سامية محمد مصطفى

شبكة المعلومات الجامعية

بسم الله الرحمن الرحيم

سامية محمد مصطفى

شبكة المعلومات الجامعية

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التوثيق الالكتروني والميكروفيلم

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قسم

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بالرسالة صفحات لم ترد بالأصل

The Role of soluble Interleukin-2 Receptor (sIL-2R) in the Pathogenesis of Pemphigus Vulgaris

Thesis

Submitted in Partial fulfillment of the Requirement for Master degree in Oral Medicine, Oral Diagnosis and Periodontology

By

Gihane Gharib Hassan Madkour

B.D.S. (Cairo University)

Oral Medicine, Oral Diagnosis and Periodontology

Department, Faculty of Oral and Dental Medicine

Cairo University

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Supervisors

Prof. Dr. Mahmoud Ibrahim El-Refaei

Dean of Faculty of Oral and Dental Medicine, and
Professor of Oral Medicine, Oral Diagnosis and
Periodontology, Cairo University

Dr. Nahed Abdel-Moneim Emara

Researcher, Clinical and Medical Pathology
Department, National Research Center,
Cairo

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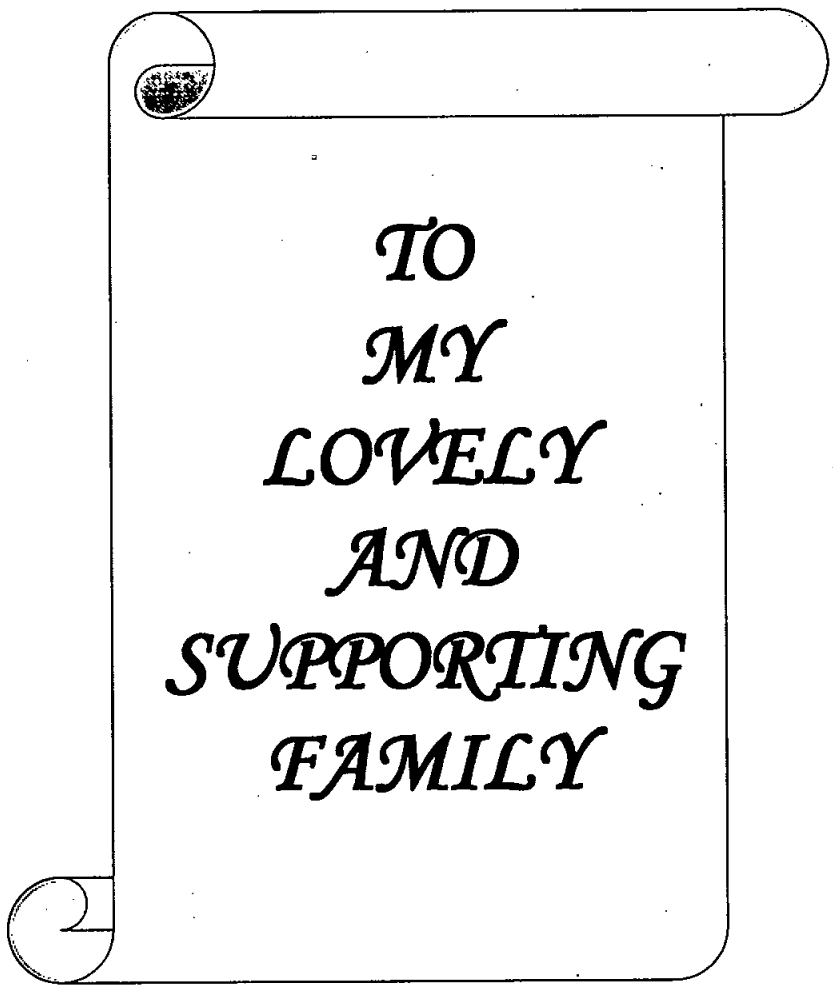
TO
MY
LOVELY
AND
SUPPORTING
FAMILY

Contents

INTRODUCTION

Introduction

Pemphigus vulgaris (PV) is a severe chronic autoimmune vesiculo-bullous skin disorder in which loss of adhesion between keratinocytes is caused by circulating IgG autoantibodies directed against Desmoglein (Dsg) adhesion molecules of keratinocytes ***(EL-Genhani and Sultan, 2003; Scott and McKinnon, 2003; Veldman et al., 2004).***

PV is characterized histologically by intraepidermal blister formation, and immunopathologically by in vivo bound and circulating IgG against Dsg1 and/or Dsg 3, resulting in acantholysis of the suprabasal layers of stratified squamous epithelium ***(Pollard and Earnshaw, 2002; Shimizu et al., 2004).***

Before the availability of corticosteroids, PV had a mortality rate of ~75%. Corticosteroids significantly improved the prognosis of PV patients, lowering the mortality rate to 21.4% ***(Toto et al., 2000).*** Furthermore, corticosteroids remain the mainstay of therapy because it is the only therapy that acts rapidly to turn off new blister activity ***(Lebwohl et al., 2002; Herzog et al., 2004).***

Interleukin-2 (IL-2) is an autocrine and paracrine growth factor secreted by activated T lymphocytes and is essential for clonal T cell proliferation ***(Peng et al., 2000; Haynes and Fauci, 2001).*** In addition to its essential role in promoting T cell division, IL-2 also potentiates B cell growth and proliferation, as well as, it enhances antibody secretion by normal B cells ***(Oppenheim and Ruscetti, 2001; Roitt et al., 2001).***

To exert its biological effect, IL-2 must interact with specific high affinity membrane receptor, Interleukin-2 Receptor (IL-2R), which is expressed by T cells responding to foreign antigens, but not by resting T cells ***(Alileche et al., 2001***; **Wesley *et al., 2004).***

Activated B lymphocytes also express high affinity IL-2R at approximately 30% the density found on activated T cells. So, B cells can respond to IL-2 at concentrations two to threefold higher than are required to obtain T cell responses ***(Oppenheim and Ruscetti, 2001).***

In addition to the expression of IL-2R by activated T and B lymphocytes, in vitro studies have shown that activated T lymphocytes continuously secrete a soluble form of the IL-2R (sIL-2R), correlating with the rate of expression of the membrane bound receptor and the degree of activation. A similar release, but at a much lower rate, has also been described in B cells and monocytes, and therefore sIL-2R is usually considered as a marker of T cell activation ***(Correia et al., 2002).***

It was shown that sIL-2R is present in vivo, at low levels in the sera of healthy persons and at markedly elevated levels in various pathological conditions including many autoimmune disorders ***(Morris and Waldmann, 2000; Correia et al., 2002; Daza et al., 2003).***

Since the release of sIL-2R appears to be a consequence of activation of various cell types that play a role in the regulation of the immune response, the plasma level of this sIL-2R may provide a new approach to the detection of lymphocyte activation in vivo, so helping in the investigation, management and prognosis of a broad spectrum of human diseases ***(Inn et al., 1996; Morris and Waldmann, 2000).***

Recent studies suggest that autoreactive T cells, secreting high levels of IL-2 and sIL-2R, are critical for the induction and regulation of auto-antibodies (AAb) production by B cells in many autoimmune diseases, including Bullous pemphigoid, Epidermolysis bullosa acquisita and Toxic Epidermal Necrolysis ***(Zillikens et al., 1992; Egan et al., 2001; Correia et al., 2002; Tsunoda et al., 2002; Veldman et al., 2003; Veldman et al., 2004)***.

So, in light of these recent evidences, the present study was thus designed to elucidate the possible role of autoreactive T cells, helping and stimulating AAb production by B cells, in the pathogenesis of PV through measuring sIL-2R levels in serum and blister fluid of these PV patients.