Review Article

Familial Lichen Palnus and Genetic Influence: A Brief Commentary

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How to cite this article: Nisheeth Saawarn, Swati Saawarn, MC Shashikant, Pinakapani R, NidhiDhakar, Raju Ragavendra T, Pearl Helena Chand. Familial lichen palnus and genetic influence: a brief commentary. International Journal of Contemporary Medicine Surgery and Radiology. 2016;1(1):16-18.

A B S T R A C T

Lichen planus (LP), considered primarily an immune mediated disorder has unknown aetiology, though there are several hypothesis proposed like genetic, infectious, oxidative stress, psychogenic, autoimmune factors etc. There have been multiple reports of LP in two or more of the family members related by blood, known as familial LP, along with evidences of certain human leukocyte antigens (HLA) in LP patients who were either related or non-related. Based on these reports a genetic aetiology of LP has been proposed. Inspite of these reports, the data available does not provide very strong evidence. This review runs a brief commentary on genetical aspects of lichen planus.

Key Words: Lichen Planus; Oral Lichen Planus; Human Leukocyte Antigen; Genetics; Familial; Hereditary.

INTRODUCTION

Lichen planus, first described by Erasmus Wilson in 1869, is a common, chronic inflammatory disease of unknown cause, that affects the skin and the mucosa of squamous cell origin.[1] It affects about 0.02 to 4% of the world population with slight female predominance.[2,3] Approximately 25% of all the patients present with only oral lesions, while about 50% of the patients with skin lesions present with oral lesions.[4]

The skin lesions are flat violaceous papules with a fine scaling on the surface. Unlike oral lesions, which are more chronic and have a typical clinical course of persistence with periods of exacerbation and quiescence, the skin lesions are usually self limiting and last for only a year or less.[5,6]

The pathogenesis has been extensively studied and the disease appears to be a result of a cell mediated immune reaction in which Langerhans cells, keratinocytes and activated T lymphocytes are involved.[7] Theetiology is not known, but there are several hypothesis involving genetic, infectious, oxidative stress, psychogenic and autoimmune factors.[7-9]

HISTORIC PERVIEW

There have been multiple reports of LP in two or more of the family members related by blood, known as familial LP, along with evidences of certain human leukocyte antigens (HLA) in LP patients who were either related or non-related.[10] Based on these reports a genetic aetiology of LP has been proposed.[10] Approximately 100 patients with familial LP has been reported in the literature.[10] As long ago as 1940, Saffron reported 60 familial cases of LP although the largest number of cases in a single family being four, a mother and three sons. LP was then recorded in two sisters; in a mother, son and daughter; three generations of another family; and in several other families. The largest family group thus far recorded is a mother and five of her children. OLP has also been recorded in twins and in husband and wife. However, all these reports are not very detailed and some are very sketchy.[11] Li J et al has reported two patients of LP with positive family history in Hunan in a survey of 124 patients.[12] Kofoed ML and Wantzin GL in a follow-up study of 140 patients found 15 patients with a clinically and/or histologically verified family history of the lichen

planus.[13] Bermejo-Fenoll and López-Jornet P in a case series of 249 cases reported 13 cases from six different families that could be considered to be family related.[14] Huang C et al in a retrospective chart review, analyzed nine consecutive familial pedigrees and found that 36 of 85 individuals (42.4%)in the nine families were affected with bullous lichen planus.[15] Singal A reported familial mucosal lichen planus in three successive generations.[16]

GENETIC INFLUENCES

The clinical presentation offamilial LP is not typical to that of idiopathic non-familial LP and therefore it is suggested that familial LP may in itself be a distinct clinical entity. The disease often present at an earlier age with generalized or disseminatedcutaneous lesions and follows a chronic and progressive course that persist for longer duration and has a increased tendency to recur. Only a minority of cases involve the oral mucosa. Females are reported to be affected mere than the males. The inheritance pattern is said to be autosomal dominant with variable penetrance.[10,13-15,17] Z Wang et al in a genetic linkage analysis of oral lichen planus in a Chinese familyperformed a whole-genome genotyping scan and found one maximal nonparametric LOD (logarithm of the odds) score of 2.32 (P = 0.0156) for single nucleotide polymorphism (SNP) marker rs2372736, defined at the chromosome 3p14-3q13 region encompassing 19 SNPs.[18] Infection, stress or any other environmental cause seems unlikely for familial LP as the disease occurs even in family members not living together in the same environment and presents at intervals ranging from 6 weeks to 30 years. It has been even reported in family members staying miles away in totally different conditions. However, as the idiopathic LP in itself is not very uncommon and there are multiple reported triggering factors, these cases may simply be coincidental and/orprobably triggered or caused by some other common unidentified factor.[10]

Human leukocyte antigens (HLA) antigens are cell surface receptors that are fundamental to cell to cell interaction in all immunologic responses. In many instances close associations have been found in disease susceptibility and the presence of one or more specific HLA antigens.[19] Furthermore, though quite sparse data are available from immunogenetic studies, it may be expected that there exists some degree of correlation between the HLA antigens of close family members.[10]

HLA-A3 was found in 54% of a group of 57 non-familial patients with cutaneous LP, compared with a control frequency of 29.7%, but a strong association was not confirmed in further studies.[11] Watanabe et al has reported a significantly raised frequency of HLA-DRw9 in Japanese oral LP patients along with increased frequency of HLA-DR3 in erosive cases.[10] Katzenelson V et al in three cases of LP from a family reported HLA DR expression in all 3 patients, however there was no increased incidence of HLA B7, HLA A3 or HLA A28.[16] The HLA-DR9 frequency was found significantly increased in a study group of OLP patients from China, however the study groups in these studies were quite small.[10]

In a British study involving 40 OLP patients' significant changes were found in both class I and class II HLA antigens.However, the frequencies of those HLA antigens previously associated with LP were not significantly changed when compared to a control group of 2,041 normal individuals, and hence did not demonstrate any consistent class I and II HLA association with LP.[19] In 5 families with familial LP, an association with HLA-B7 was reported, but this study involved only 10 cases, and was further not confirmed in other studies.[11]

CONCLUSION

Thus, the data available regarding familial LP in literature suggests that any genetic basis for LP is not of major importance, even though there are reports and evidences of familial cases. It is quite possible that etiology of LP is multifactorial with both genetic and environmental factors having interplay in its initiation, progression and probably resolution. Further elaborate researches with larger samples and more advanced markers and techniques are required to look into the genetic aspects of LP inheritance.

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Source of Support: Nil; **Conflict of Interest:** None

Submitted: 04-10-2016; **Published online**: 17-11-2016