Association between Psoriasis and the Metabolic Syndrome

A A Cross-Sectional Study

A.D. Cohen a, b M. Sherf a, b L. Vidavsky a D.A. Vardy a, b J. Shapiro a J. Meyerovitch a, c

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Abstract

Background: Previous reports have shown an association between inflammatory diseases such as systemic lupus erythematosus or rheumatoid arthritis and the metabolic syndrome. Recent data demonstrate that psoriasis is an inflammatory disease, suggesting that psoriasis may be one of the components of the metabolic syndrome. Methods: A cross-sectional study was performed utilizing the database of the Clalit Health Services. Case patients were defined as patients with a diagnosis of psoriasis vulgaris. Controls were randomly selected from the list of Clalit Health Services enrollees. The proportions of components of the metabolic syndrome (ischemic heart disease, hypertension, diabetes, obesity and dyslipidemia) were compared between case and control patients by univariate analyses. χ² tests were used to compare categorical parameters between the groups. Logistic and linear regression models served to measure the association between psoriasis and the metabolic syndrome. Results: The study included 16,851 patients with psoriasis and 48,681 controls. In the case group, there were 8,449 men (50.1%) and 8,402 women (49.9%), with a mean age of 42.7 years (SD = 20.3, range = 2–111). Diabetes mellitus was present in 13.8% of the patients with psoriasis as compared to 7.3% of the controls (p < 0.001). Hypertension occurred in 27.5% of the patients with psoriasis and in 14.4% of the controls (p < 0.001). Obesity was present in 8.4% of the patients with psoriasis as opposed to 3.6% of the controls (p < 0.001). Ischemic heart disease was observed in 14.2% of the patients with psoriasis as compared to 7.1% of the controls (p < 0.001). Multivariate models adjusting for age, gender and smoking status of the patients demonstrated that psoriasis was associated with the metabolic syndrome (OR = 1.3, 95% CI = 1.1–1.4), ischemic heart disease (OR = 1.1, 95% CI = 1.0–1.2), diabetes mellitus (OR = 1.2, 95% CI = 1.0–1.3), hypertension (OR = 1.3, 95% CI = 1.2–1.5) and obesity (OR = 1.7, 95% CI = 1.5–1.9). Limitations: The study is designed as a case-control study, thus an association alone was proven and not causality. Conclusion: Our findings demonstrate a possible association between psoriasis and the metabolic syndrome. Appropriate treatment of the metabolic syndrome may be an important part of the management of patients with psoriasis.

Introduction

The metabolic syndrome is a combination of diabetes mellitus, hypertension, obesity and hyperlipidemia. The pathophysiology of the metabolic syndrome is attributed to insulin resistance. Systemic inflammation occurs in patients with the metabolic syndrome, which is evident as a number of inflammatory markers such as TNF are often increased [1–3]. Recent studies have demonstrated an association between inflammatory diseases such as systemic lupus erythematosus or rheumatoid arthritis and the metabolic syndrome [4–6].

Psoriasis is an inflammatory disorder of the skin and in some patients the joints. The inflammatory process in psoriasis is evident histologically by the lymphocytic infiltration of the dermis and the neutrophilic infiltration of the epidermis. Inflammatory cytokines are elevated in patients with psoriasis with increased secretion of Th-1 cytokine. Inflammatory markers such as TNF play a role in both the metabolic syndrome and psoriasis [7–9].

Several reports have demonstrated a possible association between psoriasis and diabetes mellitus, hypertension, myocardial infarction and heart failure and obesity. However, the majority of these studies

Key Words

Metabolic syndrome · Psoriasis

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Arnon D. Cohen, MD, MPH
Dermatology Service, Southern District
Clalit Health Services, PO Box 4317
Omer 84965 (Israel)
Tel. +972 8 625 4202, Fax +972 8 625 4237, E-Mail arcohen@clalit.org.il

Dermatology Service, Southern District
Clalit Health Services, PO Box 4317
Omer 84965 (Israel)
Tel. +972 8 625 4202, Fax +972 8 625 4237, E-Mail arcohen@clalit.org.il

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Table 1. Proportion of diseases in the metabolic syndrome in patients with psoriasis and in the control group

<table>
<thead>
<tr>
<th></th>
<th>Psoriasis patients (n = 16,850)</th>
<th>Control group (n = 48,677)</th>
<th>OR</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic heart disease</td>
<td>2,387 (14.2)</td>
<td>3,479 (7.1)</td>
<td>2.1 [2.0–2.3]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>2,324 (13.8)</td>
<td>3,556 (7.3)</td>
<td>2.0 [1.9–2.1]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>4,627 (27.5)</td>
<td>7,017 (14.4)</td>
<td>2.2 [2.2–2.3]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Obesity</td>
<td>1,419 (8.4)</td>
<td>1,768 (3.6)</td>
<td>2.4 [2.3–2.6]</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Figures in parentheses are percentages and values in square brackets represent 95% CI.

were anecdotal, based on small sample sizes or not controlled [10–15].

The purpose of the current study was to assess the association between psoriasis and the metabolic syndrome using data mining techniques utilizing the Clalit Health Services (CHS) database.

Methods

The study was designed as a retrospective case-control study using data mining techniques utilizing the CHS database. The CHS is the largest managed care organization in Israel, serving a population of approximately 3,800,000 enrollees. The CHS has a comprehensive computerized database that has continuous real-time input from pharmaceutical, medical and administrative computerized operating systems.

In the CHS database, the diagnoses of chronic diseases such as ischemic heart disease, diabetes, hypertension and psoriasis are validated by systematic methodology. The CHS perform the process of validation by logistic checks (such as comparing diagnoses from various sources) and by direct validation of the diagnoses by the treating physicians of each patient.

Case patients were defined as having psoriasis when there was at least 1 documented diagnosis of psoriasis in the medical records between the years registered by CHS physicians. The diagnosis of psoriasis was confirmed by use of medications which are explicitly prescribed in Israel to patients with psoriasis (e.g. Neotigason) or use of PUVA therapy. Three control patients were randomly selected for each case patient. The control group was randomly selected from the list of CHS enrollees, sampling the general population. The diagnoses of obesity, hypertension, diabetes and ischemic heart disease were taken from the CHS chronic diseases registry. The metabolic syndrome was defined in the current study as obesity plus any 2 of the following criteria: raised triglycerides, reduced HDL cholesterol, hypertension or diabetes.

The proportions of patients with metabolic-syndrome-associated diseases (diabetes, hypertension, ischemic heart disease, dyslipidemia, obesity) were compared between case and control patients by univariate analyses. $\chi^2$ tests were used to compare categorical and t tests to compare continuous parameters between the groups. Logistic and linear regression models were applied to measure the association between psoriasis and the metabolic syndrome. Statistical analysis was performed with SPSS software.

Results

The study included 16,851 patients with psoriasis and 48,681 controls. The mean age of the case patients was 42.7 years (SD = 20.3, range = 2–111) and that of the controls was 51.0 years (SD = 19.1, range = 0–100). In the case group, there were 8,449 men (50.1%) and 8,402 women (49.9%). In the control group, there were 23,363 men (48.0%) and 25,318 women (52.0%).

The proportions of ischemic heart disease, diabetes mellitus, hypertension and obesity were increased in patients with psoriasis as compared to the control group (table 1). Total cholesterol and triglyceride levels were increased in patients with psoriasis as compared to the control group. HDL cholesterol level was decreased in patients with psoriasis as compared to the control group (table 2).

The associations between psoriasis and hypertension, diabetes or obesity were more pronounced in the younger age group [e.g. the OR for obesity in patients with psoriasis as compared to the control group were 2.2 (95% CI = 1.7–2.7) in patients below the age of 35 years and 1.6 (95% CI = 1.4–1.8) in patients above the age of 65 years]. The association between psoriasis and ischemic heart disease was statistically significant only in patients above the age of 35 years.

The associations between psoriasis and hypertension, diabetes or obesity were similar in females and males. The association between psoriasis and ischemic heart disease was more pronounced in males (OR = 2.3, 95% CI = 2.2–2.5) as compared to females (OR = 1.8, 95% CI = 1.7–2.0).

Multivariate models adjusting for age and gender demonstrated that psoriasis was associated with the metabolic syndrome, ischemic heart disease, diabetes mellitus, hypertension, obesity and dyslipidemia (table 3).

Discussion

In the current study we observed that psoriasis was associated with ischemic heart disease, diabetes mellitus, hypertension, dyslipidemia and obesity. Our study supports a previous observation by Hesseler and Christophers [11], Herron et al. [12], Mallbris et al. [15] and other reports that have been published previously [10, 13, 14]. Although our study was conducted retrospectively, we propose that there is an association between psoriasis and the metabolic syndrome.

The metabolic syndrome is a combination of diabetes mellitus type 2 (or insulin resistance), hypertension, central obesity and combined hyperlipidemia.
(elevated LDL, decreased HDL, elevated triglycerides). The diagnosis of the metabolic syndrome includes the diagnosis that has been recently revised by the International Diabetes Federation [16] as central obesity (according to ethnicity-specific waist circumference) plus any 2 of the following criteria: (1) Raised triglycerides: $>150$ mg/dl (1.7 mmol/l), specific treatment for this lipid abnormality. (2) Reduced HDL cholesterol: $<40$ mg/dl (1.03 mmol/l) in men, $<50$ mg/dl (1.29 mmol/l) in women, specific treatment for this lipid abnormality. (3) Raised blood pressure: systolic $>130$ mm Hg, diastolic $>85$ mm Hg, treatment of previously diagnosed hypertension. (4) Raised fasting plasma glucose: fasting plasma glucose $>100$ mg/dl (5.6 mmol/l), previously diagnosed type 2 diabetes.

Each component of the syndrome is a target for a specific treatment. Drugs that decrease insulin resistance (metformin and thiazolidinediones) and altered lifestyle reduce hyperglycemia and improve blood pressure and lipid profile. Previous studies have shown an increased risk of atherosclerosis in patients with inflammatory diseases such as systemic lupus erythematosus and rheumatoid arthritis [4–6]. Our study demonstrates that patients with psoriasis have a significant association with each of the components of the metabolic syndrome. The possible explanation is attributed to the inflammatory state mediated by altered function of specific T cell subpopulations that occurs in patients with the metabolic syndrome and psoriasis.

Although we found a statistically significant difference in lipid levels between the case and control groups, the clinical importance may be minor as the differences are very small (table 2).

In the current study cases were recruited from a large managed care organization, using diagnoses assigned by the primary care physicians. Case patients were also identified using medications which are explicitly prescribed in Israel to patients with psoriasis (e.g. Neotigason) or PUVA therapy. Therefore it is likely that more severe cases were identified. It is possible that the association between psoriasis and the metabolic syndrome occurs only in patients with moderate to severe psoriasis and not in patients with mild psoriasis. However, this distinction is beyond the scope of the current study and should be investigated in prospective studies that include psoriasis severity as an independent variable.

The regression models were adjusted for age, gender and smoking and not for other important confounders such as genetic predisposition or alcohol consumption. This was done because there is incomplete data for these fields in the CHS database.

It is important to emphasize that association alone was proven and not causality. Cross-sectional studies are not able to establish a temporal sequence. Therefore it is not clear whether metabolic syndrome and its components are cause or consequence of psoriasis as it is also likely that patients with psoriasis change their lifestyle habits including nutrition and smoking. It is possible that the first event that occurs is the onset of psoriasis, followed by lifestyle changes that include smoking and overeating, which leads to diseases that belong to the metabolic syndrome. It is known that patients with psoriasis suffer from a high proportion of depression [17], which indicates that the task of lifestyle changes would be difficult for these patients.

Further prospective studies are needed to establish our observation. However, we propose that psoriasis has a role as a new risk factor for the metabolic syndrome.

It was observed in the multivariate models (table 3) that after adjustment for age, gender and smoking status, there was a substantial association between psoriasis and obesity or hypertension, with a less imperative association between psoriasis and diabetes or ischemic heart disease. Patients with psoriasis have excessive proportions of obesity (70%), hypertension (30%), diabetes (20%) and ischemic heart

| Table 2. Cholesterol and triglyceride levels in patients with psoriasis and in the control group |
|---------------------------------|------------------------------|----------------|----------------|
|                                | Psoriasis cases (n = 16,850) | Control group (n = 48,677) | p value |
|                                | mean SD                      | mean SD          |     |
| Total cholesterol              | 194.8 39.7                   | 193.2 40.0       | $<0.001$ |
| HDL cholesterol                | 48.3 12.9                    | 49.6 13.4        | $<0.001$ |
| LDL cholesterol                | 117.0 33.5                   | 116.2 32.5       | NS    |
| Triglycerides                  | 147.8 88.8                   | 138.5 85.1       | $<0.001$ |

Figures in parentheses are 95% CI. In each model, the ORs are adjusted with age, gender and smoking status of the subjects. The metabolic syndrome was defined in the current study as obesity plus any 2 of the following criteria: raised triglycerides, reduced HDL cholesterol, hypertension or diabetes.

| Table 3. Regression models of the association between psoriasis and diseases in the metabolic syndrome |
|---------------------------------|-----------------|
|                                | OR              |
| Metabolic syndrome             | 1.3 (1.1–1.4)   |
| Ischemic heart disease         | 1.1 (1.0–1.2)   |
| Diabetes mellitus              | 1.2 (1.0–1.3)   |
| Hypertension                   | 1.3 (1.2–1.5)   |
| Obesity                        | 1.7 (1.5–1.9)   |
| Triglyceride level             | 1.0 (1.0–1.3)   |
| HDL cholesterol level          | 0.9 (0.8–1.0)   |

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disease (10%) as compared to the general population. Thus, physicians taking care of patients with psoriasis should consider the concomitant presence of ischemic heart disease, hypertension and diabetes mellitus and obesity in their patients. A targeted intervention program may be needed in the management of patients with psoriasis, in order to identify and treat the above-mentioned disease. A register of psoriasis patients, such as offered by Schmitt-Egenolf [18], may help facilitate this task. Appropriate management of the metabolic syndrome may also play a role in the treatment of psoriasis.

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