Original Article

HLA patients with an association of familial lupus-psoriasis

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Abstract

Lupus and psoriasis are autoimmune diseases of multifactorial etiology, with involvement of genetic and non-genetic factors. The most widely studied genetic factor is Human Leukocyte Antigen (HLA) or Major Histocompatibility Complex in the chromosome 6 region.
We report HLA from three generations of patients in the same family with different forms of cutaneous lupus, two of which are associated with psoriasis, and compared the results with seven healthy members of the same family. No HLA found conferred greater susceptibility or protection related to these diseases. (Dermatol Argent 2009; 15(3):196-189).

Key words: *HLA, genetic association, lupus, psoriasis.*

Introduction

Lupus is an autoimmune disease appearing in 2.6 of 100,000 inhabitants, with recognized genetic predisposition.[1] The clinical spectrum is variable, from cutaneous forms such as discoid lupus erythematosus (DLE) to systemic forms such as systemic lupus erythematosus (SLE), rapidly progressive and with multiorganic involvement, associated with HLA-DR2 and -DR3.[2-3]
Psoriasis is a chronic inflammatory disease affecting 1 to 3 percent of the world's population.[1] It has a genetic basis, immune pathogeny and receives the influence of multiple factors determining from mild forms to isolated erythematosquamous plaques, and to a generalized erythrodermal variant with joint involvement in some cases.
Only one locus has been confirmed for susceptibility to psoriasis (PSORS1), located on the major histocompatibility complex (MHC) on chromosome 6.[4] Multiple HLA alleles have been associated with psoriasis: HLA-A1, -A2, -B13, -B17, -Cw6, -DR7, and -DQ.[5]
The purpose of this work is to analyze genotypes and phenotypes of patients with associated cutaneous lupus and psoriasis suggesting susceptibility of suffering these conditions versus healthy individuals within the same family, and to compare results with the current literature.

Clinical cases

Case 1

A 61-year-old male patient, who started 30 years ago with erythematous plaques with well-demarcated edges and follicular atrophy located on the external ear and face (**Figure 1**).

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Histopathology: Dermal lymphocyte infiltrate with perivascular and periadnexial dominance was found.
Diagnosis compatible with DLE.
Laboratory: Antinuclear factor (ANF) and anti-DNA antibody: negative.
Treatment: He was treated with hydroxychloroquine 6 mg/kg/day and photoprotection, which was irregularly complied with.
Evolution: For the last three years, he has had erythematosquamous plaques on scalp and elbows (**Figure 2**) accompanied by hand arthralgia.
A new histopathological examination results in thick lamellar parakeratosis and psoriasiform acanthosis enclosing Munro's microabscesses.
Diagnosis compatible with psoriasis.
Laboratory: Rheumatoid factor (RF): negative, ANF and anti-DNA: negative.
X-ray of hands: Proximal phalangeal osteolysis. Treated with metothrexate (MTX) 15 mg/week and folic acid, with good response.
Genetic typification:
HLA haplotype:
A* 01-B* 1517-DRB1*13 -DQB1* 0604
A* 23-B* 1503/ 1554 -DRB* 11-DQB1*0301,0309,0313

Case 2

A 24-year-old male patient. Physical examination showed infiltrated erythematous plaques with cribiform scar on both preauricular regions of a three years' evolution (**Figures 3** and **4**).
Histopathology: Lymphocyte infiltrate in all dermal thickness, as well as perivascular, periadnexial, interstitial and diffuse.
Diagnosis compatible with lupus tumidus.
Laboratory: ANF and anti-DNA antibody: negative.
Treatment: Hydroxychloroquine 6 mg/kg/d and photoprotection, with good response.
Genetic typification:
HLA haplotype:
A* 01-B* 1517-DRB1*13 -DQB1* 0604
A* 31-B* 3543-DRB* 04 -DQB1*0302

Case 3

A 14-year-old female patient, starting two years ago with sharply demarcated erythematous plaques and cribiform scar located on cheeks and nose (**Figure 5**). Erythematosquamous plaques appear on the interscapular area (**Figure 6**).
Histopathology (cheek): Hyperkeratosis, suprabasal area granulosis. Thickened and undulating connective basal membrane.

Figure 1. *Case 1. Erythematosquamous plaques on forehead and follicular atrophy located on cheeks and nose.*

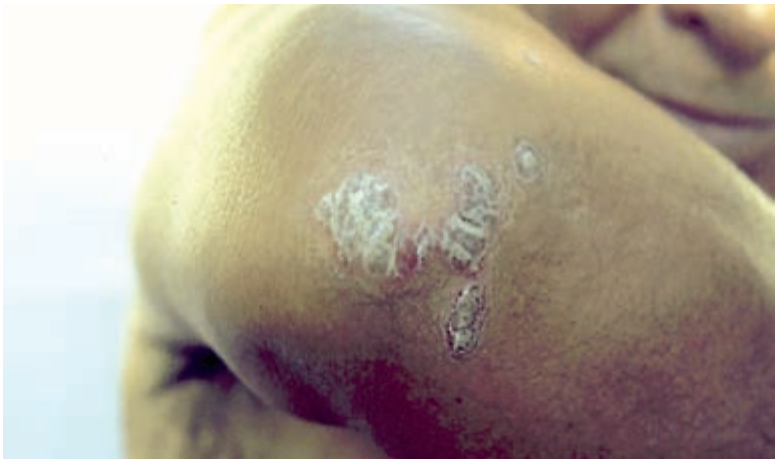

Figure 2. *Case 1. Erythematosquamous plaques on elbow.*

Diagnosis compatible with (DLE).
Histopathology (interscapular area): parakeratosis with spongiform pustule of Kogoj, acanthosis by epidermal extension of epidermal creases interdigitating with dermal papillae.
Diagnosis compatible with psoriasis.
Laboratory: ANF and anti-DNA negative.
Treatment: Hydroxychloroquine 6 mg/kg/d and sun protection.
Genetic typification:
HLA haplotype:
A* 32B* 18 -DRB1* 04 -DQB1* 0302
A* 31-B* 3543-DRB* 04 -DQB1*0302

Comment

Psoriasis and lupus are two very important genetically based diseases of multifactorial ethiology. Various genes may be involved, and environmental factors play an essential role in the development of such diseases. Familial association is found in some cases.
Scarce literature exists on lupus-psoriasis association, especially in cutaneous lupus. In the review we found that around the middle of the twentieth cen-

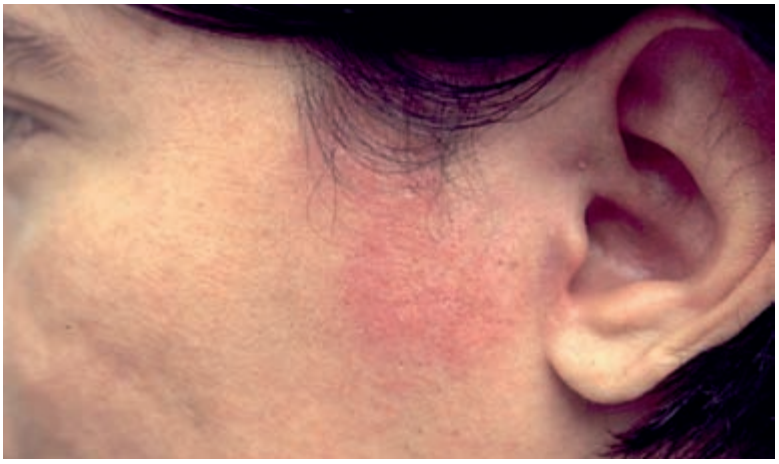

Figure 3. *Case 2. Infiltrative erythematous plaques with cribiform scar on left preauricular area.*

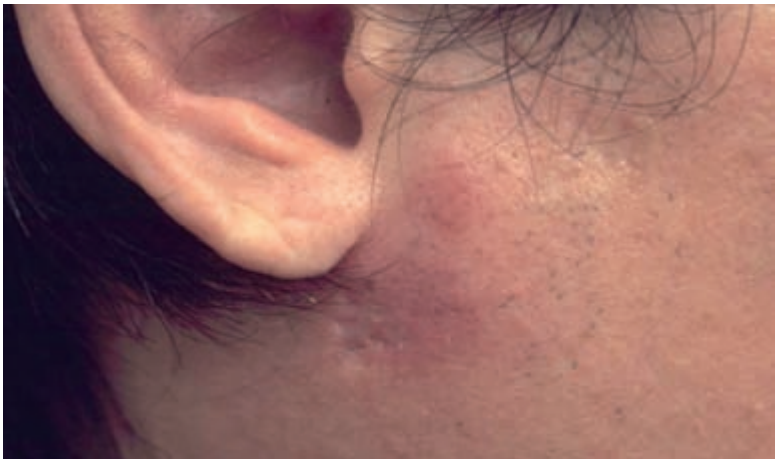

Figure 4. *Case 2. Infiltrative erythematous plaques with cribiform scar on right preauricular area.*

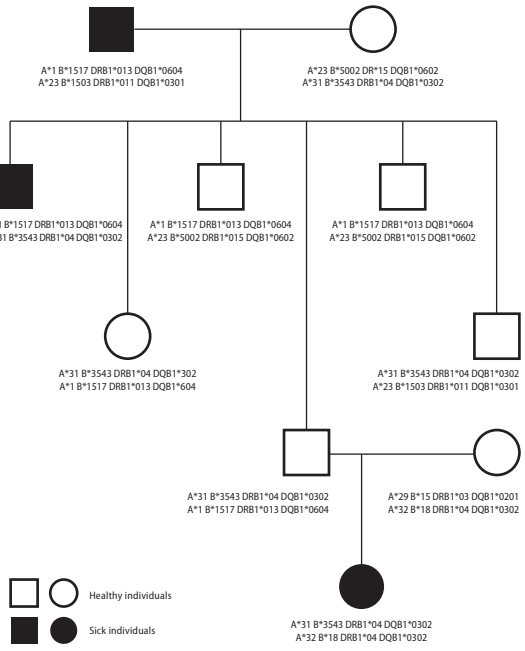

Chart 1. *Familial genetic typification scheme of three generations.*

tury, clinical observation studies were first published; then, with the development of new knowledge, associations with HLA in chromosom 6 were reported, and genes resistant to both entities have been found in recent years.

The first series on the occurrence of this association in four members of one family was published in 1962: 2 had psoriasis, 1 had DLE, and 1 had pityriasis rubra pilaris.[6]

In another study from 1964, 520 SLE cases were analysed: 0.6 percent were associated with psoriasis.[7]

In 1980, 27 patients with lupus and psoriasis were studied, where of 4 relatives had history of psoriasis and 2 of lupus.[1]

In 1984, Hays et al. added 4 patients with SLE and psoriasis, but who were not consanguineous; and finally in 2003, Astudillo et al. reported 3 cases of patients with SLE and psoriasis.[8-9]

In 1993, an increase in the relative risk of developing SLE was described in 91 patients with HLA-B8, -DR3, -DQ6 and -C4A.[10]

In 1996, it was noticed in 124 psoriasis patients that the A2,B13,Cw6,DR7,DQA1*0201 and A1,B17,Cw6,DR7,DQA1*0201 association carried higher risk of having the disease.[5]

Psoriasis was associated after 1999 to chromosome 1 and then to chromosomes 4, 5, 6, 9, 17, 19, and 20.[4,11-16]

The most studied region is the major histocompatibility complex on chromosome 6, with highest susceptibility to psoriasis.[4]

In chromosome 5, a cytokine suggests susceptibility not only to psoriasis, but also to Crohn's disease and rheumatoid arthritis.[13]

Locus 20p13 predisposes to psoriasis independently from chromosome 6, and also from other inflammatory diseases such as asthma and atopic dermatitis.[4]

After 2001, lupus was associated with chromosome 1 and in successive reports, with chromosomes 2, 3, 4, 10, 13, 16, 18, and 20.[17-21]

At first, there was a dominance of clinical communications attempting to associate phenotypical variants with filiation data.

Initial genetic studies heralded the discovery of the responsible genes, and thus the definite cure of such pathologies.

But this was not true, the inheritance pattern is still uncertain. However, great advances have been achieved in prognosis and treatment through small contributions like ours.

In reviewing the literature, we have not found a study on cutaneous lupus and psoriasis in three successive generations of the same family.

In reference to HLA performed on our patients, none showed association with susceptibility to or protection against the development of these diseases, in comparison to consanguineous healthy individuals.

Figure 5. *Case 3. Erythematous plaques with sharply defined edges and cribiform scar located on cheeks and nose.*

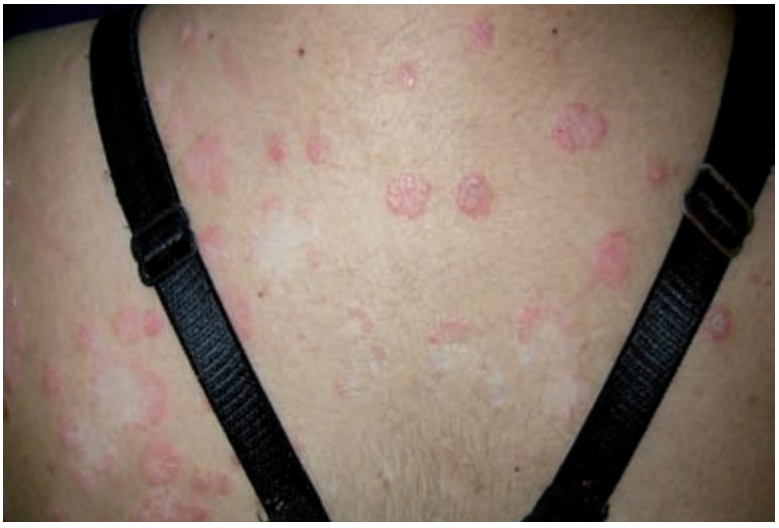

Figure 6. *Case 3. Erythematosquamous plaques on interscapular area, some with light center.*

This probably suggests that HLA may not be the main factor involved in the development of these diseases, and it is likely that others genes in this or other chromosomes are responsible. This could motivate the development of future research.

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