CASE REPORT

Keratosis pilaris and ulerythema ophryogenes in a woman with monosomy of the short arm of chromosome 18 *

Ceratose pilar e ulerythema ophryogenes em mulher com monossomia do braço curto do cromosomo 18

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Abstract: Partial monosomy of the short arm of chromosome 18 (18p- syndrome) is characterized mainly by speech delay, mild to moderate mental retardation and short stature. We describe a patient with the 18p- syndrome and widespread severe keratosis pilaris and ulerythema ophryogenes. This is the fourth case in which such an association has been reported. This association is of considerable interest because it may uncover a candidate genomic region and help to identify the gene responsible for follicular keratinization.
Keywords: Chromosome deletion; Chromosomes, human, pair 18; Keratosis

Resumo: A monossomia parcial do braço curto do cromosomo 18 (síndrome do 18p) caracteriza-se, principalmente, por atraso na aquisição da fala, retardo mental leve a moderado e baixa estatura. Relatamos o caso de uma paciente com esta síndrome associada à ceratose pilar extensa e ulerythema ophryogenes. Este é o quarto relato de caso que descreve tal associação, que desperta considerável interesse porque pode revelar uma região candidata a sede de genes responsáveis pela queratinização folicular.
Palavras-chave: Ceratose; Cromossomos humanos par 18; Deleção cromossômica

INTRODUCTION

Monosomy 18p, or 18p- syndrome, is a disorder resulting from the deletion of part or all of the short arm of chromosome 18. The condition has an estimated incidence of 1 in 50,000 among live-born infants, placing it among the commonest chromosomal anomalies. Initially described by Grouchy in 1963[1], it was the first example of a partial chromosomal anomaly compatible with life. Clinical manifestations vary greatly among patients, and in most cases a diagnosis may not be apparent at birth. Among the more common findings, the most notable are varying degrees of mental retardation, speech delay and short stature. Less frequently, craniofacial dysmorphisms may be observed. In approximately two thirds of cases the deletion is a de novo one. Familial transmission of the 18p deletion from a parent to an offspring has already been described in six families. An extensive review of this syndrome was recently published by Turleau. [2]

The association between this syndrome and the genodermatoses keratosis pilaris and ulerythema ophryogenes was first reported in 1994 by Zouboulis et al[3] and was subsequently lent further weight by two other case studies. [4,5] The finding of this association suggested that the genes responsible for follicular keratinization could be located on the short arm of chromosome 18. We describe a case of keratosis pilaris / ulerythema ophryogenes in a patient with 18p- syndrome.

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CASE REPORT

A 19-year-old female patient was referred to the genetics outpatient clinic for dermatological examination. She had been diagnosed with 18p- syndrome at the age of eight years. She is the third daughter of healthy non-consanguineous parents. Gestation was normal and both the patient's sisters are healthy. She was born at term, when she weighed 3320 g (50th percentile) and measured 49 cm (25th percentile), and had normal motor development during infancy and childhood. At the end of the first year of life a significant speech delay was noted, and as a result an investigation was started, leading to the diagnosis of 18p- syndrome. Her medical history showed that she had had German measles at the age of two years, asthma (the symptoms of which stopped at around seven years of age) and hypothyroidism, which is currently being treated with levothyroxine.

The high-resolution karyotype was 46,XX, del(18)(p11.1p11.32), indicating that the whole short arm of chromosome 18 had been deleted. No other alterations were observed. The parents' karyotypes were normal.

At 19 years of age she measured 144.5 cm (below the 3rd percentile), had a head perimeter of 54.5 (25th to 50th percentile) and weighed 41.5 kg (below the 3rd percentile). Dysmorphology examination revealed down-slanting palpebral fissures, a left pre-auricular pit, a high-arched palate and a short neck. Cardiology assessment, including echocardiogram, and abdominal ultrasound were normal. Pelvic ultrasound revealed the presence of a uterine septum. Menarche and the appearance of secondary sex characteristics occurred at the appropriate age, and her menstrual cycles at the time of the examination were regular. She had mild mental retardation and was studying in a regular secondary school.

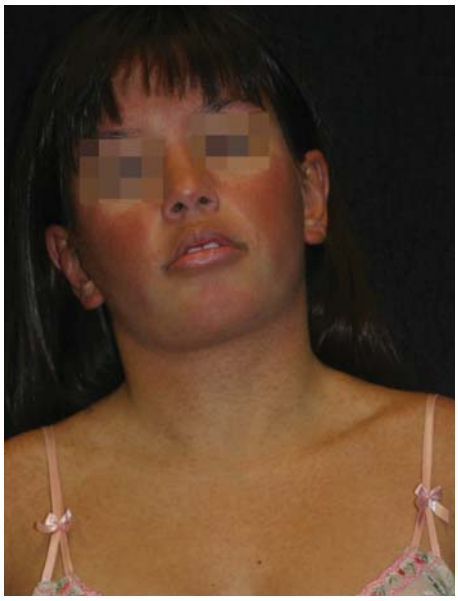

Figure 2: Short neck

Dermatologic examination revealed small hyperkeratotic follicular papules 1 to 2 mm in diameter distributed evenly on the back, anterior thorax, abdomen, neck and upper and lower limbs (Figure 3). On her face, she had erythema and small hyperkeratotic follicular papules distributed symmetrically on the malar and masseteric regions, as well as on her forehead and chin (Figure 4). Her skin was rough to the touch in all these areas. The scalp, palm of her hands and soles of her feet were not affected. Skin alterations had been reported since birth and had worsened significantly during adolescence. A skin punch biopsy was performed in the lumbar region

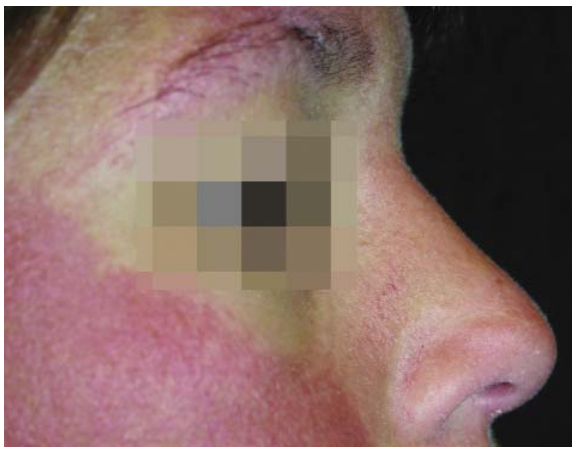

Figure 1: Down-slanting palpebral fissure

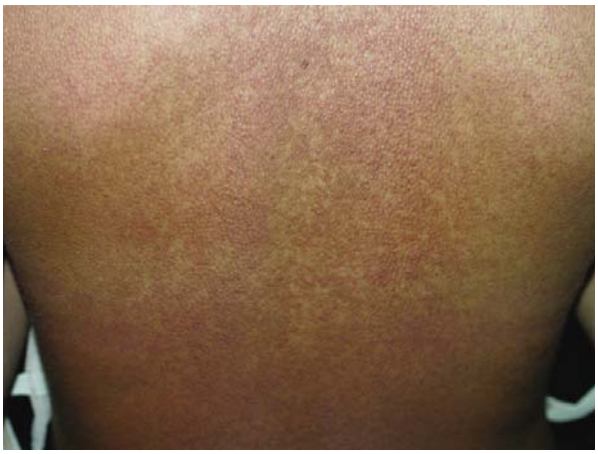

Figure 3: Very abundant keratotic follicular papules on the back

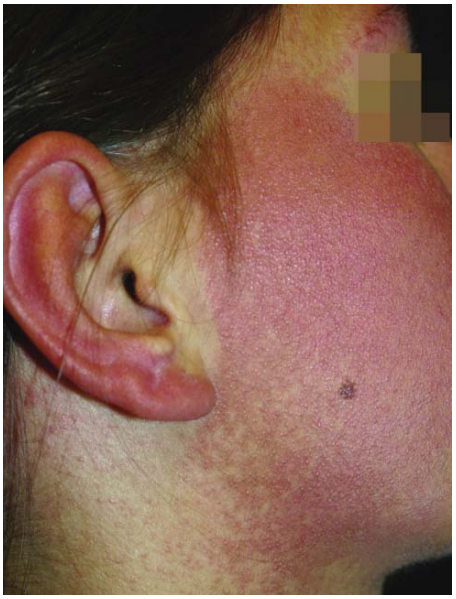

Figure 4: Ulerythema ophryogenes. Distal madarosis, erythema and keratotic papules can be observed

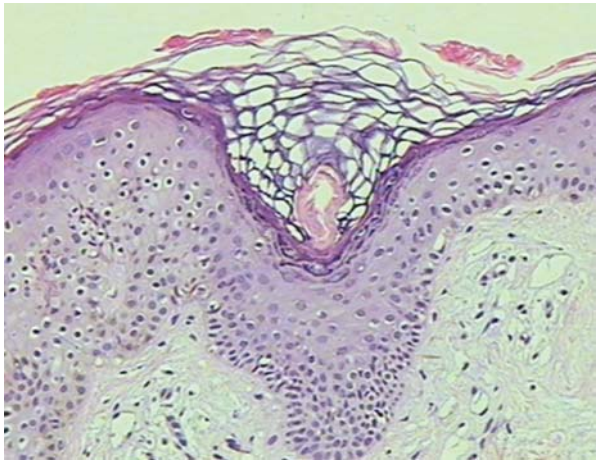

Figure 5: A compact keratin plug blocking the upper third of the follicular infundibulum. A discrete, nonspecific inflammatory infiltrate can be seen in the dermis

and revealed hyperkeratosis in the upper region of the infundibulum and a discrete inflammatory infiltrate (Figure 5).

The patient was treated with topical keratolytic agents and showed a modest improvement.

DISCUSSION

When limited to typical areas (the upper outer side of the arms and thighs), keratosis pilaris is an extremely common, benign condition. Although its etiology has not been clearly defined, the condition is frequently described in association with other conditions that cause xerodermia, such as ichthyosis vulgaris and atopic dermatitis. Its pathophysiology is based on genetically determined excessive follicular keratinization. In the case described here, keratosis pilaris affected nearly the whole body and was accompanied by ulerythema ophryogenes, a rare disorder affecting mainly children and young adults. The latter condition is characterized by inflammatory keratotic facial papules on an erythematous background. Its pathogenesis remains unknown, and the disease has been described in association with other conditions, such as Noonan syndrome.

The clinical and cytogenetic findings suggest that this case should be grouped with the three previous reports of an association between 18p- syndrome and keratosis pilaris / ulerythema ophryogenes, reinforcing the hypothesis that follicular keratinization may be under the control (to an extent yet to be determined) of gene(s) located on the short arm of chromosome 18. Since most patients with this chromosomal anomaly do not present with either keratosis pilaris or ulerythema ophryogenes, it is possible that the dermatological alterations in the patient described here and in the patients in the three reports referred to above may be the result of phenotypic expression of a recessive mutation that is only being expressed because of the loss of the wild allele in the deleted portion of the short arm of chromosome 18. ❑

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