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SHORT COMMUNICATION

Cardiovascular Risk Factors in Children and Adolescents with Psoriasis: A Case-control Study

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Population-based and case-control studies have shown that adults with psoriasis are at greater risk of developing cardiovascular comorbidity, metabolic syndrome, and endothelial dysfunction (a marker of early atherosclerosis) than healthy individuals (1–3). However, data are more limited with regards to cardiovascular risk factors in children and adolescents with psoriasis. A population-based study from Germany showed an association between juvenile psoriasis and increased prevalence of hyperlipidaemia, obesity, hypertension and diabetes (4). In addition, it has been demonstrated that there is a positive association between childhood psoriasis and overweight (5, 6). A recent study by Koebnick et al. (7) showed that obesity was associated with higher odds of psoriasis in children and adolescents. Other epidemiological data indicate that the greatest risk of myocardial infarction and incident diabetes mellitus is observed in young adult patients with severe psoriasis (8, 9).

Cardiovascular events occur rarely in children and adolescents, and therefore surrogate markers of cardiovascular disease are important for these subjects. Endothelial dysfunction is a sign of early atherosclerosis (10, 11). Microvascular endothelial function can be assessed by peripheral arterial tonometry (PAT) (12).

Up to one-third of patients with psoriasis have their disease debut during childhood, and if the presence of excess cardiovascular risk can be firmly established at that time it may warrant closer monitoring and early intervention to minimize the risk of future cardiovascular events (13). Here we measure cardiovascular risk factors in juvenile patients with psoriasis compared with healthy controls matched according to age and gender.

MATERIALS AND METHODS

Between June 2011 and July 2012, we enrolled 30 consecutive patients between the age of 10 and 18 years with plaque-type psoriasis, who were attending the dermatology outpatient clinics at Copenhagen University Hospital Gentofte, and Aarhus University Hospital. As controls, we included 30 healthy children, recruited through advertising on the website of our institution. We obtained written informed consent from the custodial parent(s) before enrolment, and the study was approved by the ethics committee of the Capital Region of Denmark (approval no. H-2-2011-008). Exclusion criteria were: smoking > 10 cigarettes per day; and other autoimmune diseases.

On enrolment, we measured the subject's weight, height, waist and hip circumferences, systolic and diastolic blood pressures, and resting heart rate. In addition, we recorded information about the duration of psoriasis, current systemic anti-inflammatory treatment and psoriatic arthritis. We assessed the severity of psoriasis with the Psoriasis Area and Severity Index (PASI). Blood was drawn in the non-fasted state for analysis of glucose, urate, high-sensitivity C-reactive protein (hs-CRP), glycated haemoglobin (HbA1c), total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, very-low-density lipoprotein cholesterol, and triglycerides.

To assess microvascular endothelial function, we measured the pulse wave amplitude before and during reactive hyperaemia by PAT using the Endo-PAT2000© device (Itamar Medical Ltd, Caesarea, Israel). We measured the reactive hyperaemia index (RHI), a measure of endothelial function, with Endo-PAT2000©-software (version 3.2.4).

For a 2-sample pooled *t*-test of a normal mean difference with a 2-sided significance level of 0.05, assuming a common standard deviation (SD) of the RHI score of 0.68 units, a sample size of 30 participants per group was required to obtain a power of at least 0.8 (80%) to detect a mean difference between the groups of 0.5 RHI units. We performed the statistical analysis with IBM SPSS software (version 19.0, Chicago, IL, USA) and GraphPad Prism (version 5.00, GraphPad Software, San Diego, CA, USA). Results are expressed as the difference between the group means and 95% confidence intervals (CIs) with associated *p*-values based on the independent samples *t*-test. Skewed variables were logarithmically transformed to improve normality for statistical purposes, and then back-transformed to their natural units. We used the Mann–Whitney test to compare continuous variables between the groups in case normality did not improve after logarithmic transformation of skewed variables, and these data are presented as median (interquartile range). A $p < 0.05$ was considered statistically significant.

RESULTS

Demographics and group comparisons are shown in Table I. The groups were matched according to age and gender, and there was no difference in smoking status. Median (interquartile range) PASI was 1.7 (0.6–3.0). Five patients (17%) received systemic anti-inflammatory treatment with methotrexate and/or biologics and 3 (10%) had psoriatic arthritis.

Body mass index (BMI) (mean difference 1.7 kg/m^2, 95% CI 0.1–3.2), abdominal circumference (mean difference 6 cm, 95% CI 2–10), systolic blood pressure (mean difference 6 mmHg, 95% CI 1–11), plasma glucose (mean difference 0.4 mmol/l, 95% CI 0.01–0.9), and hs-CRP were significantly higher ($p < 0.05$) in patients with psoriasis than in controls. There was no difference between the groups with regards to RHI, height, weight, hip circumference, diastolic blood pressure, resting heart rate, urate, HbA1c, and lipid levels.

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Table I. *Clinical and biochemical characteristics of the study population*

	Psoriasis $n=30$	Controls $n=30$	Difference in means (95% CI)	p-value
Boys/girls, *n*	16/14	15/15		0.8
Age, years, mean ± SD	14.5 ± 2.3	14.3 ± 2.1		0.476
Current smokers, *n* (%)	1 (3.3)	0		
Psoriasis Area and Severity Index, median (IQR)	1.7 (0.6–3.0)	–		
Duration of psoriasis, years, median (IQR)	3.5 (2–10)	–		
Current systemic anti-inflammatory treatment, *n* (%)	5 (17)	–		
Psoriatic arthritis, *n* (%)	3 (10)	–		
Height, cm, mean ± SE	162 ± 2	164 ± 2	–2 (–8–4)	0.462
Weight, kg, mean ± SE	53.5 ± 2.7	50.8 ± 2.0	2.7 (–3.9–9.4)	0.408
Body mass index, kg/m^2, mean ± SE	20.3 ± 0.6	18.7 ± 0.5	1.7 (0.1–3.2)	0.036
Abdominal circumference, cm, mean ± SE	72.0 ± 1.8	66.0 ± 1.0	6.0 (2–10)	0.004
Hip circumference, cm, mean ± SE	87.0 ± 1.4	83.5 ± 1.4	3.5 (–0.5–7.5)	0.082
Systolic blood pressure, mmHg, mean ± SE	105 ± 2	99 ± 2	6 (1–11)	0.023
Diastolic blood pressure, mmHg, mean ± SE	66 ± 2	64 ± 1	2 (–2–6)	0.354
Resting heart rate, beats per min, mean ± SE	75 ± 2	77 ± 2	–2 (–7–4)	0.611
Reactive hyperaemia index, median (IQR)	2.03 (1.53–2.19)	1.69 (1.25–2.00)		0.083*
Glucose, mmol/l, mean ± SE	5.3 ± 0.2	4.9 ± 0.1	0.4 (0.01–0.9)	0.043
Urate, mmol/l, mean ± SE	0.25 ± 0.0	0.25 ± 0.0	0	
High-sensitivity C-reactive protein, mg/l, median (IQR)	0.78 (0.01–1.77)	0.01 (0.01–0.35)	–	0.011*
Glycated haemoglobin, %, mean ± SE	5.25 ± 0.11	5.19 ± 0.04	0.06 (–0.17–0.29)	0.596
Total cholesterol, mmol/l, mean ± SE	3.8 ± 0.1	3.9 ± 1.4	–0.1 (–0.5–0.3)	0.702
HDL cholesterol, mmol/l, mean ± SE	1.25 ± 0.05	1.29 ± 0.06	–0.05 (–0.20–0.10)	0.519
LDL cholesterol, mmol/l, mean ± SE	2.1 ± 0.1	2.2 ± 0.1	–0.1 (–0.4–0.3)	0.67
VLDL cholesterol, mmol/l, median (IQR)	0.4 (0.2–0.6)	0.4 (0.3–0.4)	–	0.913*
Triglycerides, mmol/l, mean ± SE	0.96 ± 0.09	0.95 ± 0.10	0.02 (–0.24–0.28)	0.876

HDL: high-density lipoprotein; LDL: low-density lipoprotein; VLDL: very-low-density lipoprotein; IQR: interquartile range.
*Independent-samples Mann–Whitney test.

DISCUSSION

We show that children and adolescents with psoriasis had significantly higher BMI, abdominal circumference, systolic blood pressure, plasma glucose, and hs-CRP compared with healthy controls matched according to age and gender.

Decreased endothelial function has been reported in adults with more severe psoriasis compared with healthy controls (3). However, our data showed that PAT in children and adolescents with mild-to-moderate psoriasis, was comparable to that of healthy controls. Indeed, we also reported recently that PAT variables were not altered in adults with mild-to-moderate psoriasis (14). More studies are warranted to assess the impact of PAT investigations in subjects with more severe psoriasis.

Psoriasis appears to be an independent risk factor for the development of atherosclerosis and cardiovascular disease, and it is likely that the persistent systemic low-grade inflammation contributes to this association (15). The children and adolescents in the present study had only mild-to-moderate psoriasis, but their hs-CRP levels were suggestive of a systemic inflammatory state.

Cardiovascular risk assessment is currently advised for adult patients with moderate-to-severe psoriasis. Based on the current evidence, we believe that children with psoriasis and their parents should be informed of the association between psoriasis and cardiovascular risk, and that a healthy lifestyle should be encouraged in these patients.

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