Study of HLA-Cw6 in psoriatic patients

Thesis

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Abstract

Introduction:

Psoriasis is a multifactorial disease, some studies showed that the inheritance of psoriasis is autosomal dominant with reduced penetrance, eight loci giving statistical evidence of linkage to psoriasis have been identified, PSORS1 locus resides within the major histocompatibility complex (MHC) on the short arm of chromosome 6, as predicted by HLA association studies.

The putative gene at PSORS1 is considered to be the major genetic determinant for psoriasis, perhaps accounting for 35-50% of the heritability of the disease. HLA-C genes are considered as potential psoriasis susceptibility genes.

Psoriasis has bimodal distribution of age of onset; an early peak around 20 years and the later is around 60 years .The bimodal peak in disease onset could be taken as evidence for the existence of two pathogenetically distinct froms of the disease, similar to the model of diabetes mellitus. Thus, type 1 is hereditary, strongly HLA associated (particularly HLA- Cw6),with an early onset and more likely to be severe. Type 2 is sporadic, HLA unrelated, of late onset and usually mild.

Aim of the work:

Is to assess the association of HLA-Cw6 with psoriasis among Egyptian patients.

Material and Methods:

This study included 30 patients with psoriasis vulgaris and 10 healthy volunteers as controls.

The patients included 20 males and 10 females with age ranging from 20-60 years.They had psoriasis vulgaris with various degrees of severity.

All patients were subjected to :

1- Full history taking including personal history, family history, .History of present illness and History of other skin or systemic diseases.
2- Clinical examination including General examination and dermatological examination.
3- PASI score calculation.
4- Skin biopsy.
5- Molecular study including DNA extract,PCR amplification for HLACw6 alleles using Dynal SSP (sequence specific primer), detection of the amplification by agrose gel electrophoresis and lastly detection of Cw6 alleles .

Results:

The study included 30 psoriasis vulgaris patients, 20 males (66.7 %) & 10 females (33.3 %)with a ratio of 2:1 . Their ages ranged from 20 to 60 years Patients with positive family history had an earlier age of onset.

Twenty six patients out of 30 for HLA-Cw6 Gene, 4 patients were negative.

HLA-Cw6 gene was positive in 4 persons.

significant difference was observed as (P= 0.05), Patients who are HLA-Cw6 positive had more severe disease.

Patients having the HLA-Cw6 gene tend to get the psoriasis at an earlier age than those who were negative for the gene .

Conclusion:

HLA-Cw6 is strongly expressed in psoriatic patients .It has a strong influence on age of onset , extent of involvement and severity of the disease. However, its presence in non psoriatic patients suggest that psoriasis is a multifactorial disease. Patients with positive HLA-Cw6 and those with positive family

history, tend to get psoriasis earlier in age . This may highlight the importance of the genetic factor in etiopathogenesis of psoriasis.

Key words: Psoriasis – HLACw6.

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Abbreviations table:

ACE	***Angiotensin converting enzyme***
AD	***Autosomal dominant***
AR	***Autosomal recessive***
BSA	***Body surface area***
BP	***Base pair***
CLA	***Cutaneous lymphocyte antigen***
DC	***Dendritic cell***
DNA	***Deoxyribonucleic acid***
DIP	***Distal interphalangeal***
DZ	***Dizygotic***
EGF-R	***Epidermal growth factor receptor***
FDA	***Food &drug administration***
GM-CSF	***Granulocyte macrophage colony stimulating factor***
HLA	***Human leucocytes antigen***
HB	***Hemoglobin***
HIV	***Human immune deficiency virus***
ICAM	***Intercellular adhesion molecule***
IFN	***Interferon***
IL	***Interleukin***
LMP	***Large multifunctional protease***
LS-PGA	***Lattice system physician global assessment***
LFA	***Lymphocyte functional associated antigen***
LD	***Linkage disequilibrium***
mRNA	***Messenger ribo nucleic acid***
MZ	***Monozygotic***
MHC	***Major histocompatability complex***
NK	***Natural killer***
PCR	***Polymerase chain reaction***
PASI	***psoriasis area severity index***
PGA	***Psoriasis global assessment***

QOL	***Quality of life***
RNA	***Ribo nucleic acid***
RANTES	***Regulated upon activation normal T-cell expressed&secreted***
RF	***Rheumatoid factor***
SSP	***Sequence specific primer***
SPI	***Salford psoriasis index***
t-RNA	***Transfer ribo nucleic acid***
Th	***T helper***
Tc	***T cytotoxic***
TNF	***Tumor necrosis factor***
TGF	***Transforming growth factor***
VCAM	***Vascular cell adhesion molecule***
VLA	***Very late antigen***

Introduction

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Aim of work

Introduction and aim of the work:

Psoriasis is a common chronic recurrent inflammatory disease of the skin characterized by round circumscribed erythematous dry scaling plaques of various sizes, covered by grayish white or silvery white imbricated and lamellar scales. The lesions have a predilection for the scalp, nails, extensors surface of the limbs, elbows, knees, umbilical, and sacral region.The eruption usually develops slowly but may be exanthematous, with the sudden onset of numerous lesions , such as itching or burning , that may cause extreme discomfort ***(Odom et al,2000).***

Prevalence of psoriasis is 2% in white population , 8% in relatives with equal frequency in both sexes***(Odom et al,2000).***

Psoriasis is a multifactorial disease, some studies showed that the inheritance of psoriasis is autosomal dominant with reduced penetrance, eight loci giving statistical evidence of linkage to psoriasis have been identified , PSORS1 locus resides within the major histocompatibility complex (MHC) on the short arm of chromosome 6 , as predicted by HLA association studies***(Veal et al,2002).***

The putative gene at PSORS1 is considered to be the major genetic determinant for psoriasis , perhaps accounting for 35-50% of the heritability of the disease***(Asumalahti et al,2002)***

Psoriasis has bimodal distribution of age of onset ; an early peak around 20 years and the later is around 60 years .The bimodal peak in disease onset could be taken as evidence for the existence of two pathogenetically distinct forms of the disease ,similar to the model of diabetes mellitus . Thus, type 1 is hereditary, strongly HLA associated particularly HLA- Cw6, early onset and more likely to be severe. Type 2 is sporadic, HLA unrelated, of late onset and usually mild ***(Henseler&Christopher, 1985).***

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Chapter 1