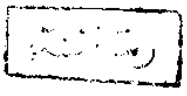
URTICARIAL VASCULITIS
ESSAY

Submitted for Partial Fulfilment of the
Master Degree in Dermatology and Venereology



By

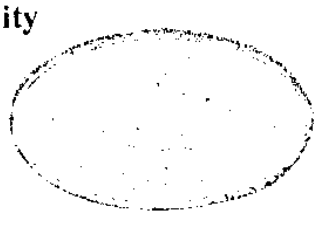
MOHAMED ABDUL AZIM HAMOUDA
M.B., B.Ch.
Faculty of Medicine, Ain Shams University

Supervised by

Prof. Dr. ZENAB EL-GOTHAMY
Professor of Dermatology and Venereology
Faculty of Medicine, Ain Shams University

Dr. MAY HUSSEIN EL-SAMAHY
Assistant professor of Dermatology and Venereology
Faculty of Medicine, Ain Shams University

Faculty of Medicine
Ain Shams University



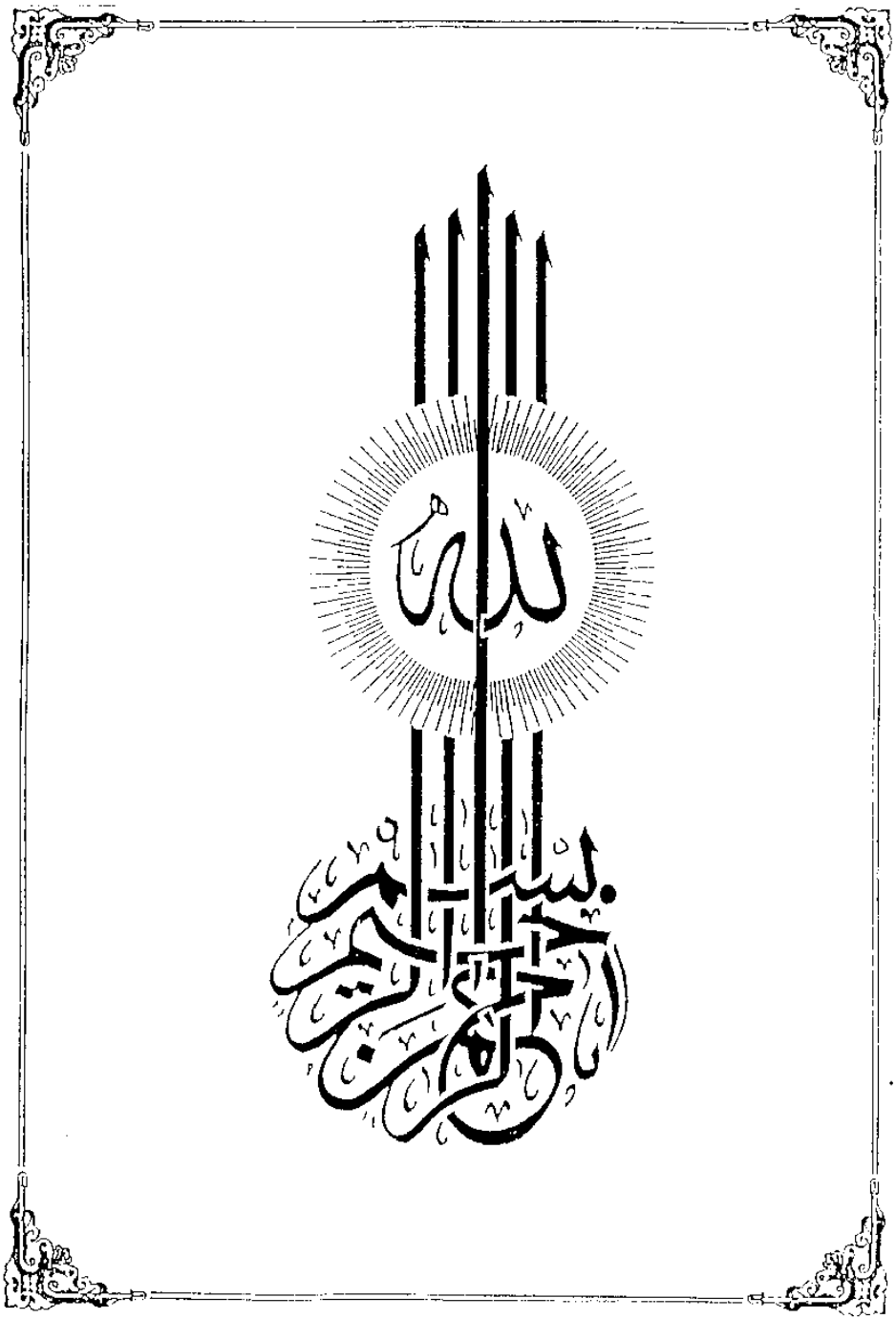
1995

بسم الله الرحمن الرحيم

﴿ قالوا سبحانك لا علم لنا إلا ما علمتنا إنك أنت العليم الحكيم ﴾

صدق الله العظيم

(سورة البقرة ٣٢)



To the memory of my father, who

died hoping to see this work

CONTENTS

LIST OF FIGURES

Page

ACKNOWLEDGEMENT

*Thanks to **GOD** helping me to complete this work.*

*I would like to express my utmost gratitude, deepest appreciation, and great thanks to **Prof. Dr. Zenab El-Gothamy** Professor of Dermatology and Venereology Faculty of Medicine, Ain Shams University for her close supervision, kind instructions, and advices that were very helpful in finishing this work.*

*I would like also to express my great thanks and deepest appreciation to **Dr. May Hussein El Samahy** Assistant Professor of Dermatology and Venereology Faculty of Medicine, Ain Shams University for her precious guidance, valuable suggestions and kind support throughout the whole work.*

*Last but not least, my warmest thanks to my **family** for their patience and encouragement.*

Mohamed Abdul Azim Hamouda

INTRODUCTION AND AIM OF THE WORK

Vasculitis, like urticaria, is not a specific disease per se, but it represents a reaction pattern in the skin caused by a wide variety of substances, involving different pathogenic mechanisms which result in the deposition of immune complexes. The lesions of cutaneous vasculitis may be pleomorphic, but most often they are represented by palpable purpura *(Monroe, 1980)*.

In *1973, McDuffie et al.* described a syndrome in which urticaria was the sole cutaneous manifestation of leukocytoclastic vasculitis. Subsequently, urticarial vasculitis, emerged as a spectrum of disease ranging from urticaria without evidence of systemic disease to the lupus like syndrome *(Berg et al., 1988)*.

With respect to the complement system, patients have been divided into two groups, one with hypocomplementemia and another with normal complement system *(Soter, 1977)*.

The majority of cases of urticarial vasculitis are of unknown aetiology *(Berg et al., 1988)*.

Jones et al. (1983) reported that the pathogenesis of urticarial vasculitis is thought to involve type III hypersensitivity reaction, similar to other forms of cutaneous leukocytoclastic vasculitis.

Urticarial vasculitis represents a clinical spectrum of disease ranging from localized cutaneous manifestations to multisystem disease. Patients with hypocomplementemia are more likely to have systemic involvement than patients with normocomplementemia *(Mehregan et al., 1992).*

Skin biopsies usually reveal the classic features of leukocytoclastic vasculitis *(Berg et al., 1988).* The essential histologic findings are neutrophils, nuclear dust, and fibrin within and around capillaries and venules in the dermis *(Ackerman, 1980).* On direct immunofluorescence examination of the skin, immunoreactants are deposited at the basement-membrane zone, about the vessels, or in normal skin *(Soter, 1985).*

The most consistent laboratory abnormality which occurs in the majority of patients, is an elevated erythrocyte sedimentation rate (ESR) *(Soter, 1985).* In hypocomplementemic patients, the striking serologic features are hypocomplementemia and the presence of a substance which precipitates with C1q *(Agnello, 1978).*

The results of treatment of urticarial vasculitis have been inconsistent. Among the drugs used are antihistamines, indomethacin, corticosteroids, antimalarials, and cytotoxic agents *(Mehregan et al., 1992).*

Sanchez et al. (1982) reported that most of the patients with systemic urticarial vasculitis have had a relatively benign course.

The disease has been found in association with systemic lupus erythrematosus (SLE), Sjögren's syndrome, and hepatitis B infection. It has also been reported in a patient with IgA myeloma and after cimitidine therapy *(Berg et al., 1988)*.

The aim of this work is to review the literature on one form of cutaneous leukocytoclastic vasculitis in which urticaria is the sole cutaneous manifestation, urticarial vasculitis, in order to get an overall view of this syndrome.

HISTORICAL REVIEW AND NOMENCLATURE

Historical review

In *1971, Agnello et al.* described a female patient with erythema-multiforme like disease, C1q precipitins, and profound hypocomplementemia. This patient may have been the first described case of hypocomplementemic urticarial vasculitis syndrome (HUVS) *(Sturgess and Littljohn, 1988). McDuffie and co workers, (1973)* described four patients with similar clinical manifestations and considered that these patients had a previously undescribed illness. There have since then multiple case reports describing patients with clinical and complement abnormalities similar to those observed in those patients *(Zeiss et al., 1980).*

Soter, (1977) reported that although serum complement abnormalities have been reported, serum complement level may be normal. Assessement of the complement system showed two groups of patients - some with hypocomplementemia and others with a normal complement system.

Asherson et al. (1991) reported that approximately 50% of cases had hypocomplementemia.

In *1982, Schwartz et al.* suggested that the patients with urticarial vasculitis and hypocomplementemia had so many similar systemic features, that they should be grouped together.

McDuffie et al. (1973) believed that their patients represent a possible new immune complex disease syndrome.

This concept has been supported by many authors in their case reports and reviews untill *Wisnieski and Naff (1989)* reported that IgG antibodies to C1q are present in HUVS serum, and it is likely that these antibodies are C1q - precipitins. Their findings support the concept that HUVS is an autoimmune syndrome.

Nomenclature

The variety of skin lesions and extra - cutaneous manifestations occuring in these patients has led to a plethora of diagnostic appelations *(Soter, 1985)*. Names suggested for the syndrome include unusual SLE-related syndrome *(Agnello et al., 1971 and 1976)*, Hypocomplementemic vasculitis *(McDuffie et al., 1973)*, Urticaria with vasculitis *(Mathison et al., 1977)*, Urticarial vasculitis *(Gammon and Wheeler, 1979)*, Hypocomplementemic vasculitic urticarial syndrome *(Zeiss et al., 1980)*, Hypocomplementemic urticarial vasculitis syndrome *(Schwartz et al., 1982)* and McDuffie syndrome *(Palazzo et al., 1993)*.

In many reviews the term urticarial vasculitis is used synonymously with hypocomplementemic vasculitis. However these terms are not synonymous since only about half of the patients reported in the literature with urticarial vasculitis had hypocomplementemia *(Callen and Kalbfleisch, 1982)*.

AETIOLOGY

The majority of cases of urticarial vasculitis are of unknown aetiology *(Berg et al., 1988)*. It has been postulated that it is an immune complex disease *(McDuffie et al., 1973)* or an auto immune disease *(Wisnieski and Naff, 1989)*. Some authors reported other causes such as intake of herbs, Cogan's syndrome, BCG-vaccination, sulfite, cimitidine or ultraviolet irradiation.

Immune complex theory

In *1973, McDuffie and Coworkers* described the syndrome in 4 patients and although the cause of the illness was unknown, they postulated that chronic vascular inflammation resulting from deposition of immune complexes in vessel walls seemed most likely. That complexes actually may be present in the circulation was suggested by the precipitin reaction with monoclonal rheumatoid factor and C1q. By immunofluorescence, the presence of lumpy deposits of immunoglobulin and complement in the renal glomeruli and the finding of IgM and complement in the walls of skin vessels are the immunopathologic hallmarks of immune complex disease.

In support of this concept, circulating immune complexes were detected in 30 to 75% of patients with urticarial vasculitis *(Mehregan et al., 1992)*. Other indirect evidence was presented by *Jones et al. (1983)* when

they used plasma exchange as a therapeutic tool in one patient with urticarial vasculitis. They documented a clear correlation between C1q binding and disease activity. Plasma exchange removed C1q binding activity and was followed by a period of disease remission which lasted from 4 - 6 weeks. These findings are consistent with the hypothesis that circulating immune complexes (CIC) cause the cutaneous lesions.

Sisson et al. (1974) reported that immune complexes may be the responsible factor, but an alternative, and in many respects more acceptable explanation, is that the complement activation results from an intrinsic abnormality of the complement system itself, such as an absent inhibitor or abnormal component; the resultant hypocomplementemia could then predispose to the formation and persistence of circulating immune complexes and a consequent SLE-like illness or glomerulonephritis.

Autoimmune theory

Wisnieski and Naff, (1989) reported that IgG antibody to C1q is present in HUVS serum, and it is likely that these antibodies are C1q precipitins. They showed that IgG molecules present in HUVS serum bind C1q under physiological condition. This binding is Fab dependent not Fc dependent. Therefore, HUVS contains an IgG antibodies to C1q. This supports the concept that HUVS is an autoimmune syndrome.

Unusual aetiology

Urticarial vasculitis possibly induced by herbs

Lee and Kim, (1991) described a 19-year-old woman who had urticarial lesions on her calves persisting for longer than 24 hours. Histological examination showed leukocytoclastic vasculitis. Direct IF revealed IgG, IgM, and C3 in the wall of blood vessels of the upper dermis. The prime suspected causative factor was herbs prescribed by a herb doctor as an energizer to maintain her good health. They pointed out that the patient seemed to have had leukocytoclastic vasculitis in the fashion of serum sickness, which supposedly was precipitated by the intake of herbal antigens.

Herbal remedies are not entirely free of risk of adverse reactions ***(Smith et al., 1992).***

Cogan's syndrone

Cogan's syndrome is an uncommon disease of young adults typically characterized by episodes of acute non syphilitic interstitial keratitis associated with vestibuloauditory dysfunction resembling Menier's disease. The diagnosis of atypical Cogan's syndrome is proposed when one of the two principal symptoms is not typical. Atypical Cogan's syndrome is more often associated with systemic vasculitis than the typical form ***(Haynes et al., 1980).***