7

Metabolic Features in Psoriasis

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1. Introduction

Psoriasis is a chronic inflammatory disease affecting about 3% of the worldwide population (Gottlieb A et al, 2007).

Recent findings have shown that the previous concept " psoriasis as a disease of healthy people" must be revisited into psoriasis as a complex entity with multisistemic involvement.

Although the overall mortality attributed to psoriasis is about 0.64 deaths per 100 000 psoriatic patients annually in the USA, erythrodermic and generalized pustular soriasis, are associated with a greater risk of mortality and morbidity (Boyd AS et al, 1989; Prystowsky JH et al, 1995).

Psoriasis can be associated with other disease, such as metabolic syndrome, which may have a major impact on quality of life, morbidity and mortality.

The aim of this chapter is to focus on two newly emergent comorbidities in psoriatic patients, the cardiovascular disease (CVD) and the metabolic syndrome (MetS).

2. The metabolic syndrome

The metabolic syndrome (MetS) is a cluster of risk factors including obesity, atherogenic dyslipidaemia, hypertension, glucose intolerance and a proinflammatory and prothrombotic state predisposing the patients to cardiovascular diseases (CVD), type 2 diabetes (DM), renal failure and stroke (Gisondi et al, 2007).

Furthermore, it has recently been suggested that the metabolic syndrome might be a risk factor for cancer, in particular colon cancer (Gottlieb A et al, 2007).

The MetS prevalence in Western Europe population ranges from 15% to 35% and it strictly correlates with age, increasing sharply after the age of 60 (Gisondi et al, 2007).

The National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) have proposed the criteria for the metabolic syndrome diagnosis; other organizations, such as The World Health Organization (WHO) and the European Group on Insulin resistance, agree with it in the essential components, differing from it in the details and criteria (Chung CP et al, 2005).

According to NCEP ATPIII the diagnosis of MetS requires at least three of these following criteria:

- Abdominal obesity, defined as waist circumference ≥ 102 cm in men and ≥ 88 cm in women
- Tryglicerides plasma levels ≥ 150 mg/dl
- HDL cholesterol plasma levels less than 40 mg/dl in men and 50 mg/dl in women
- Blood pressure more than 130 mmHg (systolic) and 85 mmHg (diastolic)
- Fasting plasma glucose levels more than 100 mg/dL [Grundy et al., 2005]

It is now thought that non-alcoholic fatty liver disease (NAFLD) is a component of metabolic syndrome, that may progress to steatoepatitis (NASH) with complications of fibrosis and cirrhosis (Capeau J, 2008).

Recent study have demonstrated that the prevalence of metabolic syndrome is significantly higher in psoriatic patients compared to controls after the age of 40 years and psoriatic patients have an increased risk for the individual components of MetS (Gisondi et al, 2007).

Moreover, the association between psoriasis and metabolic syndrome is also true for mild severity psoriasis and it is independent from the tendency of psoriatic patients to be obese (Mallbris L et al, 2006; Neimann AL et al, 2006; Sommer DM et al, 2006).

Although the link between psoriasis and metabolic syndrome is not completely elucidated, the pathophysiology of both these entities shows many shared cytokines contributing to the underlying chronic inflammatory status.

It is known that both innate and adaptive immunity are involved in psoriatic pathogenesis and, in particular, NK cells appear crucial in the inflammatory process initiation, with an increased release of proinflammatory cytokines, such as TNF-alpha and IFN-gamma and the subsequent interaction with TH1 and Th17 cells (Teunissen MBM et al , 2007).

Dysregulation of T-cell antigen presenting cell interactions and overexpression of proinflammatory cytokines lead to the hyperproliferation of keratinocytes and the activation of neutrophils and endothelial cells until the development of the characteristic psoriatic skin lesions (Kimball AB et al, 2008).

The molecular mechanisms involved in psoriasis-associated dysregulation of metabolic functions are believed to be due to an underlying low and persistent inflammatory status with increased levels of proinflammatory factors, such as tumor necrosis factor-alpha and IL-6 (Fig.1).

TNF-alpha is a proinflammatory cytokine produced by many cell lines, such as keratinocites, T cells, NK cells, dendritic cells, neutrophils, mast cells and adipocytes (Ronti T et al, 2006).

It is expressed as a 26-kD cell surface trans-membrane protein that undergoes cleavage to produce a 17-kD soluble, biologically active form of TNF-α (Ronti T et al, 2006).

IL-6, a pleiotropic circulating cytokine, shows multiple effects ranging from inflammation to host defence and tissue injury. It is secreted by many cell types, including immune cells, fibroblasts, endothelial cells, skeletal muscle and adipocytes (Ronti T et al, 2006).

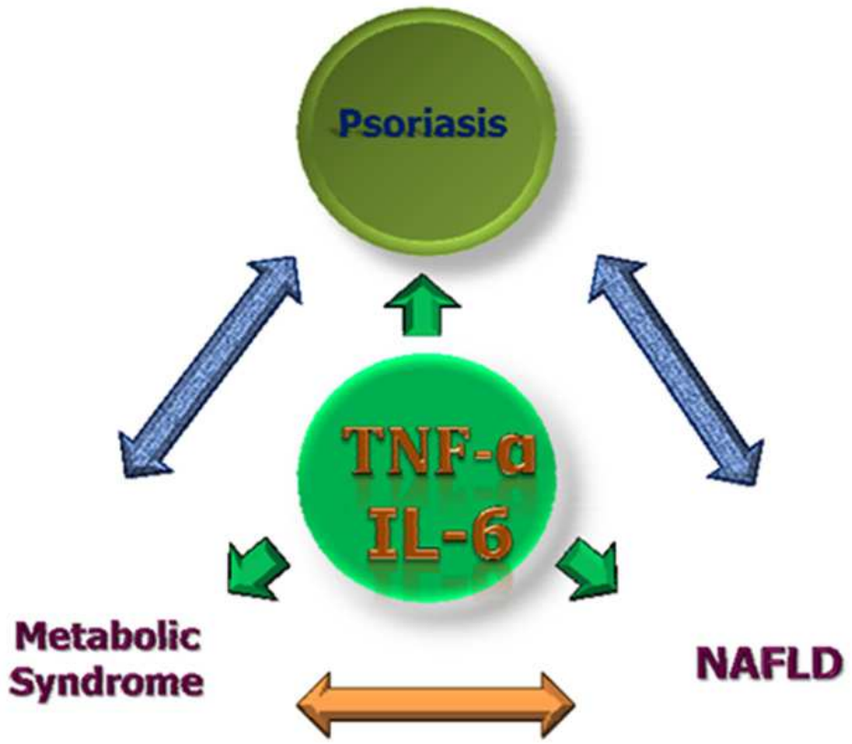


Fig. 1. The molecular mechanisms involved in psoriasis-associated dysregulation of metabolic function.

3. Obesity and psoriasis

Among different MetS components, the association between obesity and psoriasis is the best documented.

Several studies have shown that the severity of PsO may be linked to obesity and a population-based study of mild or severe PsO has demonstrated that the risk of obesity was significantly increased in PsO patients compared with healthy controls. Unlike in other inflammatory diseases, such as rheumatoid arthritis, the risk of obesity is strongly associated with disease severity (Sterry W et al, 2004).

Although it is controversial if psoriasis is the result or the cause of obesity itself , recent data support the obesity is a consequence of psoriasis (Henseler T et al, 1995; Neimann AL et al, 2006; Herron MD et al. 2005).

Obesity is considered the main pathogenic factor in the metabolic syndrome and it is characterized by a low and persistent sistemic inflammatory status, whose mainstay is the adipose tissue (Greenberg et al., 2006).

Adipose tissue is principally divided into two compartments, subcutaneously and centrally: the central one is characterized by omental adipose tissue and other intra-abdominal fat sources such as mesenteric fat. Central adipose tissue, also called visceral fat, is considered more metabolically active than peripheral subcutaneous fat (Kershaw EE et al, 2004; Galic S et al, 2010).

The importance of adipose tissue location in terms of dysmetabolism risk is evident: patients with excess visceral fat (central obesity) show an higher risk of developing insulin resistance and the features of the metabolic syndrome than patients with excess subcutaneous fat (Kissebach AH et al, 1982).

One of the most commonly used antropometric indexes is BMI (Body mass index), which measures adiposity and body composition as weight in kilograms divided by the square ofthe height measurement in metres (kg/m2). BMI have high specificity, but low sensitivity to identify adiposity and excess body fat (Okorodudu DO et al, 2010).

Waist circumference (WC), alone or in combination with BMI, has been shown to be an accurate predictor of visceral fat directly reflecting total abdominal fat mass but failing to quantify the visceral and subcutaneous fat compartments individually (Kashihara H et al, 2009).

The visceral adipose tissue is not only an energy storage organ, but also an important component of the immune system through the adipocytes' expression of toll receptors and a real active endocrine organ producing proinflammatory cytokines (TNF-alpha, IL-6), free fatty acids, procoagulant molecules and bioactive products called adipokines (Ronti et al, 2006).

Many adipokines have been identified, such as leptin, visfatin, resistin and adiponectin; they act in a communications network with other tissues and organs such as the skeletal muscle, adrenal cortex, brain and sympathetic nervous system and participate in appetite and energy balance, immunity, insulin sensitivity, angiogenesis, blood pressure, lipid metabolism and haemostasis (Ronti T et al, 2006).

In particular, leptin and resistin appear to be two proinflammatory cytokines, while adiponectin has anti-inflammatory properties (Ronti T et al, 2006).

Leptin, a 16-kD adipocyte-derived cytokine, is synthesized and released from fat cells in response to changes in body fat. Leptin circulates partially bound to plasma proteins and enters the CNS by diffusion through capillary junctures in the median eminence and by saturable receptor transport in the choroid plexus. In the hypothalamus, leptin binds to receptors that stimulate anorexigenic peptides such as proopiomelanocortin and cocaine- and amphetamine-regulated transcript and inhibit orexigenic peptides, such as neuropeptide Y. Leptin reduces intracellular lipid levels in skeletal muscle, liver and pancreatic beta cells, thereby improving insulin sensitivity. There is strong evidence showing that the dominant action of leptin is to act as a 'starvation signal': leptin declines rapidly during fasting.Therefore, leptin deficiency was perceived as a state of unmitigated starvation, leading to compensatory responses, such as hyperphagia, decreased metabolic rate and changes in hormone levels, designed to restore energy balance. The concept of 'leptin resistance' was introduced when increased adipose leptin production was observed in obese individuals, who were not leptin-deficient. Moreovere, some studies suggest leptin may affect vascular structure with an angiogenic activity and contributes to arterial thrombosis through the platelet leptin receptor. Leptin also stimulates production of reactive oxygen species as a result of monocyte activation. Therefore, in an obese subject leptin may no longer be able to regulate caloric intake and energy balance, but may still

exert its angiogenic activity and production of reactive oxigen species, which affect vessel walls (Ronti T et al, 2006).

Resistin is a dimeric protein. In murine models, obesity is associated with rises in circulating resistin concentrations. Resistin increases blood glucose and insulin concentrations and impairs hypoglycaemic response to insulin infusion. In obese mice, antiresistin antibodies decrease blood glucose and improve insulin sensitivity: these data support the hypothesis that in obese rodents, resistin induces insulin resistance and contributes to impaired insulin sensitivity. In humans, the physiological role of resistin must be elucidated and its role in obesity and insulin resistance and/or diabetes is controversial. In humans, as resistin is primarily produced in peripheral blood monocytes and its levels correlate with IL-6 concentrations. the question of its inflammatory role has been raised (Ronti et al, 2006).

Four genes encode for resistin in the mouse and two in humans. Some genetic case control studies demonstrated genetic variations in the resistin gene are associated with insulin resistance and obesity in humans. Others show that the very low resistin mRNA expression in isolated human adipocytes does not correlate consistently with insulin resistance or obesity, making the role of human resistin in insulin resistance unclear. No differences have been observed in resistin expression in adipocytes from normal, insulin-resistant, and type 2 diabetic individuals. Mc Ternan et al. reported greater resistin mRNA expression in fat depots in the abdomen than in the thigh, suggesting human resistin could play a role in obesity-related insulin resistance (McTernan et al, 2002; Ronti et al, 2006).

Adiponectin is almost exclusively expressed in white adipose tissue, whose expression is inhibited by IL- 6 and TNF-α. Unlike most adipokines, adiponectin expression and serum concentrations are reduced in obese and insulin-resistant states and, in vivo, high plasma adiponectin levels are associated with reduced risk of myocardial infarction. Although further studies are needed to clarify whether adiponectin independently predicts coronary heart disease events, in men with type 2 diabetes, increased adiponectin levels are associated with a moderately decreased risk of coronary heart disease. The association seems to be mediated in part by the effects of adiponectin on high-density lipoprotein cholesterol (HDL), through parallel increases in both. Moreover, it has been demonstrated that weight loss, caloric restriction and thiazoladinedione treatment increase adiponectin plasma levels and gene expression in white adipose tissue (Ronti et al, 2006).

Recent studies have evidenced a high leptin levels and decreased serum levels of adiponectin in obesity, insulin-resistent PsO patients and they emphasized an inverse correlation between serum levels of adiponectin and IL-6 (Satapathy SK et al, 2004).

The precise physiological events leading to the initiation of the inflammatory response in obesity remain incompletely understood. One theory underlined that the expansion of adipose tissue leads to adipocyte hypertrophy and hyperplasia with a consequent local oxygen supply, cell hypoxia and the activation of cellular stress pathways releasing proinflammatory cytokines and signals. These proinflammatory chemokines attract pro-

inflammatory macrophages into the adipose tissue with the creation of crown-like structures around hypertrophic dead or dying adipocytes. Furthermore, these macrophages release cytokines that stimulate an inflammation in neighboring adipocytes developing a vicious circle (Esposito K et al, 2004; Das UN, 2001).

Thus, excess adipose tissue results in elevated levels of pro-inflammatory adipokines, resulting in an imbalance between increased inflammatory stimuli and decreased anti-inflammatory mechanism leading to persistent low-grade inflammation (Wajchenberg BL et al, 2000; Esposito K et al, 2004; Das UN, 2001).

Among proinflammatory cytokines, TNF-a and IL-6 represent two driving cytokines, which link psoriasis with many MetS components, such as obesity-related insulin-resistance (Ronti T et al, 2006).

In humans TNF-α is synthesized and secreted by adipocytes and stromovascular cells: adipose tissue TNF-α is not secreted in systemic circulation and acts in an autocrine and paracrine pathways. Adipose tissue TNF-α mRNA correlates with body mass index, percentage of body fat and hyperinsulinaemia; weight loss decreases TNF-α levels (Ronti T et al, 2006).

TNF-α modifies the gene expression profile of adipocytes and liver with an increased release and production of FFAs, cholesterol and VLDL; elevated IL-6 levels appears to be associated with decreased levels of HDL cholesterol, which may contribute to a state of chronic inflammation (Gottlieb A et al, 2008).

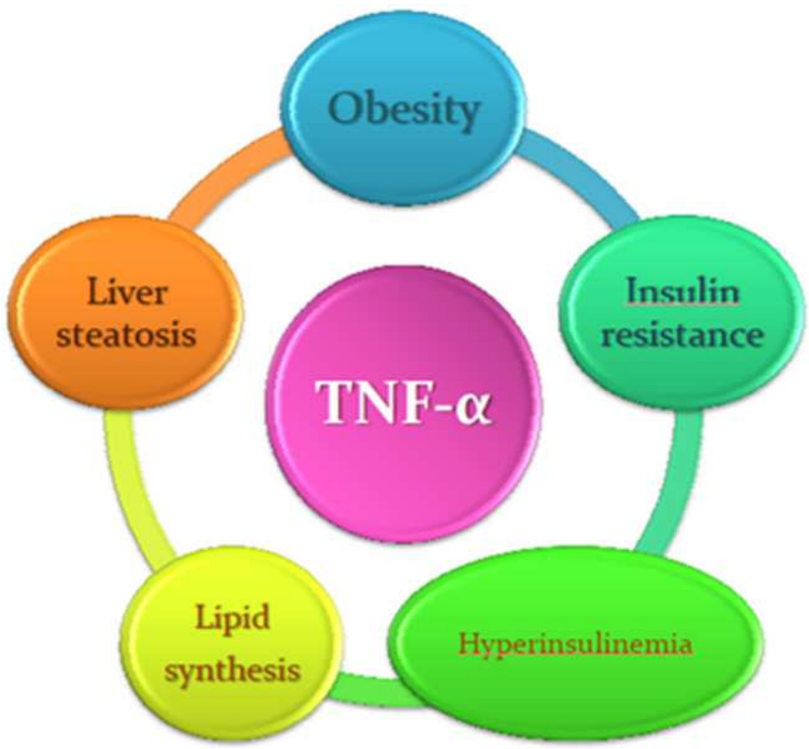


Fig. 2. The vicious circle linking obesity and hyperinsulinemia

Moreover, levels of soluble TNF-α receptors are directly proportional to total and LDL cholesterol concentrations and inversely correlated with certain HDL cholesterol subfraction levels (Gottlieb A et al, 2008).

Obesity-induced chronic inflammation is a key component in the pathogenesis of insulin resistance (Fig.2).

4. Insulin-resistance

Several studies have demonstrated a potential association between PsO and increased serum fasting glucose levels, hyperinsulinemia, insulin-resistance, and type 2 diabetes. However, insulin resistance does not significantly correlate with PsO disease severity and duration (Gottlieb A et al, 2008).

Insulin resistance is a characteristic feature of most patients with Type 2 diabetes mellitus and is one of the MetS clinical features. Insulin is a pleiotropic hormone stimulating nutrient transport into cells, regulating gene expression, modifying enzymatic activity and regulating energy homeostasis (De Luca C et al, 2008).

Insulin exerted to these multiple functions through several intracellular signaling cascades, such as the phosphatidylinositol 3-kinase (PI3K)-AKT (also called protein kinase B (PKB)) pathway and the Ras-mitogen activated protein kinase (MAPK) pathway. PI3K-AKT is largely responsible for insulin action on glucose uptake and in the suppression of gluconeogenesis, while MAPK mediates gene expression and controls cell growth and differentiation, interacting with the first pathway. The insulin action is evidenced on target tissue, such as liver, adipose tissue and skeletal muscle (De Luca C et al, 2008).

In the liver, insulin regulates glucose metabolism depending on the meal or starvation, while in adipose tissue insulin signaling results in decreased hormone sensitive lipase activity and this anti-lipolytic effect inhibits free fatty acid efflux out of adipocytes (De Luca C et al, 2008).

Increased levels of TNF-alpha, IL-6 and FFAs produced by excess visceral adipose tissue can cause insulin resistance in adipose tissue, skeletal muscle and liver by inhibiting insulin signal transduction and they can determine the production of other inflammatory-related factors, such as CRP (Gottlieb A et al, 2008).

TNF-alpha causes a decrease in the autophosphorylation of tyrosine residues of insulin receptor (IR) and phosphorylation of insulin receptor substrate 1 (IRS-1) (Hotamisligil GS, 2003).

Thus, in psoriasis obesity and insulin resistance have a proinflammatory effect perpetuated through a positive feedback loop in PsO patients.

5. NAFLD

The liver plays a central role in lipid metabolism, importing serum free fatty acids and manufacturing, storing and exporting lipids and lipoproteins (Adams LA et al, 2005).

NAFLD is the acronym for nonalcoholic fatty liver disease and it includes a wide spectrum of liver pathology, from hepatocellular steatosis to nonalcoholic steatohepatitis (NASH) (Browning JD et al, 2004).

The prevalence of NAFLD is 10–25% in the western world and it is a an emergent condition now recognized as the most frequent cause of abnormal liver tests, especially in obese individuals (Papatheodoridis GV et al, 2007).

NAFLD is considered the hepatic manifestation of the metabolic syndrome closely associated to visceral obesity and insulin resistance (Marchesini G et al, 2003; Tsochatzis EA et al, 2009).

Adipocytokines, free fatty acids, mitochondrial dysfunction, bacterial endotoxin and vascular disturbance have all been implicated in the development of hepatic inflammation and fibrosis in patients with NAFLD (Adams LA et al, 2005).

The pathogenesis of NAFLD is currently seen as a two steps process, initially characterized by the accumulation of liver fat followed by the development of necroinflammation and fibrosis (Day CP et al,1998).

Insulin resistance results in both increased adipose tissue lipolysis and increased hepatic lipogenesis leading to lipid accumulation in the hepatocytes, mainly in the form of triglycerides and FFAs (Emmanuel A et al, 2009).

The increased liver deposition of TG and FFAs contributes to lipotoxicity and predisposes hepatocytes to the second step: the mythocondrial disfunction and the oxidative stress (Emmanuel A et al, 2009).

A recent study has emphasized that NAFLD is highly prevalent among psoriasis patients and it seems that patients with NAFLD and psoriasis are at higher risk for severe liver fibrosis than their age, sex and BMI-matched counterparts with NAFLD without psoriasis (Marra M et al, 2007).

Psoriasis, metabolic syndrome and NAFLD might share a common underlying mechanism characterized by a low level inflammatory status characterized by a pro-inflammatory cytokines generalized activation (Marra M et al, 2007).

As in obesity and insulin resistance, TNF-alpha seems to have a pivotal role: both serum and hepatic levels of TNF-alpha are elevated in patients with NAFLD and it is directly correlated considering the markers of liver damage (Marra M et al, 2007).

AST, ALT and mostly AST/ALT ratio are considered important parameters of liver damage and they appear correlated to the severity of the hepatic damage to histological disease severity.[Pulzi FBU et al, 2011]

It has already demonstrated that psoriatic patients with NAFLD show a higher mean AST/ALT ratio, a parameter proved to be an independent predictor factor of liver fibrosis in NAFLD patients (Angulo P et al, 2007).

AST serum levels increase more than those of ALT with the progression of the hepatic disease; therefore, an higher than 1 AST/ALT ratio may be one element of more advanced disease (Vanni E et al, 2010).

6. Atherogenic dyslipidemia

Many evidences suggest a strong link between PsO and abnormalities in fatty acid metabolism: psoriatic patients show dyslipidemia with increased plasma cholesterol, triglycerides (TG), low-density lipoprotein (LDL) cholesterol, very low-density lipoprotein (VLDL) cholesterol, and decreased HDL cholesterol and antioxidant capacity. In particular, a recent study has underlined that the dyslipidemic profile could precede the psoriasis manifestations (Gottlieb A et al, 2008).

Studies on lipid profile in psoriatic patients have been conducted since 1994 focusing on the presence of a significant content in total cholesterol and of the cholesterol/protein ratio in low-density lipoproteins (LDL) and in high-density lipoproteins (HDL) of psoriatic children. The compositional changes were associated with alterations of fluidity in LDL and HDL of psoriatic patients (Offidani AM et al, 1994).

In PsO patients, the detection of raised levels of LDL and low levels of HDL cholesterol is associated with coronary artery disease and with accelerated mortality for cardiovascular disease (Jones SM et al, 2000).

7. Hypertension

In PsO patients a higher occurrence of hypertension compared with controls has been reported. The underlying mechanism of hypertension in psoriasis has been discussed and multiple hypothesis have been emerged on this topic (Gottlieb A et al, 2008).

The pathogenesis of hypertension in psoriasis seems to be linked to increased production of angiotensinogen by adipose tissue, subsequently converted to angiotensin II through angiotensin converting enzyme (ACE) (Armstrong AW et al, 2011).

ACE serum levels are increased in psoriasis patients (Gottlieb A et al, 2008).

Angiotensin II not only promotes salt retention by kidney but also it regulates vascular tone, acting a vasoconstrictor and stimulates T-cell proliferation promoting inflammation and the development of atherosclerosis (Armstrong AW et al, 2011).

The association between psoriasis and hypertension may also be attributed to the increased oxidative stress in psoriasis patients. Greater levels of reactive oxygen species can damage endothelium-dependent vasodilation (Armstrong AW et al, 2011).

Other studies emphasized the role of endothelin-1 in hypertension development among PsO patients. Endothelin-1 is a protein produced by several different cell types including keratinocytes; it induces blood vessels vasoconstriction increasing blood pressure. In PsO patients endothelin-1 expression appears to be altered in lesional skin and serum and correlated to psoriasis disease severity (Armstrong AW et al, 2011).

8. Protrombotic state

A proinflammatory and/or prothrombotic state has been associated with MetS and PsO, probably linked to elevated serum levels of PAI-1, fibrinogen and CRP. Elevated CRP levels are induced by IL-6 and they have been shown to be predictive of future CVD in initially

healthy individuals, and the risk of CVD in patients with either diabetes or MetS is significantly increased in the presence of elevated CRP levels (Gottlieb A et al, 2008).

9. Anti-TNF-alpha in psoriasis and metabolic syndrome

TNF-alpha is an inflammatory cytokine promoting inflammation via the activation and induction of proinflammatory cytokines (IL-1, IL-6, IL-8) and by the upregulation of adhesion molecules on endothelial cells leading to increased leukocyte extravasation (Channual J et al, 2009).

Given that TNF-a show a pivotal role in many inflammatory conditions and that it represents one of possible link between psoriasis and metabolic syndrome, theoretically the TNF-alpha blockade might have a widespread potential in the treatment of both pathological entities (Channual J et al, 2009).

Although it is well known the TNF-alpha inhibitors efficacy on PsO and Psoriatic arthritis (PsA), little is known about their effects on the MetS components in PsO patients.

Currently, three available in the United States are approved for psoriasis and psoriatic arthritis (PsA): infliximab, etanercept, and adalimumab (Channual J et al, 2009).

Infliximab is a chimeric monoclonal antibody binding the human tumor necrosis factor alpha (Staidle JP et al, 2011).

Actually there are no data in literature about infliximab effect on insulin resistance or sensitivity in PsO patients.

About lipid profiles, studies have shown that infliximab does not significantly modify total cholesterol, triglycerides and, interestingly, the patient's lipid profile reverted to baseline values after infliximab discontinuation (Gisondi P et al, 2008; Antoniou KM et al, 2008).

Studies investigating the effect of infliximab on body weight have reported significant increase in weight gain and in BMI, without differences among males and females (Saraceno R et al, 2009).

Etanercept is a fusion protein consisting of two molecules of extracellular domain of human p75 TNF-alpha receptor attached to the Fc domain of human immunoglobulin G1 (IgG1), that binds to TNF-alpha with greater affinity than natural receptor. The binding makes TNF-alpha biologically inactive, with consequent reduction of inflammation (Weinberg JM, 2003).

Although there are conflicting results on the effect of Etanercept in insulin-resistance, etanercept have shown an interesting action on reducing serum insulin levels and improving insulin sensitivity. Similar to Infliximab, Etanercept does not significantly modify lipid profiles; furthermore, PsO patients treated by etanercept gradually and progressively gain weight, in particular lean ones (Marra M et al, 2007).

Adalimumab is human monoclonal antibody against TNF-alpha (Staidle JP et al, 2011).

Although there are no reports in literature discussing about adalimumab effect on insulin resistance or sensitivity in PsO patients, a recent case revealed episodes of hyperglycemia in

a PsO-PsA patient; these increased serum glucose levels resolved after adalimumab discontinuation (Wu JJ et al, 2008).

Similar to Infliximab and Etanercept, Adalimumab does not modify lipid profiles and it increases BMI and weight gain (Saraceno R et al, 2009).

10. Conclusion

Despite further studies on anti-TNF-alpha drug effect on MetS syndrome are required, an examination of literature data suggest that the combined effects of improved insulin resistance and sensitivity and a significant reduction in systemic inflammation may interrupt inflammatory cascade linking PsO and MetS.

Taking into consideration the high potentiality of biological therapies to reduce the metabolic effect of TNF-alpha, the future goal might be to demonstrate a real in vivo preventing effect on development of cardiovascular comorbidities in Pso/PsA patients. For these reason other longitudinal long term clinical studies are needed.

11. References

Adams, LA. & Lindor, KD. (2005). Nonalcoholic fatty liver disease. *CMAJ.*,172,899–905.

Angulo, P.; Hui, JM.; Marchesini, G.& al. (2007). The NAFLD fibrosis score: a non invasive system that identifies liver fibrosis in patients with NAFLD. *Hepatology.*,45(4),846-54.

Antoniou, KM.; Mamoulaki, M.; Malagari, K.; Kritikos, HD.; Bouros, D.; Siafakas, NM. & Boumpas, D. (2007). Infliximab therapy in pulmonary fibrosis associated with collagen vascular disease. *Clin Exp Rheumatol*.,25(1),23-8.

Armstrong, AW.; Lin, SW.; Chambers, CJ.; Sockolov, ME. & Chin, DL. (2011) Psoriasis and Hypertension Severity: Results from a Case-Control Study. *PLoSONE.*,6(3),e18227. doi:10.1371/journal.pone.0018227.

Browning, JD.; Szczepaniak, LS.; Dobbins, R. & al. (2004). Prevalence of hepatic steatosis in an urban population in the United States: impact of ethnicity. *Hepatology*, 40(6),1387–1395.

Capeau, J. (2008). Insulin resistance and steatosis in humans. *Diabet and Metab.*, 34,649-57.

Channual, J.; Wu, JJ. & Dann, FJ. (2009) Effects of tumor necrosis factor-alpha blockade on metabolic syndrome components in psoriasis and psoriatic arthritis and additional lessons learned from rheumatoid arthritis. *Dermatol Ther.*,22(1),61-73.

Chung, CP.; Oeser, A.; Raggi, P.; Gebretsadik, T.; Shintani, AK.; Sokka, T.; Pincus, T.; Avalos, I. & Stein, CM. (2005). Increased coronary-artery atherosclerosis in rheumatoid arthritis: relationship to disease duration and cardiovascular risk factors. *Arthritis Rheum.*, 52(10),3045-53.

Das, UN. (2001). Is obesity an inflammatory condition? *Nutrition.*, 17,953-966.

Day, CP. & James OFW. Steatohepatitis: a tale of two "hits"?. (1998). *Gastroenterology*, 114(4),842–845.

de Luca, C. & Olefsky, JM. (2008). Inflammation and Insulin Resistance. *FEBS Lett.*, 582(1), 97–105.

Esposito, K. & Giugliano, D. (2004). The metabolic syndrome and inflammation: association or causation? *Nutr Metab Cardiovasc Dis.*,14,228-232.

Ferretti, G.; Alleva, R.; Taus, M.; Simonetti, O.; Cinti, B.; Offidani, AM.; Bossi, G. & Curatola, G. (1994). Abnormalities of plasma lipoprotein composition and fluidity in psoriasis. *Acta Derm Venereol*.,74(3),171-5.

Galic, S.; Oakhill, JS. & Steinberg, GR. Adipose tissue as an endocrine organ. (2010). *Mol Cell Endocrinol.*,316,129-139.

Gisondi, P.; Cotena, C.; Tessari, G. & Girolomoni, G. (2008). Anti-tumour necrosis factor-alpha therapy increases body weight in patients with chronic plaque psoriasis: a retrospective cohort study. *J Eur Acad Dermatol Venereol*.,22(3), 341-4.

Gisondi, P.; Tessari, G.; Conti, A.; Piaserico, S.; Schianchi, S.; Peserico, A.; Giannetti, A. & Girolomoni, G. (2007). Prevalence of metabolic syndrome in patients with psoriasis: a hospital-based case-control study. *Br J Dermatol*., 157(1),68-73.

Henseler, T. & Christophers, E. (1995). Disease concomitance in psoriasis. *J Am Acad Dermatol*., 32,982–6.

Herron, MD.; Hinckley, M.; Hoffman, MS.; Papenfuss, J.; Hansen, CB., Callis, KP. & al. (2005). Impact of obesity and smoking on psoriasis presentation and management. *Arch Dermatol*.,141,1527–34.

Hotamisligil, GS. (2003). Inflammatory pathways and insulin action. *Int J Obes.,* 27(S), 53.

Jones, SM.; Harris, CPD.; Lloyd,J.; Stirling, CA.; Reckless, JPD & McHugh, NJ. (2000). Lipoproteins and their subfractions in psoriatic arthritis: identification of an atherogenic profile with active joint disease. *Ann Rheum Dis.*,59,904–909

Kashihara, H.; Lee, J.; Kawakubo, K.; Tamura, M. & Akabayashi, A. (2009). Criteria of Waist Circumference According to Computed Tomography-Measured Visceral Fat Area and the Clustering of Cardiovascular Risk Factors. *Circ J.*,73,1881-1886.

Kershaw, EE. & Flier, JS. Adipose tissue as an endocrine organ. (2004). *J Clin Endocrinol Metab*, 89,2548-2556.

Kissebach, AH.; Vydelingum, N.; Murray, R.; Evans, DJ.; Kalkhoff, RK. & Adams PW. (1982). Relation of Body Fat Distribution to Metabolic Complications of Obesity. *J Clin Endocrinol Metab.*,54,254-260.

Mallbris, L.; Ritchlin, CT. & Stahle, M. (2006). Metabolic disorders in patients with psoriasis and psoriatic arthritis. *Curr Rheumatol Rep*,8,355–63.

Marchesini, G.; Bugianesi, E.; Forlani, G. & al. (2003). Nonalcoholic fatty liver, steatohepatitis, and the metabolic syndrome. *Hepatology*., 37(4),917–923.

Marra, M.; Campanati, A.; Testa, R. & al. (2007). Effect of Etanercept on insulin sensitivity in nine patients with psoriasis. *Int J Physiol Pharmacol*, 20(4),731-36.

McTernan, C.L.; McTernan, P.G.; Harte, A.L.; Levick, P.L.; Barnett,A.H. & Kumar, S. (2002) Resistin, central obesity, and type 2 diabetes. *Lancet*, 359, 46–47.

Neimann, AL.; Shin, DB.; Wang, X.; Margolis, DJ.; Troxel, AB. & Gelfand, JM. (2006). Prevalence of cardiovascular risk factors in patients with psoriasis. *J Am Acad Dermatol*.,55, 829–35.

Okorodudu, DO.; Jumean, MF.; Montori, VH.; Romero-Corral, A.; Somers, VK.; Erwin, PJ. & Lopez-Jimenez, F. (2010). Diagnostic performance of body mass index to identify obesity as defined by body adiposity: a systemic review and meta-analysis. *Internation Journal of Obesity*.,34,791-799.

Papatheodoridis, GV.; Goulis, J.; Christodoulou, D. & al. (2007). High prevalence of elevated liver enzymes in blood donors: associations with male gender and central adiposity. *European Journal of Gastroenterology & Hepatology*.,19,(4), 281–287.

Saraceno, R.; Schipani, C.; Mazzotta, A.; Esposito, M.; Di Renzo, L.; De Lorenzo, A. & Chimenti, S. (2008). Effect of anti-tumor necrosis factor-alpha therapies on body mass index in patients with psoriasis. *Pharmacol Res*.,57(4),290-5.

Satapathy, SK.; Garg, S.; Chauhan, R.; Sakhuja, P.; Malhotra, V.; Sharma, BC. & Sarin, SK. (2004). Beneficial effects of tumor necrosis factor-alpha inhibition by pentoxifylline on clinical, biochemical, and metabolic parameters of patients with nonalcoholic steatohepatitis. *Am J Gastroenterol*.,99(10),1946-52.

Sommer, DM.; Jenisch, S.; Suchan, M; Christophers, E. & Weichenthal, M. (2006). Increased prevalence of the metabolic syndrome in patients with moderate to severe psoriasis. *Arch Dermatol Res*,(298):321–8.

Staidle, JP.; Dabade, TS. & Feldman, SR. (2011). A pharmacoeconomic analysis of severe psoriasis therapy: a review of treatment choices and cost efficiency. Expert Opin Pharmacother., Jul 8.

Sterry, W.; Barker, J.; Boehncke, WH.; Bos, JD.; Chimenti, S.; Christophers, E.; De La Brassinne, M.; Ferrandiz, C.; Griffiths, C.; Katsambas, A.; Kragballe, K.; Lynde, C.; Menter, A.; Ortonne, JP.; Papp, K.; Prinz, J.; Rzany, B.; Ronnevig, J.; Saurat, JH.; Stahle, M.; Stengel, FM.; Van De Kerkhof, P. & Voorhees J. (2004). Biological therapies in the systemic management of psoriasis: International Consensus Conference. *Br J Dermatol*.,151 Suppl 69,3-17.

Teunissen, MBM.; Piskin, G.; Res, PCJM.; De Groot, M.; Picavet, DI.; De Rie, MA. & Bos, JD. (2007). State of the art in the immunopathogenesis of psoriasis. *G Ital Dermatol Venerol*., 142, 229-42.

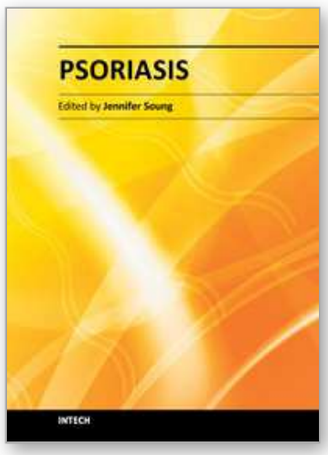
Tsochatzis, S.; Manolakopoulos, GV.; Papatheodoridis, A. & Archimandritis,AJ. (2009). Insulin resistance and metabolic syndrome in chronic liver diseases: old entities with new implications. *Scandinavian Journal of Gastroenterology*, 44(1),6–14.

Vanni, E.; Bugianesi, E.; Kotronen, A.; De Minicis, S.; Yki-Jarvinen, H. & Svegliati Baroni, G. (2010). From the metabolic syndrome to NAFLD or vice versa?. *Dig Liver Dis*, 42(5),320-30.

Wajchenberg, BL. (2000). Subcutaneous and visceral adipose tissue: their relation to the metabolic syndrome. *Endocr Rev*.,21,697-738.

Weinberg, JM. (2003). An overview of infliximab, etanercept, efalizumab, and alefacept as biologic therapy for psoriasis. *Clin Ther*.,25(10),2487-505.

Wu, JJ. & Tsai, TF. (2008). Recurrent hyperglycemia during adalimumab treatment in a patient with psoriasis. *Arch Dermatol.,*144(10),1403-4.



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We hope you enjoy and find the information provided in this book useful in your research or practice. We urge that you continue to keep abreast of the new developments in psoriasis and share your knowledge so that we may advance treatment and cures of psoriasis.

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