شبكة المعلومات الجامعية

بسم الله الرحمن الرحيم

شبكة المعلومـــات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

﴿ قَسَـــم ﴾

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
علي هذه الأفلام قد اعدت دون آية تغيرات

يجب أن

تحفظ هذه الأفلام بعيداً عن الغبار

في درجة حرارة من 15 – 20 مئوية ورطوبة نسبية من 20-40 %

To be kept away from dust in dry cool place of
15 – 25c and relative humidity 20-40 %

بعض الوثائق الأصلية تالفة

بالرسالة صفحات

لم ترد بالأصـــل

B ١٩٢٢

E-SELECTIN IN CERTAIN PHOTORESPONSIVE DERMATOSES BEFORE AND AFTER PHOTOCHEMOTHERAPY

Thesis submitted for partial fulfillment of M.D. degree in Dermatology.

BY
SHEREEN OSAMA MOHAMED TAWFIC
M.S.c Dermatology and Andrology.

SUPERVISORS

Prof. Dr. Medhat Abdl El-Monem El-Mofty.
Professor of Dermatology
Faculty of Medicine
Cairo University.

Prof. Dr. Manal Mohamed Wagedy El-Masery.
Assistant Prof. of Clinical Pathology.
Faculty of Medicine.
Cairo University.

Dr. Randa Mohamed Ahmed Youssef.
Lecturer of Dermatology.
Faculty of Medicine.
Cairo University.

Faculty of Medicine.
Cairo university.
2001.

جامعة القاهرة / كلية الطب
القسم المختص

محضر

أجتماع لجنة الحكم على الرسالة المقدمة من

الطبيب / شيرين أسامة محمد توفيق

توطئة للحصول على درجة الماجستير / الدكتوراة

في الامراض الجلدية

عنوان : باللغة الانجليزية :

: باللغة العربية : " دور الاى سيلكتين فى بعض الامراض الجلدية التى تستجيب للعلاج الضوئى قبل وبعد العلاج بالاشعة الفوق بنفسجية "

بناء على موافقة الجامعة بتاريخ / / ١٩ تم تشكيل لجنة الفحص والمناقشة للرسالة المذكورة أعلاه على النحو التالي :-

السيد الاستاذ الدكتور/ مدحت عبد المنعم المفتى - أستاذ بالقسم عن المشرفين

" " " / جلال عبد المقصود العنانى - أستاذ (متفرغ) بالقسم ممتحن داخلي

" " " / عاصم محمد فرج - أستاذ الامراض الجلدية والتناسلية بكلية ممتحن خارجي

فحص الرسالة بواسطة كل عضو منفردا وكتابة تقارير منفردة لكل منهم إنعقدت اللجنة مجتمعة في الاربعاء بتاريخ ٢٤ / ١٠ / ٢٠٠١ بقسم الامراض الجلدية مدرج العيادة الخارجية

الطب - جامعة القاهرة وذلك لمناقشة الطالب في جلسة علنية في موضوع الرسالة والنتائج التي توصل اليها وكذلك الأسس العلمية التي قام عليها البحث .

اللجنة : توصي اللجنة بالاجماع قبول الرسالة ومنح الدرجة العلمية

توقيعات أعضاء اللجنة :-

المشرف الممتحن	الممتحن الداخلي	الممتحن الخارجي
.... [signature]	.... [signature]	.... [signature]
(أ.د. مدحت المفتى)	(أ.د. جلال العنانى)	(أ.د. عاصم فرج)

Abstract

E-selectin, an endothelial specific adhesion molecule, is best known for its role in leukocyte adhesion. It is not detected in quiescent endothelial cells, but secondary to its activation. A soluble isoform of E-selectin is found in the plasma. Although, PUVA could down regulate sE-selectin, this effect is limited by the phenomenon of tachyphylaxis. This thesis was conducted to study the role of sE-selectin before and after PUVA in different photoresponsive dermatoses, psoriasis was chosen as an example of the inflammatory dermatosis, and mycosis fungoides as an example of the neoplastic skin conditions. Vitiligo was studied as a control for the previous two conditions, since vitiligo is a non-inflammatory, non-neoplastic dermatoses, but responsive to PUVA, so it was aimed to study the link between sE-selectin, PUVA and pigmentation. **Methods**: This study included 45 patients, divided into three groups; the first group included 15 psoriatic patients, the second group included 15 mycosis fungoides patients and the third group included 15 vitiligo patients, besides 20 normal controls. The PASI score was done for the psoriatics, while staging was done for M.F. patients, both of these were done pre, mid and after PUVA therapy. Also serum was taken for all patients pre, mid and post PUVA, but only pre treatment samples was taken for the control. **Results:** It was found that the mean sE-selectin in psoriasis, mycosis fungoides and vitiligo before and after PUVA was lower than control. In psoriasis, the PASI score was significantly correlated to pre treatment sE-selectin level, while there was no post treatment correlation. Regarding the response to PUVA therapy, there was a minimal difference in the mean pre, mid and post treatment sE-selectin levels in psoriasis, while in mycosis fungoides and vitiligo, there was a statistically significant difference. But in vitiligo there was an apparent increase in the sE-selectin level with the clinical improvement, i.e. serum level of sE-selectin rises with better pigmentation. **Conclusion**: 1) In psoriasis, sE-selectin is released secondary to endothelial activation, and is related to disease severity. 2) In mycosis fungoides, sE-selectin was not related to early stages of M.F and PUVA therapy raises its level to reach near that of normal controls. 3) As regards vitiligo, sE-selectin rises with clinical improvement (more pigmentation). 4) PUVA raises sE-selectin level, but is limited by the phenomenon of tachyphylaxis.

Keywords: sE-selectin, psoriasis, mycosis fungoides, vitiligo, PUVA.

Acknowledgment

I would like to express my deepest gratitude to Prof. Dr. Medhat Abd EL-Monem EL-Mofty, Professor of Dermatology, Cairo University, for his continuous and sincere guidance, and expert remarks during all phases of this work. He offered me a lot of time and effort in revising this work despite his tight schedule.

I would also wish to extend my thanks to Dr. Randa Mohamed Youssef, Lecturer of Dermatology, Cairo University, for her support and advice during conducting this work. Her precise remarks were of utmost help in guiding me towards attempting perfection of the work.

I am also grateful to Dr. Manal El Masry, Assistant Professor of Clinical Pathology, for her valuable contributions in the laboratory part of this work

Last but not least, I would like to express my gratitude to my family for their unceasing encouragement and support throughout the various steps of conducting this work. Words fail to describe my overwhelming feelings towards them.

Contents

page

- **Introduction and Aim of work**----------1.
- **Section I**: *Review of Literature*

*Chapter1: Cell adhesion molecules----------3
-Role of adhesion molecules----------8
-Selectins----------9
*Selectin structure---------- 9
*Selectin expression---------- 10
*Effect of the selectins on leukocytes---------- 13
*Selectin deficient mice---------- 15
*Selectin ligands---------- 17
-Soluble selectins---------- 18

*Chapter2: Psoriasis----------23
-Clinical forms---------- ---------- 23
-Etiology of psoriasis---------- ---------- 26
*Mode of inheritance---------- - 27
*Provocation and exacerbation---------- 27
-Psoriatic epidermis and keratinocytes---------- 32
*Growth factors---------- 32
*Signal transduction---------- 33
*Second messenger and intracellular mediators----- 34
*Regulatory enzymes----------36
*Enzymes of oxireduction----------37
-Changes associated with psoriasis and---------- 37
contributing to its pathogenesis
*Cellular changes---------- 37
*Microcirculation in psoriasis----------39
*Immunopathogenesis----------40
-E-selectin and psoriasis----------46

*Chapter3: Mycosis fungoides---------- 50
-Clinical features---------- 50
*Classic mycosis fungoides---------- 51
*Clinicopathologic syndromes---------- 52
*Immunophenotypic syndromes---------- 54
*Erythrodermas---------- 55
*Tumor stage mycosis fungoides---------- 56
*Rare presentations---------- 56
-Etiopathogenesisof mycosis fungoides---------- 58

*Genetic factors---------- 58
*Oncogenes---------- 59
*Environmental factors---------- 61
*Viruses----------61
*Bacterial superantigens----------64
*Immunopathogenesis----------65
*Thymus by pass model----------73
-Diagnosis of cutaneous T cell lymphoma---------- 74
-Staging systems---------- 77
-E-selectin and mycosis fungoides---------- 78

*Chapter4: Vitiligo---------- 82
-Diseases associated with vitiligo---------- 83
*Cutaneous diseases---------- 83
*Systemic diseases---------- 84
-Heritability of vitiligo---------- 85
-Pathogenesis of vitiligo---------- 86
*Autoimmune theory---------- 86
*Self destructive theory---------- 88
*Neural theory---------- 90
-Vitiligo and E-selectin---------- 92

*Chapter5:Photochemotherapy and its mechanism ---------- 93
of action in psoriasis, M.F. and vitiligo.
-Photochemotherapy---------- 93
-Principles of PUVA therapy---------- 94
-Psoralens---------- 94
-Oral treatment protocol---------- 94
-PUVA side effects---------- 95
-Mechanism of action of PUVA---------- 97
*Antimitotic effect ---------- 97
*Reactive oxygen species---------- -98
*Effect on apoptosis---------- -98
*Immunological effects---------- 99
*Effect on pigmentation----------102
-Ultraviolet light phototherapy----------106
and E-selectin.

- **Section II:** *Patients and methods*---------- 109
- **Section III:** *Results*----------117
- **Section IV:** *-Discussion*----------147
-Conclusion---------- 156