PITYRIASIS LICHENOIDES - CLINICAL AND IMMUNOGENETIC STUDIES

PITIRÍASE LIQUENÓIDE - ESTUDOS CLÍNICOS E IMUNOGENÉTICOS

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ABSTRACT: Type of study: Prevalence study**.**

Objectives: Despite pityriasis lichenoides is an uncommon dermatosis, we observed 12 cases in the last 3 years. By this means, we review clinical and histopathologic findings of all patients with pityriasis lichenoides seen at our Division. Furthermore, since pathogenic features of the disease are unknown, we performed HLA class I and II typings to search for possible immunogenetic markers for pityriasis lichenoides.

Methods: Twenty-one patients with biopsy-proven diagnosis of pityriasis lichenoides were evaluated. HLA class I and II antigens were typed using conventional serological procedures.

Results: Children and young adults were predominantly affected. Most of the cases were seen in fall and winter time. Typical disseminated lesions were observed more frequently. Both acute and chronic patterns were observed at histology. Compared to controls, the HLA-B17 antigen was overrepresented in patients ($P < 0.005$).

Conclusions: Although pityriasis lichenoides remains a cutaneous disease of undetermined origin, our findings show that the disease is associated with the HLA-B17 antigen.

UNITERMS: Pityriasis Lichenoides. HLA Antigens. Histology. Immunogenetics.

1. INTRODUCTION

Pityriasis lichenoides (PL) is an uncommon self-limited dermatosis which occurs at any age, particularly in children and young adults[1,2,3]. Two variants of the disease are described: a mild chronic form referred to as pityriasis lichenoides chronica (PLC), and an acute form also known as pityriasis lichenoides et varioliformis acuta (PLEVA)[2]. Despite the treatment with antimicrobials are somewhat beneficial, etiopathogenic mechanisms have not been elucidated. Immune complexes, cell-mediated immunity and endothelial cells bearing HLA class II antigens have been implicated in the pathogenesis of the disease[4/8]. Immunogenetic studies on the susceptibility to this dermatosis have never been accomplished. In this study, besides clinical and laboratory evaluation of, we typed HLA class I and II antigens in a series of patients presenting with pityriasis lichenoides.

2. MATERIAL AND METHODS

2.1. Patients

A total of 21 patients seen at the University Hospital of the Faculty of Medicine of Ribeirão Preto, São Paulo, Brazil, from 1978 to 1993, were retrospectively studied. The men to women ratio was 1.6, with ages varying from 10 to 60 years (median 20). Diagnosis of pityriasis lichenoides was performed on the basis of clinical and histopathological features.

2.2. Controls

A total of 100 blood donors from same geographical area and presumably of similar ethnic background were also typed for HLA antigens.

2.3. HLA antigens

Mononuclear peripheral cells were isolated using Ficoll-Hypaque gradient at a density of 1.077 g/l. B lymphocytes were obtained by adherence to nylon wool. HLA typing was performed by a microlymphocytotoxicity assay[9], using commercially available antisera (Pel Freez, Gen Track-USA; Biotest-Germany). A total of 72 HLA class I (A, B) and class II (DR.DQ) specificities were used. Complement was obtained from a pool of normal rabbit sera.

2.4. Statistical analysis

Comparisons of HLA frequency between patients and controls was performed using the bicaudal Fisher exact test, correcting the ***P*** value according to the number of HLA specificities. Differences were considered significant at $P < 0.05$. The relative risk (RR) which indicates how many times more often the disease occurs in individuals with the HLA antigen compared to those without it, and the etiologic fraction (EF) which defines the attributable risk at the population level were also calculated [10].

3. RESULTS

Most of the cases was observed among children and young adults (**Figure 1**). More than 79% of the cases occurred in Brazilian fall and winter seasons (April to June and July to September, respectively). With regard to distribution of cutaneous lesions, 71% of patients presented typical lesions disseminated along the whole body, whereas 19% presented with lesions restricted to the trunk, neck, and proximal aspects of extremities. Only 10% of patients presented peripheral lesions confined to upper and lower limbs. Fever preceded cutaneous lesions in 14% of patients, and pruritus was seen along with lesions in 76% of

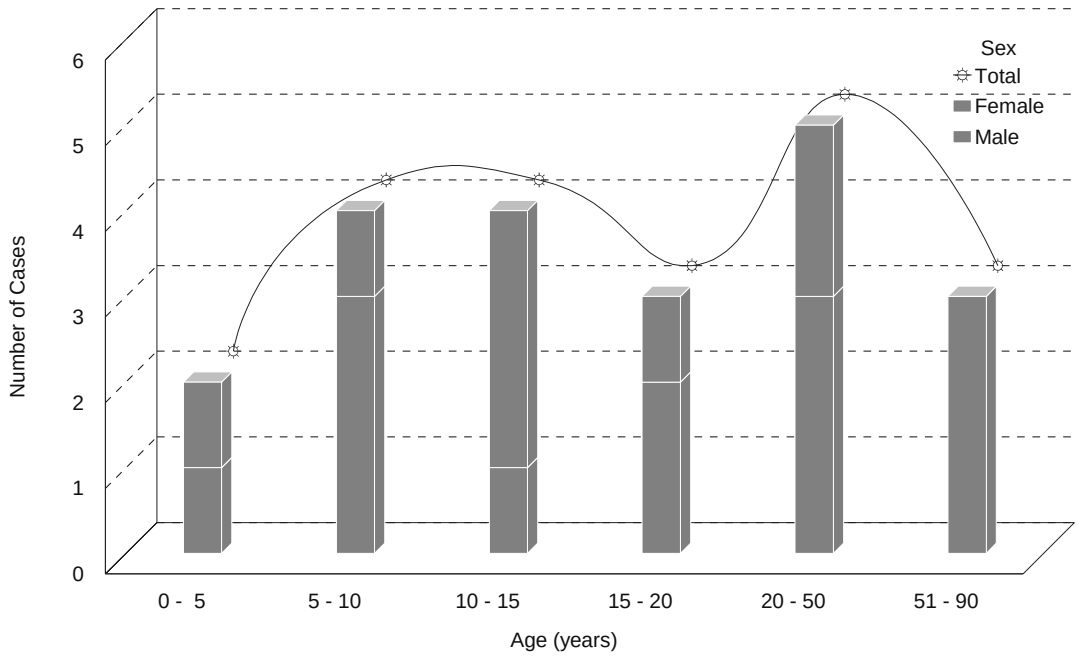

Figure 1: *Bimodal distribution of pityriasis lichenoides cases according to age (years) from 1978 to 1993. Sex distribution is also shown.*

patients. Hypopigmented macules were observed in 48% even on the first cutaneous examination. Both erythematous papules with central scales (affecting also the scalp) and mucous membranes involvement were seen in 14% of cases, respectively. Adenomegaly was observed in 38% of patients. Nineteen percent of patients had both lesions of PLEVA and PLC, however, histological features of typical PLEVA or PLC were observed in 33% and 44% of the cases, respectively.

HLA typing was performed in only 14 patients. The frequency of HLA-B17 antigen in patients was 36% whereas in control individuals this antigen was observed only in 1% **(Figure 2)**.

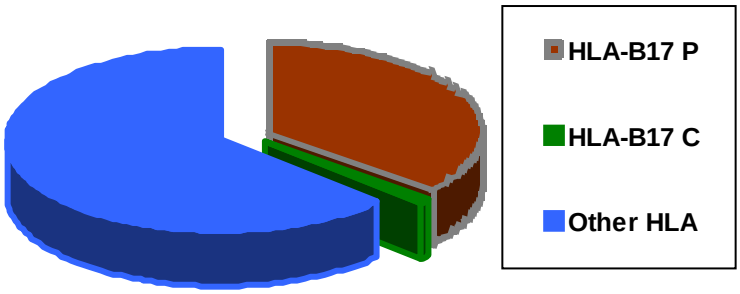

Figure 2: *Relative frequency of HLA-B17 in patients and controls in comparison with other HLA-B antigens.*

The comparison of the frequency of HLA-B17 antigen in patients was significantly increased when compared to controls **(*P* = 0,005)**. The HLA-B17 antigen conferred an RR of 55 and an EF of 35. The frequency of HLA class I and II antigens is shown in **(Table I)**, where the comparisons of HLA class I or II antigens between patients and controls disclosed no significant differences.

4. DISCUSSION

The clinical and laboratory features presented by the patients of this series were similar to those reported by other authors[1,2,3], emphasizing the predominance of the disease in children and young adults, and the occurrence of the disease predominantly in fall and winter time.

Table I - Frequency (%) of HLA class I (A and B) and class II (DR and DQ) antigens in patients presenting with pityriasis lichenoides (n = 14) and controls (n = 100). Frequencies observed in controls are shown in parenthesis. Although 72 specificities were tested, only those seen in patients are shown

	HLA-A %			HLA-B %			HLA-DR %			HLA-DQ %	
	P	C		P	C		P	C		P	C
A1	7	(21)	B7	21	(14)	DR1	36	(26)	DQ1	78	(64)
A2	7	(46)	B15	7	(2)	DR2	28	(31)	DQ2	21	(40)
A3	7	(12)	B17	36	(1)*	DR3	50	(28)	DQ3	57	(44)
A9	7	(27)	B44	36	(16)	DR4	21	(23)	DQ7	36	(37)
A10	14	(27)	B49	7	(6)	DR6	7	(6)			
A11	21	(16)	B51	21	(14)	DR7	28	(21)			
A28	21	(10)	B60	7	(6)	DR9	14	(2)			
A30	40	(4)				DR11	14	(12)			
A33	42	(2)									

* HLA-B17 corrected P value < 0.005, relative risk = 55, etiologic fraction = 35.
P = patients C= controls

Compared to controls, the class I HLA-B17 antigen was overrepresented in patients presenting with pityriasis lichenoides, conferring high RR and E.F. The most striking association of a HLA class I antigen with a disease is the observation that HLA-B27^{+} Caucasian individuals have 91 times the risk of developing ankylosing spondylitis than HLA-B27^{-} individuals[11]. Besides ankylosing spondylitis, HLA-B27 antigen has also been associated with Reiter's syndrome and acute anterior uveitis. Particularly, Reiter's syndrome encompasses a reactive arthritis seen after episodes of infection caused by several enteric and/or urogenital pathogens such as *Shigella*, *Salmonella*, *Yersinia*, *Campylobacter*, *Chlamydia* and *Ureaplasma*[12]. One of the mechanisms of HLA class I molecule association with disease is the mimicry between certain epitopes of the causative agents with those of HLA molecules[13]. Corroborating this hypothesis is the observation of a stretch of 5 amminoacid residues shared by *Shigella* strain plasmids and the HLA-B27 molecule[12,13]. Although an infectious agent has not been implicated in the pathogenesis of pityriasis lichenoides, the involution of cutaneous lesions following an antibiotic treatment suggest the participation of an infectious pathogen. Paralelling the hypotheses which have been proposed to explain the pathogenesis of Reiter's syndrome, when susceptible individuals carrying the HLA-B17 antigen upon contact with an yet undetermined environmental agent may trigger the development of pityriasis lichenoides.

Increased diffuse expression of HLA-DR molecules have been reported on the cell surface of epidermal keratinocytes of patients presenting with pityriasis lichenoides[4/8], suggesting the participation of cells bearing HLA class II molecules in the pathogenesis of the disease. However, the comparisons of the frequency of HLA-DR and HLA-DQ antigens between patients and controls revealed no significant differences. Although we were not able to define a specific association between HLA class II antigen with pityriasis lichenoides, an association with HLA class II specificities cannot be ruled out. In this study, only serologically defined specificities were tested, perhaps the utilization of more discriminative methods such as the molecular ones may disclose such an association.

In conclusion, few reports have focused on the study of the immunopathogenic events which are going on pityriasis lichenoides, and much has to be learned about them. Notwithstanding, the findings reported here showed that an HLA class I antigen is overrepresented in patients. presenting with pityriasis lichenoides, and indicate that the HLA-B17 antigen as a susceptible marker for the development of the disease.

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RESUMO: Modelo de estudo: Estudo de prevalência.

Objetivos: Embora a pitiríase liquenóide seja uma dermatose incomum, 12 casos foram por nós observados nos últimos três anos. Assim, neste estudo, avaliamos os perfis clínicos e histopatológicos dos pacientes com pitiríase liquenóide, atendidos na Divisão de Dermatologia. Além disso, tipificamos os antígenos HLA de classes I e II nesses pacientes.

Metodologia: Foram estudados 21 pacientes com diagnóstico clínico e histopatológico de pitiríase liquenóide. As tipificações dos antígenos de histocompatibilidade de classes I e II foram realizadas, utilizando-se métodos sorológicos.

Resultados: A maioria dos casos ocorreu entre crianças e ou adultos jovens, no outono e inverno. As lesões típicas de forma disseminada foram as mais freqüentes. Os achados histopatológicos mostraram lesões dos tipos agudo e crônico. O antígeno HLA-B17 estava significantemente aumentado nos pacientes em relação aos controles (***P*** < 0,005).

Conclusões: Embora a etiologia da pitiríase liquenóide não seja conhecida, os achados aqui relatados mostram que o marcador HLA-B17 é prevalente entre os doentes.

UNITERMOS: Pitiríase Liquenóide . Antígenos HLA. Histologia. Imunogenética.

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