Singapore Med J 1998; Vol 39(5):220-221

Linear Epidermolytic Epidermal Naevus – A Case Report

P Ang, Y K Tay

ABSTRACT

A 25-year-old man presents with linear verrucous epidermal naevus since birth. A biopsy done showed histological features of epidermolytic hyperkeratosis. Patients with epidermolytic epidermal naevi can give rise to children with a rare but serious condition known as congenital bullous icthyosiform erythroderma. Recently, keratin mutations have been described in both conditions and the relationship between the two can be explained using the concept of genetic mosaicism.

Keywords: epidermal naevus, epidermolytic hyperkeratosis, mosaicism, keratin mutations

INTRODUCTION

In the past, there have been case reports of epidermal naevi showing histological features of epidermolytic hyperkeratosis. More recently, it was reported that patients with such naevi can actually give rise to offspring with congenital bullous icthyosiform erythroderma (CBIE). We describe a patient who presented with a linear epidermal naevus with histological features of epidermolytic hyperkeratosis and discuss its relationship with CBIE.

CASE REPORT

Chan KP is a 25-year old man who presented with widespread skin lesions since birth. The lesions were stable with no increase in size. He was previously asymptomatic but now complained of pruritus over these lesions for the last four months. There was no significant medical or family history. His parents were non-consanguinous.

Physical examination revealed multiple verrucous papules and plaques over his trunk and limbs arranged along the lines of Blaschko, with some areas of erythema and excoriation (Figs 1& 2). Systemic review was otherwise normal. A skin biopsy showed a hyperplastic epidermis with alternating hyperkeratosis and parakeratosis. Vacuolisation in the keratinocytes were seen in the upper Malpighian layers. Some epidermal cells were hypereosinophilic, showing premature keratin differentiation. In addition, coarse keratohyaline granules were seen in the granular layer. All these were consistent with epidermolytic hyperkeratosis. The patient was diagnosed to have systematised linear epidermal naevus with epidermolytic hyperkeratosis.

DISCUSSION

Epidermal naevi are developmental or hamartomatous disorders characterised by hyperplasia of epidermal structures in a circumscribed area of skin. There is no proliferation of naevus cells.

They can be classified into seven types: linear verrucous epidermal naevus, naevus sebaceous, naevus comedonicus, eccrine naevus, apocrine naevus, Becker's naevus and white sponge naevus[1].

Epidermal naevi, especially the systematised forms, can show features of epidermolytic hyperkeratosis. What is peculiar are recent reports of such patients giving rise to offspring with generalised epidermolytic hyperkeratosis, more specifically the variant of congenital bullous ichthyotic erythroderma (CBIE)[2,3]. CBIE was first described by Brocq in 1902 and is now known to be an autosomal dominant condition resulting from mutation of either the keratin 1 or 10 genes[4]. Affected children present with severe blistering and ichthyotic erythroderma soon after birth. There are two components to this disease: bullous and keratotic. The former prevails during the first few years of life, gradually subsiding with the development of keratoses. The hyperkeratosis forms distinctive ridge patterns over the flexural areas. There is blistering after minor trauma and patients are prone to impetigo and body odour.

How do we explain this phenomenon of patients with epidermolytic epidermal naevi giving birth to CBIE offspring? Two hypotheses were proposed: variable expression of the keratin gene mutation, and genetic mosaicism with both somatic and gonadal mutations[4].

Support for the mosaic hypothesis comes from the following: patients with epidermolytic epidermal naevi may beget CBIE children, never vice versa. This could be explained by a somatic mutation occurring early during embryogenesis manifesting itself in the parent as a localised epidermolytic naevus. At the same time, such a somatic mutation can also affect the germline and result in gonadal mosaicism. Some gametes will carry the defective gene so that offspring can show

National Skin Centre
1 Mandalay Road
Singapore 308205

P Ang, MBBS, MRCP (UK)
Registrar

Y K Tay, M Med (Int Med), MRCP (UK), MRCP (Ireland),
Senior Registrar

Correspondence to:
Dr Y K Tay

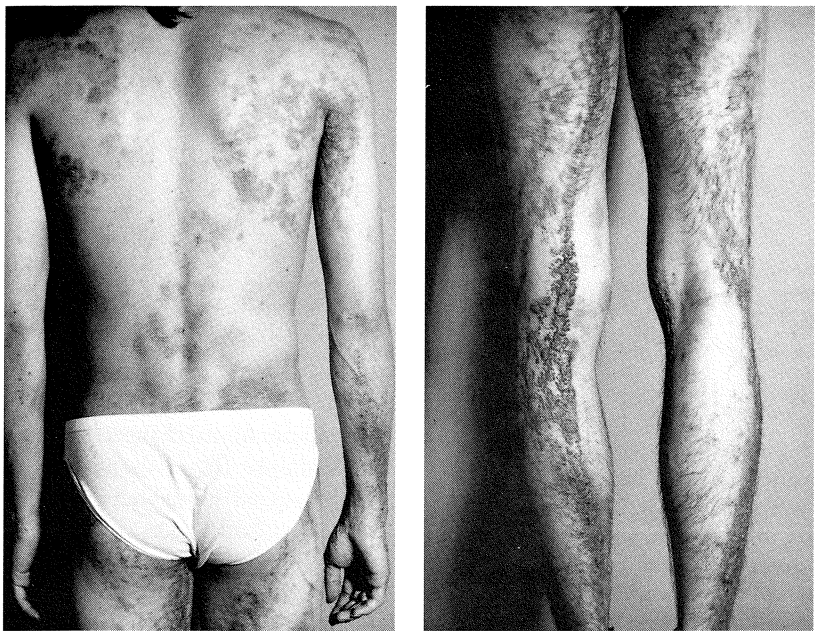
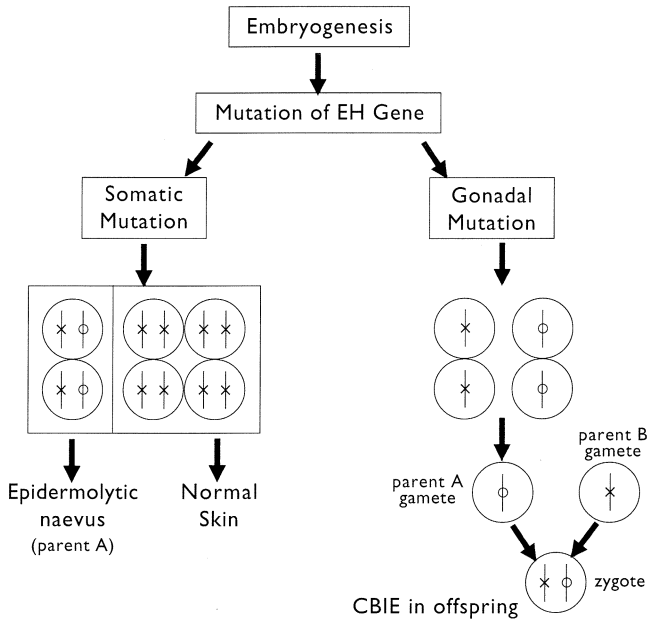


Fig 1& 2 – Patient with systematised linear verrucous epidermolytic naevus

generalised CBIE. This hypothesis has been confirmed recently at the molecular level by Paller et al[5] who studied the keratin genes in the blood, fibroblasts and keratinocytes of lesional and non lesional skin from 3 parents with epidermolytic naevi and 4 of their offspring with CBIE. They demonstrated point mutations in 50% of K10 alleles of keratinocytes in lesional skin in the parents with no mutation in normal skin, fibroblasts or blood. In the offsprings, mutations were found in 50% of K10 alleles from all cell types and they corresponded to the parental mutation. The last study has proven convincingly the mosaicism theory and provided evidence that genetic mosaicism can cause clinical mosaicism. This can be summarised into the following schema:



So, how do we apply this knowledge to our clinical practice? This can be done from two perspectives:

1. Epidermal naevi
   It is recommended that all epidermal naevi (especially systematised linear forms) be screened for epidermolytic hyperkeratosis by doing a skin biopsy. If such features are present, the patient should receive genetic counselling.
2. CBIE
   All parents of CBIE infants should be screened for the presence of any epidermal naevus and if present, be informed of the possibility of another child developing CBIE.

There are limitations in terms of genetic counselling and prenatal diagnosis. Firstly, there is no way of determining the percentage of gonadal cells involved in the mutation. As such, it is impossible to estimate the risk of a child developing CBIE. Secondly, prenatal diagnosis is time consuming and requires special expertise. Presently, there are several methods available. Foetoscopy and foetal skin biopsy can be done at 20 weeks of gestation and the cells can be examined for the ultrastructural characteristics of CBIE[4]. Recently, gene sequencing using molecular analysis has been used successfully at the 15th week by Rothnagel et al[6] to identify the presence of foetal gene mutation via chorionic villus sampling. The risk of foetal loss is far less than with foetoscopy.

In summary, parents with epidermolytic naevi can produce children with CBIE due to gonadal mosaicism. Ideally, all linear epidermal naevi (especially if extensive) should be biopsied. If epidermolytic hyperkeratosis is present, the parents should be given genetic counselling and offered prenatal diagnosis. In the future, DNA techniques will permit prenatal diagnosis at a much earlier gestational age.

REFERENCES

1. Ho VCY, McLean DI. Benign epithelial tumours. In: Fitzpatrick TB, Eisen AZ, Wolff K, Freedberg IM, Austen KF, 4th eds. Dermatology in General Medicine. New York: McGraw-Hill, 1993:855-72.
2. Lookingbill DP, Ladda RL, Cohen C. Generalised epidermolytic hyperkeratosis in the child of a parent with naevus comedonicus. Arch Dermatol 1984; 120:223-6.
3. Nazzaro V, Ermacora E, Santucci B, Caputo R. Epidermolytic hyperkeratosis: Generalised form in children from parents with systematised linear form. Br J Dermatol 1990, 122:417-22.
4. Traupe H, ed. The Ichthyoses. A guide to clinical diagnosis, genetic counselling and therapy. Berlin: Springer-Verlag, 1989:139-53.
5. Paller AS, Syder AJ, Chan YM, et al. Genetic and clinical mosaicism in a type of epidermal naevus. N Engl J Med 1994; 331:1408-15.
6. Rothnagel JA, Longley MA, Holder RA, Kuster W, Roop DR. Prenatal diagnosis of epidermolytic hyperkeratosis by direct gene sequencing. J Invest Dermatol 1994; 102:13-6.