Ain Shams University
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Detection of hepatitis C virus RNA in keratinocytes from patients with cutaneous Lichen planus and chronic hepatitis C virus by PCR

Thesis

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كلية الطب

تقييم الحمض النووي الريبوسي للفيروس سي فى آفة الحزاز المسطح الجلدي في المرضي الذين يعانون من التهاب الكبد الوبائي سي

رسالة
توطئة للحصول علي درجة الماجستيرفي الأمراض الجلدية والتناسلية والذكورة

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LIST OF ABBREVIATIONS

ALK phos	Alkaline phosphatase
ALT	Alanine amino transferase
ANA	Antinuclear antibodies
AST	Aspartate amino transferase
BCL	Bank confirmation letter
BM	Basal membrane
BMT	Bone marrow transfer
CCL20	Chemokine ligand 20
CCL5	Chemokine ligand 5
CCR5	Chemokine receptor type 5
CCR6	Chemokine receptor type 6
CD	Cluster of differentiation
CD4	Antigenic marker of helper T cell
CD8	Antigenic marker of suppressor / cytotoxic T cell
CDC	Centers for disease control
cDNA	Complementary DNA
CXCL10	Chemokine ligand 10
CXCL9	Chemokine ligand 9
CXCR1	Chemokine receptor 1
CXCR3	Chemokine receptor 3
DM	Diabetes mellitus
DNA	Deoxyribo nucleic acid
dNTPs	Deoxy ribo nucleoside triphosphates
DS	Double stranded
E	Envelope glycoprotein
ECP	Exrtacorporeal photoheresis
ELISA	Enzyme linked immunosorbent assay

GVHD	Graft versus host disease
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
HHV-6	Human herpes virus 6
HHV-7	Human herpes virus 7
HIV	Human immune deficiency virus
HLA	Human leucocyte antigen
HSV	Herpes simplex virus
IDU	Intravenous drug user
INF	Interferon
INF-gamma	Interferon gamma
IP-10	Inducible protein -10
ISSR	Intersequence specific PCR
LFA-1	Lmphocyte function associated antigen 1
LP	Lichen planus
LPSA	Lichen planus specific antigen
m RNA	Messenger ribosomal nucleic acid
MCP-1	Macrophage chemo-attractant protein -1
MHC	Major histocompatibility complex
MIG	Monokine induced by interferon gamma
MIP-1 alpha	Macrophage inflammatory protein -1 alpha
MMF	Mycophenolate mofetil
NK	Natural killer
NS	Non structural protein
OLP	Oral lichen planus
P53	Protein 53
PAMPS	Pathogen associated molecular patterns
PCA	Polymerase cycling assembly
PCR	Polymerase chain reaction
PRR	Pattern recognition receptors

PUVA	Psoralen ultraviolet A therapy
q.d.s	4 times a day
RANTES	Regulated on Activation, Normal T cell Expressed and Secreted
RCT	Randomized clinical trials
RIBA	Recombinant immunoblot assay
RNA	Ribosomal nucleic acid
RPM	Round per minute
RT- PCR	Reverse transcriptase- polymerase chain reaction
SS	Single stranded
T reg	Regulatory T cell
TAIL PCR	Thermal a symmetric interlaced PCR
Tc	T- cytotoxic
Th	T- helper
TLR	Toll like receptors
TNF	Tumer necrosis factor
TNF- alpha	Tumer necrosis factor alpha
USA	United States of America
VZV	Varicella zoster virus

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INTRODUCTION

Hepatitis C virus (HCV) is a small-enveloped virus belonging to the Flaviviridae family of animal viruses. Its genome consists of a single-stranded RNA of positive polarity **(Kato et al., 1990)**.

Chronic HCV infection causes a wide range of types of liver damage, ranging from mild chronic hepatitis to liver cirrhosis and hepato-cellular carcinoma **(Di Bisceglie, 1997)**; however, besides liver disease, chronic HCV infection is associated with several extrahepatic manifestations, with skin disorders frequently observed in these patients as cryoglobulinemic purpura, psoriasis, urticaria, porphyria cutanea tarda and lichen planus (LP) **(Doutre, 1999).**

In relation to these skin diseases, several epidemiologic studies have shown that lichen planus lesions are more prevalent in patients with chronic hepatitis C than in the general population **(Carrozzo et al., 1996.)**

LP is an inflammatory mucocutaneous condition with characteristic violaceous polygonal flat-topped papules and plaques **(Breathnach and Black, 2004).** Pruritus is often severe. Skin, nail and hair lesions may be disfiguring and involvement of the oral mucosa or genital mucosa in severe cases may be

debilitating. LP most commonly affects middle-aged adults of both sexes, with a slight predominance in women **(Daoud and Pittelkow, 1999).**

The widespread and chronic viral disease, hepatitis C (HCV), has been implicated in triggering LP. **(Gimenez-Garcia and Perez-Castrillon, 2003).**

The virus may play a potential pathogenic role by replicating in cutaneous tissue and triggering lichen planus in genetically susceptible HCV-infected patients. **(Lazaro, 2002).**

In the few studies evaluating HCV in LP lesion, confirmed a significant association with HCV **(Gimenez-Garcia and Perez-Castrillon, 2003)**. Other studies did not find the virus in LP lesion **(Harden et al., 2003)**.

AIM OF WORK

The aim of this work is to assess the presence of HCV RNA in lesions of cutaneous lichen planus

REVIEW OF LITERATURE

Lichen Planus

Lichen Planus (LP) is a chronic inflammatory mucoutaneous disease that was first described clinically by Wilson (1869) **(Mignogna et al., 2000).**

Lichen rubber pemphigoides was the first variant of LP reported by Kaposi (1892). Pringle (1895) described the association between LP and follicular Keratotic lesions, using the term "Lichen-plano-pilaris". In 1941, Katzenellenbogen described lichen planus actinicus **(Hallag, 1993).**

Natural History

Although few cases evolve rapidly and clear within few weeks, the onset in most cases is insidious and it is some weeks or months before the patient seeks advice. The skin lesions subside within nine months in about 50% of cases. Chronicity is usually attributable to the development of local hypertrophic lesions or to mucous membrane involvement **(Black, 1992).** The duration of the disease varies from 1 month to 7 years, with history of recurrence of the disease in 10.3% of patients **(Bhattacharya et al., 2000).**

Incidence and Prevalence

The prevalence of lichen planus is unknown, but it is estimated to occur in less than 1 percent of the population. Estimates of the prevalence vary among different populations, but the condition does not appear to exhibit a racial predilection. LP is rarely reported in childhood **(Sharma and Maheshwari, 1999)**, as it most commonly affects middle-aged adults of both sexes, with a slight predominance in women, although equal sex incidence has been reported. LP constituted 0.38% of the total dermatology, outpatients diagnosed in Postgraduate Institute of Medical Education and Research, Chandigarh, India **(Bhattacharya et al., 2000).** At Al-Minya University Hospital (Egypt) LP was present in 0.28% of patients, the age range was 10-65 years and the majority fall in the 21-50 age group. At St John's Hospital for diseases of the skin (London), about 200 new cases are registered each year. This represents approximately 1.20% of all new cases. At the Finsen institute in Copenhagen, 0.9% of all new cases registered were diagnosed as LP, occasionally LP can develop within the same family. It has also been reported in monozygotic twins, suggesting a genetic predisposition nature of the disorder **(Black, 1992).**

The incidence of LP increased in Egypt due to increase