Study of the Relation between Psoriasis and Atherosclerosis

Thesis

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Presented by

Marwa Mohamed Mahmoud Abd Ellah
(M.B., B.Ch.)

Under Supervision of

Prof. Dr. Hanan Mohamed Ahmed Saleh
Professor of Dermatology, Venereology and Andrology
Faculty of Medicine - Ain Shams University

Dr. Enas Attia Saad El Din Attia
Assistant Professor of Dermatology, Venerelogy and Andrology
Faculty of Medicine - Ain Shams University

Dr. Ahmed Mohamed Onsy Ibrahim
Lecturer of Cardiology
Faculty of Medicine - Ain Shams University

Faculty of Medicine
Ain Shams University
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List of Contents

List of Contents (Cont.)

List of Contents (Cont.)

List of Table

List of Table (Cont.)

INTRODUCTION

Psoriasis is a common, chronic, and recurrent inflammatory disease of the skin affecting 2 to 3 % of the general population characterized by circumscribed, erythematous, dry, scaling plaques of various sizes. The lesions are usually covered by silvery white lamellar scales ***(Henseler and Christophers, 1995).***

The lesions have a predilection for the scalp, nails and extensor surfaces of the limbs, umbilical region, and sacrum. The eruption is usually symmetrical. The eruption usually develops slowly but may be exanthematous, with the sudden onset of numerous, guttate (drop like) lesions. Subjective symptoms, such as itching or burning, may be present and may cause extreme discomfort ***(Griffiths and Barker, 2007).***

The psoriatic skin lesions are the result of inflammation in the dermis and hyperproliferation with abnormal differentiation of the epidermis ***(Brunner et al., 2005).***

The primary pathologic process is most likely dysregulation of activated T-cell interactions with antigen presenting cell and over production of proinflammatory cytokines such as interferon-α (INF-α) and tumor necrosis factor-α (TNF-α). Evidence for this theory derives from the dramatic improvement of severe psoriasis in patient treated with broadly immunosuppressive drugs used in

organ transplantation, such as cyclosporin and tacrolimus ***(Gudjonsson et al., 2004).***

It has been suggested that psoriasis is associated with atherosclerosis ***(Wakkee et al., 2007).*** Endothelial dysfunction is a characteristic of most conditions associated with atherosclerosis and, thus, is considered as an early feature in atherogenesis ***(Neimann et al., 2006).***

Endothelial dysfunction may be defined as impaired ability of the artery to dilate in response to physical and chemical stimuli because of a decreased release or increased breakdown of nitric oxide (NO). Endothelial function can be none invasively evaluated by post occlusion flow-mediated dilation (FMD) of the brachial artery using high sensitivity brachial ultrasonography ***(Deanfield et al., 2005).***

Platelets have an important role in increasing inflammation. An increased incidence of occlusive vascular disease has been reported in patient with psoriasis and pathomechanism of psoriasis may involve platelet activation ***(Tamagawa et al., 2009).*** An association between the increased platelet activation and the pathogenesis of atherosclerosis has also been demonstrated ***(Jenning, 2009).***

Mean platelet volume (MPV) is used as a marker of platelet activation ***(Jenning, 2009).*** Platelet selectin (CD62) is also a marker for platelet activation and its level is increased in ischemic cardiovascular event during both acute and subacute periods, and this was associated with atherosclerotic complication ***(McCabe et al., 2004).***

AIM OF THE WORK

This thesis is designed to evaluate the relationship between psoriasis and atherosclerosis by assessment of endothelial function using FMD, MPV and platelet reactivity by means of platelet expression of CD62 (P-selectin) in psoriatic patient compared to controls.

PSORIASIS: AN OVERVIEW

Psoriasis is a common chronic inflammatory, immune-mediated disease that predominantly affects the skin and joints ***(Griffiths and Barker 2007).*** It is characterized by sharply demarcated, red, and scaly symmetrical plaques on the elbow, knee or scalp ***(Christopher, 2001).***

The course of the disease is characterized by relapses and remissions but the condition tends to persist throughout life. Over the past 20 years there have been many developments in the understanding of the genetic, molecular and cellular mechanisms that underlie these inflammatory processes and many effective treatments have been developed ***(Mrowietz et al., 2011).***

1.1. Epidemiology

Psoriasis is found worldwide, although its frequency varies widely among different ethnic groups. According to published reports, prevalence in different populations varies from 0% to 11.8% ***(Icen et al., 2009)*** Nevertheless, examination of available population-based studies reveals prevalence ranging from 0.2% to 4.8%. The highest prevalence, observed in Norway, was obtained by relying on ascertainment by questionnaire without validation of positive responses ***(Gudjonsson and Elder, 2007).***

With the exception of the Norwegian questionnaire study, the highest reported incidences in Europe have been in Denmark (2.9%) and the Faeroe Islands (2.8%), with the average for northern Europe being around 2%. Population-based (but not examination-validated) studies in the United States (US) have yielded prevalence ranging from 2.2% to 2.6% with approximately 150000 newly diagnosed cases per year ***(Gelfand et al., 2005).***

The incidence of psoriasis appears to be lower in Asians, with several large population-based studies recording prevalence around 0.3% ***(Yip, 1984),*** but one large (incompletely described) study yielded a prevalence of 1.2% ***(Lin, 1993).***

Although the only available studies are clinic-based, and several are rather small, investigations from Africa revealed a generally higher prevalence of psoriasis in East Africans (average of 7 studies = 2.0%) as opposed to West Africans (average of 5 studies = 0.3%) ***(Farber and Nall, 1998).***

Psoriasis is a disorder with a relatively high prevalence in the general population, mainly as a result of its chronicity and the absence of a cure. Because psoriasis is present throughout life, when examining population data, it is expected that point prevalence and lifetime prevalence would increase with age. On

the contrary, in many studies, prevalence does not increase with age and even decreases ***(Naldi, 2004)***.

The most obvious deduction from these data is that mortality among psoriatic patients may be increased as compared with the general population in the late decades of life. The association of psoriasis with smoking and components of the metabolic syndrome may be responsible for such a trend ***(Adams et al.*, 2006**).

1.1.1 Age at onset

Psoriasis may first appear at any age. It is most likely to appear between the ages of 15 and 30 years but its age of onset ranges from birth to the eighth or ninth decade ***(Buntin et al.*, *1983)*.**

Henseler and Christophers (1985) showed that the possession of certain human leucocytic antigen (HLA) class I antigens, particularly HLA-Cw6, is associated with an earlier age of onset and with a positive family history, these findings led them to propose that 2 different forms of psoriasis exist: type I psoriasis with age of onset before 40 years and HLA-associated and type II, with age of onset after 40 years and lacking HLA associations. Not all age-at-onset studies have observed this bimodality ***(Farber and Nall, 1998).***

1.1.2 Sex ratio

Although some studies found minor deviations, psoriasis is equally common in males and females ***(Fry, 1988; Farber and Nall, 1998)***. There is no evidence for morphological differences in psoriasis between males and females ***(Gudjonsson and Elder, 2007).***

1.2. Predisposing Factors

1.2.1 Genetic factors

1.2.1.1 Familial studies

It has been known for quite a long time that psoriasis occurs with increased frequency in some families. Depending upon series, a positive family history has been reported by 35% to 90% of patients. With regard to the risk of a child developing psoriasis, a large German survey found that if both parents were affected with psoriasis, the risk for the child developing the disorder was 41%, whereas if one parent was affected, the risk was 14%; and if one sibling was affected, the risk was 6% ***(Gudjonsson and Elder, 2007).***

1.2.1.2 Twins studies

Analysis of concordance rates amongst monozygotic and dizygotic twins is another method for examining the influence of genetic factors on a disease. ***Farber and Nall (1998)***

reviewed the published data from twin pair studies in psoriasis. Of 141 monozygotic twin pairs, 82 were concordant for psoriasis and 59 were discordant. Of 155 dizygotic twin pairs, only 31 were concordant and 124 were discordant for psoriasis. The distribution of the lesions, the severity of the lesions, and the age of onset were similar in the monozygotic twin pairs, whereas these features differed in the dizygotic twin pairs. This observation suggested that genetic factors also play a role in the clinical course of psoriasis ***(Sagoo et al., 2004).***

1.2.1.3 Influence of HLA

HLA-Cw6 was expressed in 90% of the patients with early-onset psoriasis, in 50% of those with late-onset psoriasis, and only in 7.4% of a control population ***(Oka et al., 2012).*** As a result, some clinicians have designated patients with early-onset psoriasis, a positive family history of psoriasis, and expression of HLA-Cw6 as having *Type I psoriasis* and those with late-onset disease, no family history, and a lack of expression of HLA-Cw6 as *Type II psoriasis* ***(Farber and Nall, 1998).***

1.2.1.4 Linkage studies

Based upon analyses of family pedigrees, a polygenic inheritance provides the best model for the complex genetics of psoriasis. Genome wide linkage scans have demonstrated