1/L2 morphology FAB classification). Further identification of the ALL could not be performed at our laboratory. High resolution banding showed no abnormality or rearrangement involving chromosome 14 and in particular band q11.

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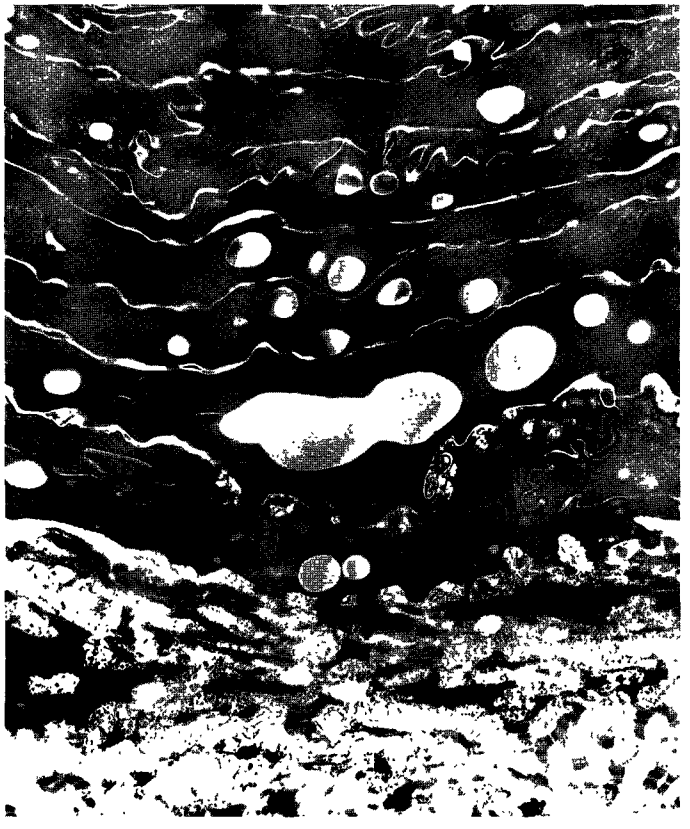

Fig. 1. Electron micrography of skin biopsy showing numerous lipid vacuoles in the stratum corneum. × 10,000.

Light microscopy of a skin biopsy from the trunk showed hyperkeratosis, parakeratosis and acanthosis. Electron microscopy revealed numerous lipid vacuoles in the stratum corneum (fig. 1); these are all features of erythrodermic lamellar ichthyosis.

She was treated according to the UKALL X, standard risk leukemia protocol (arm A) [8] but unfortunately died 2 weeks later of severe chemotherapy-related toxicity.

Discussion

The clinical, histological and ultrastructural features of this patient's skin are in keeping with the erythrodermic variant of ARLI (synonym: nonbullous congenital ichthyosiform erythroderma). The more severe nonerythrodermic variant characterized by generalized plate-like scales was initially linked to chromosome 14q11 [2]. The TGK gene, which encodes one of the enzymes responsible for cross-linking epidermal proteins during formation of the stratum corneum, maps to 14q11 [5] and subsequently mutations in the TGK gene were identified in families with both variants of ARLI [3, 4].

Chromosomal rearrangements involving 14q11 occur in T cell ALL [6]. On the other hand, T lineage ALL is associated with L1 or L2 morphology of lymphoblasts in similar relative frequencies as B lineage ALL [9]. In our patient, further identification of the leukemia type could not be done at our laboratory, and although no mediastinal mass was present, T cell ALL could still be the diagnosis.

The concomitant occurrence of ARLI and ALL, possibly of T cell origin, in one individual suggests a common causal factor for both conditions. Since high resolution banding did not reveal a deletion of the band 14q11, we think there is either a submicroscopic cryptic deletion involving the two genes or a deletion involving a control element that regulates the expression of both genes. In this family, individuals with the skin disease may be at risk of developing ALL. Although the carriers of ARLI in this family and the other affected sib have not developed any malignancy to date, they should perhaps be observed closely for early diagnosis of such a complication.

Despite modest treatment intensity and the availability of good supportive care, our patient died 2 weeks after induction treatment because of chemotherapy-related toxicity. It is difficult to draw conclusions from a single case report, but this may suggest that our patient had an unusual sensitivity to chemotherapy.

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