Actas Dermosifiliogr. 2014;105(1):31–44

ACTAS Dermo-Sifiliográficas

Full English text available at www.actasdermo.org

REVIEW

Obesity and Psoriasis: Inflammatory Nature of Obesity, Relationship Between Psoriasis and Obesity, and Therapeutic Implications☆

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Received 10 June 2012; accepted 1 August 2012
Available online 30 December 2013

KEYWORDS
Psoriasis;
Obesity;
Metabolic syndrome;
Adipokine;
Therapy

Abstract Obesity, particularly abdominal obesity, is currently considered a chronic low-grade inflammatory condition that plays an active role in the development of the pathophysiologic phenomena responsible for metabolic syndrome and cardiovascular disease through the secretion of proinflammatory adipokines and cytokines. In recent years clear genetic, pathogenic, and epidemiologic links have been established between psoriasis and obesity, with important implications for health. The relationship between the 2 conditions is probably bidirectional, with obesity predisposing to psoriasis and psoriasis favoring obesity.

Obesity also has important implications in the treatment of psoriasis, such as a greater risk of adverse effects with conventional systemic drugs and reduced efficacy and/or increased cost with biologic agents, for which dosage should be adjusted to the patient's weight.

PALABRAS CLAVE
Psoriasis;
Obesidad;
Síndrome metabólico;
Adipocinas;
Terapéutica

Obesidad y psoriasis: naturaleza inflamatoria de la obesidad, relación entre psoriasis y obesidad e implicaciones terapéuticas

Resumen La obesidad, en particular la abdominal, se considera en la actualidad como un proceso inflamatorio crónico de bajo grado que participa de forma activa en el desarrollo de los fenómenos fisiopatológicos responsables del síndrome metabólico y la morbilidad

☆ Please cite this article as: Carrascosa JM, Rocamora V, Fernandez-Torres RM, Jimenez-Puya R, Moreno JC, Coll-Puigserver N, et al. Obesidad y psoriasis: naturaleza inflamatoria de la obesidad, relación entre psoriasis y obesidad e implicaciones terapéuticas. Actas Dermosifiliogr. 2014;105:31–44.

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1578-2190/$ - see front matter

cardiovascular a través de la secreción de adipocinas y citocinas proinflamatorias. En los últimos años se ha establecido un vínculo firme entre psoriasis y obesidad que abarca aspectos genéticos, patogénicos y epidemiológicos, con importantes repercusiones en la salud del individuo. Es probable una relación bidireccional, en la que la obesidad predispone a la psoriasis, pero también la psoriasis favorece la obesidad.

La obesidad tiene también importantes implicaciones terapéuticas, como el mayor riesgo de efectos adversos en el caso de los fármacos sistémicos convencionales y la disminución de la eficacia y/o el incremento del coste en el caso de los fármacos biológicos, que hace recomendable ajustar la dosis al peso del paciente.

Background

Obesity is defined as a chronic condition characterized by excess weight due to an increase in energy deposits stored as body fat. A defect in the symbiosis and equilibrium of food intake associated with a deregulation of energy expenditure, whether due to inflammatory or genetic disease or caused by excesses or alterations in food intake, will lead to a state of obesity or thinness.[1]

A diagnosis of obesity is established by determining the patient's body mass index (BMI) using the formula weight in kilograms divided by the square of the height in meters. The current World Health Organization weight classification for BMI in adults is as follows: a BMI of between 18.5 and 24.9 is normal, 25 to 29.9 is overweight, and a BMI greater than 30 is diagnostic of obesity.[2,3]

The establishment in recent years of a clear association between psoriasis and obesity coincided with a growing awareness that both diseases are chronic inflammatory processes that have significant repercussions on the individual's health, largely in terms of increased risk of cardiovascular disease and the elements of metabolic syndrome. Although there is still considerable debate about this association with psoriasis, the evidence points to a bidirectional relationship. Several epidemiological studies have provided evidence supporting the hypothesis that obesity is an independent risk factor associated with a high risk of psoriasis and a poor long-term prognosis in that setting; however, the findings of other studies appear to indicate that obesity may be a consequence of psoriasis rather than a risk factor for the condition.[4–6]

The aim of the present review is to provide a general analysis of the relationship between psoriasis and obesity. Starting with an account of the currently accepted view of the inflammatory nature of obesity, we will review the relationship between psoriasis and obesity and the pathogenic basis of this association. Finally, we will discuss the challenges and implications of the association in the treatment of psoriasis.

Inflammatory Nature of Obesity

Before the first adipokine—leptin—was discovered in 1994, it was thought that the only role of adipose tissue (AT) was to store energy in the form of fat; however, it is now clear that AT is an endocrine, autocrine, and paracrine organ that performs other functions in addition to storing energy reserves.[7]

AT, the largest organ in the adult human body, is composed of adipocytes, cells that are responsible for storing energy in the form of triglycerides. Recent evidence indicates that AT, and especially abdominal fat, is an active endocrine organ which helps to regulate several body functions, including insulin-mediated processes, lipid and glucose metabolism, and vascular biology, and plays a role in coagulation and some aspects of inflammation.[8,9]

All these effects are mediated by various adipokines—regulators secreted by adipocytes—and a wide variety of proinflammatory cytokines, including C-reactive protein (CRP), transforming growth factor β, plasminogen activator inhibitor-1 (PAI-1), interleukin (IL) 1β, IL-6, and tumor necrosis factor-alpha (TNF-α). The direct and indirect effects of these molecules are the key to the inflammatory nature of obesity and its relationship with other inflammatory processes including psoriasis.

In obesity, the structure and composition of AT is altered and these changes enhance the proinflammatory effect. Leptin, and possibly other factors produced by adipocytes and macrophages, upregulate or markedly increase endothelial cell adhesion molecules, such as intercellular adhesion molecule-1 (ICAM-1) and platelet endothelial cell adhesion molecule-1 (PECAM-1). It is also possible that monocyte-chemoattractant molecule-1 (MCP-1), a chemokine expressed in adipocytes that can be correlated with body weight, contributes to the recruitment and transmigration of bone marrow–derived monocytes, thereby producing an increase in macrophages in AT. Fusions with resident macrophages would generate multinucleated giant cells. It is proposed that this accumulation of macrophages, which are increased in both number and size and may account for as much as 60% of cells depending on the patient's fat mass, triggers the expression of proinflammatory molecules, thereby contributing to the ongoing inflammatory state.

Another important finding is that lymphocytes, which do not form part of the adipose tissue, are often found in close proximity to the adipocytes surrounding the lymph node; consequently, there may be paracrine relationships between the lymphocytes and adipocytes, allowing the exchange of information between the two.[10,11]

Figure 1 shows the cytokines secreted by activated macrophages and adipocytes present in AT. In fact, some