Short Communication

CARDIOVASCULAR COMORBIDITIY IN PSORIASIS

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Abstract

The chronic inflammatory nature of psoriasis is also thought to predispose patients to other diseases with an inflammatory component, the most notable being cardiovascular and metabolic (cardiometabolite) disorders. This concept is supported by studies showing that psoriasis is associated with cardiovascular risk factors like diabetes, obesity, hypertension, dyslipidemia, smoking and diseases including MI. Given the increased prevalence of cardiovascular co morbidities in patients, dermatologists treating psoriasis need to approach the disease as a potentially multisystem disorder and must alert these patients to the potentially negative effects of their disease.

Key Words: *Carsiovascular disease, metabolic syndrome, psoriasis*

Introduction

Psoriasis is a chronic immune-inflammatory-mediated disease affecting approximately 1–3% of the population worldwide.[1] There is an overwhelming data to substantiate that psoriasis is not just a disease of skin and joints but is a systemic, inflammatory autoimmune disease that is connected with a range of comorbidities such as Crohn's disease, depression, sleep-apnoea, etc.[2,3] Environmental risk factors including streptococcal pharyngitis, stressful life events, low humidity, drugs, HIV infection, trauma, smoking, alcohol, obesity have been associated with psoriasis and psoriatic arthritis.[4,5]

The chronic inflammatory nature of psoriasis is also thought to predispose patients to other diseases with an inflammatory component, the most notable being cardiovascular and metabolic (cardiometabolite) disorders. This concept is supported by studies showing that psoriasis is associated with cardiovascular risk factors such as diabetes, obesity, hypertension, dyslipidemia, smoking, and diseases including myocardial infarction (MI).[6–10] A recently population-based study showed an increased rate of death at a younger age in patients with severe psoriasis.[11]

Pathogenetic Linkage

An antigen-presenting cell (APC) identifies and processes a yet-to-be identified antigen in the skin. APC then presents, in a major histocompatibility class II-restricted fashion, processed antigen and activates naive T-cells in the local lymph nodes, resulting in a clonal expansion of the Th1 arm under the influence of interleukin (IL)-2.

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The result of T-cell activation is release of IFNγ, the defining cytokine of type 1 T-cells, and also TNF, which is co-produced by activated type 1 T-cells. Due to effect of these cytokines, there is keratinocyte proliferation, neutrophil migration, potentiation of Th-1 type response, angiogenesis, up-regulation of adhesion molecule, and epidermal hyperplasia.[12,13]

During the rupture of an unstable atherosclerotic plaque, activated inflammatory cells within the plaque secrete matrix proteases leading to the degradation of the extracellular matrix proteins, weakening of the fibrous cap, leading to rupture, and thrombus formation. The activation of the inflammatory process and upregulation of Th1-mediated cytokine cascades (with IFN-γ, TNF-α, IL-1, and IL-6) is a probable trigger for acute coronary syndromes as well as psoriasis, as described above.[14]

Recently, cytokines interleukin-12 and interleukin-23 have also been implicated in the pathogenesis of psoriasis. IL-12 promotes growth and differentiation of naïve T-cells into Th1 and cytotoxic T-cells (Tc)1 where as IL-23rd imulates survival and proliferation of a unique set of T-cells, termed Th17 cells.[15,16] Recent studies shows that IL-12 is thought to provide a link between inflammation and Th1-type cytokine production in coronary atherosclerosis.[17]

Linking Psoriasis with Cardiovascular Disease and Metabolic Syndrome

Recent studies have shown that psoriasis is associated with

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atherosclerosis. This association applies to coronary artery, cerebrovascular, and peripheral vascular diseases and results in increased mortality.[18-21]

The presence of psoriasis is an independent risk factor for subclinical atherosclerosis. Psoriasis patients had impaired endothelial function and thicker intima-media thickness (IMT) of the common carotid artery, compared with the healthy control subjects.[22]

A spiral computer tomography study demonstrated a significantly higher prevalence and severity of coronary artery calcification as an indicator for CVD in patients with psoriasis compared to control subjects without psoriasis, supporting the notion that psoriasis is an independent risk factor for CVD.[23] Interestingly, the excessive relative risk of MI seems to persist even after adjustment for the major risk factors for CVD, suggesting that psoriasis might be considered as an independent risk factor for MI.[9]

Recently, a descriptive cohort study has shown that patients with psoriasis had higher risks of incident myocardial infarction, angina, atherosclerosis, peripheral vascular disease, and stroke.[24] Moreover, the prevalence of MI is higher in mild and severe psoriasis than in patients without psoriasis.[25,26]

In recent years, there have been studies which have linked psoriasis to metabolic syndrome.[27-30] In addition, one study reviews all the recent studies regarding epidemiology and pathophysiology connecting psoriasis and metabolic syndrome.[31]

Patients with psoriatic arthritis have a very high prevalence of metabolic syndrome, which predisposes them to an increased risk of both diabetes and atherosclerotic cardiovascular disease (ASCVD).[32]

The metabolic syndrome is a constellation of lipid and nonlipid cardiovascular risk factors of metabolic origin. Multiple groups have issued slightly different criteria for definition of the metabolic syndrome. The most widely accepted criteria are issued by the Adult Treatment Panel III which defines metabolic syndrome as the presence of at least three of the following conditions.[33]

- Elevated waist circumference
  Men ≥40 inches (102 cm)
  Women ≥35 inches (88 cm)
- Elevated triglycerides ≥150 mg/dL
- Reduced HDL cholesterol
  Men < 40 mg/dL
  Women <50 mg/dL
- Elevated blood pressure <130/85 mmHg
- Elevated fasting glucose <110 mg/dL or use of medication for hyperglycemia

Despite different criteria used to define metabolic syndrome across studies a significant association between metabolic syndrome and psoriasis was consistently found.[34]

The Relationship Between Psoriasis and Cardiometabolite Risk Factors

In one large population study from the UK that included over 130,000 patients with psoriasis, Neimann *et al*. used the General Practice Research Database and found higher rates of diabetes mellitus, hypertension, hyperlipidemia, obesity, and smoking in patients with psoriasis than in controls. Furthermore, those patients with severe psoriasis had higher rates of obesity and diabetes than those with mild psoriasis.[8]

Obesity

Persons with BMI >25 kg/m^2 and >30 kg/m^2 are defined as overweight and obese, respectively. The suggested BMI cutoff point for Asian Indians is 23 kg/m^2. Young Asian Indians with a mean (SD) BMI of 23 kg/m^2 were found to have a higher abdominal and visceral fat mass and were significantly more insulin resistance as compare to BMI-matched Caucasian subjects.[35]

Patients with severe psoriasis have a higher BMI that is directly related to the risk of cardiovascular mortality.[36]

The combination of obesity and psoriasis is an important health care concern. Both conditions are associated with chronic inflammation, which may exacerbate the cardiovascular disease pathogenic process such as atherosclerosis.[37]

Lifestyle factors such as decreased physical activity due to social stigma or depression, the presence of psoriatic arthritis and increase alcohol consumption may further exacerbate the obesity in patients with psoriasis.[38-40]

Diabetes

According to recent studies, psoriasis is related to diabetes, independent of factors such as obesity, hypertension, and hyperlipidemia. Diabetes is more prevalent in patients with severe psoriasis than in those with mild disease.[8]

TNF-α which plays a central role in the immunopathogenesis of psoriasis may be involved in the increased insulin resistance observed in patients with psoriasis.

In one Indian study of the systemic disorders associated with psoriasis, diabetes showed the highest frequency with an *O*/*E* ratio of 2.6.[41] Furthermore, data from large cross-sectional studies also reveal that, when compared with control subjects, the risk for diabetes mellitus rises substantially in patients with psoriasis, with a 62% increase in risk noted in patients with severe psoriasis.[8,42]

A recent large observational study shows that the risk of incident DM was increased for patients with psoriasis as compared with a psoriasis-free comparison group.[43]

Dyslipidemia

Several studies, although with relatively small patient

populations, have demonstrated that an atherogenic dyslipidemic profile consisting of increased levels of total cholesterol, triglycerides, low-density lipoprotein cholesterol, oxidatively modified lipids, and decreased levels of HDL cholesterol is exhibited by patients with psoriasis.[40,44,45]

It has been proposed that lipoprotein (a) [Lp(a)] which is a genetically determined molecule whose role has been implied in cardiovascular pathology, and whose levels have been reported to be elevated in patients with psoriasis may be a factor contributing to an increased cardiovascular risk in patients with psoriasis.[46]

Hypertension

The link between psoriasis and hypertension may be related to the increased levels of angiotensin-converting enzyme, endothelin-1 (ET-1) and rennin in patients with psoriasis.[47,48]

More recently, Sommer *et al*. reported that inpatients with psoriasis had a >3-fold higher prevalence of hypertension compared with inpatients without psoriasis (OR: 3.3; 95% CI: 2.4–4.4).[10]

One prospective study demonstrated an increased risk of diabetes and hypertension in women with psoriasis, even after adjustment for age, BMI, alcohol intake, and smoking status.[49]

Smoking

Smokers are more likely to have psoriasis than nonsmokers, and smoking plays a role in developing the condition.[38]

Recently, current or past smoking was associated with an increased risk of incident psoriasis in the large Nurses' Health Study II (20) and was an independent risk factor for psoriasis in another large study of patients in the UK.[39,50]

Alcohol

Animal studies and the measurements of human transdermal alcohol monitoring devices show that skin alcohol concentrations can reach such levels that induce proinflammatory cytokine production and enhance lymphocyte and keratinocyte proliferation.[51]

A recent study showed that smoking and alcohol intake are independently associated with severe forms of psoriasis. Disease severity is correlated with smoking in both genders as well as with alcohol intake in female patients.[52] In another study, modest but significant association between physical severity of psoriasis and weekly alcohol consumption was shown.[53]

Conclusion

Psoriasis is associated with comorbidities that include metabolic syndrome and increased cardiovascular risk. These conditions share etiologic features and health consequences that directly correlate with the severity of psoriasis.

Given the increased prevalence of comorbidities in patients, dermatologists who treat psoriasis especially more severely affected patients need to approach the disease as a potentially multisystem disorder and must alert these patients to the potentially negative effects of their disease.

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