Comorbidities in patients with palmoplantar plaque psoriasis

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Background: Psoriasis has been shown to be associated with several comorbidities. Whether the palmoplantar subtype of plaque psoriasis carries similar risks for comorbidities as generalized plaque psoriasis remains to be defined.

Objective: To examine the association between palmoplantar plaque psoriasis and comorbidities known to be associated with generalized plaque psoriasis.

Methods: We retrospectively compared the prevalence of comorbidities previously found to be associated with generalized plaque psoriasis among 163 patients with palmoplantar plaque psoriasis who had been treated with topical psoralen and ultraviolet A from 2009 to 2017 and a cohort of 781 control individuals. Each patient with psoriasis was matched according to sex and age (±1 year) with up to 5 control individuals. Conditional logistic regression was used to evaluate the associations after matching.

Results: Diabetes mellitus (odds ratio [OR], 2.296), cardiovascular disease (OR, 1.797), and most remarkably, mood disorders (OR, 6.232) were significantly associated with palmoplantar plaque psoriasis. Dyslipidemia, hypertension, and psoriatic arthritis were more frequent among patients with palmoplantar plaque psoriasis, but those associations did not reach statistical significance.

Limitations: The retrospective nature of this study, the fact that some data were collected through a survey questionnaire, and the relatively small sample size suggest the need to validate the present data in a prospective manner. Additionally, within the psoriasis group, patients were assessed for the presence of comorbidities during the whole follow-up period, whereas the comorbidities of individuals in the control group were assessed during a baseline visit.

Conclusions: Several comorbidities known to be associated with psoriasis vulgaris were also found to be prevalent in a series of patients with plaque palmoplantar psoriasis. Individuals affected with plaque palmoplantar psoriasis showed a particularly high risk for mood disorders. (J Am Acad Dermatol 2021;84:639-43.)

Key words: palmoplantar plaque psoriasis; psoriasis; psoriasis comorbidities; psoriatic arthritis; PUVA.

Although psoriasis is a common disorder, estimated to affect 2% to 4% of the population of the Western world,[1] it encompasses a wide range of often much rarer clinical subtypes.[2] Palmoplantar plaque psoriasis (PaPP) is defined by the presence of plaques on the palms and soles either exclusively or chiefly, and it accounts for approximately 12% of all cases of psoriasis.[3]

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A steadily growing body of data supports an association between psoriasis and a wide range of extracutaneous disorders such as the metabolic syndrome, cardiovascular disease, inflammatory bowel diseases, and mood disorders.[4] These associations are mostly evident among patients affected with moderate to severe psoriasis. Whether all clinical subtypes of psoriasis are associated with comorbidities remains to be determined. Here, we conducted a retrospective study to ascertain the prevalence of comorbidities previously found to be associated with generalized plaque psoriasis in a series of patients with PaPP.

CAPSULE SUMMARY

- Generalized plaque psoriasis is associated with multiple comorbidities.
- Similar associations, albeit of varying strengths, were identified in a series of patients with palmoplantar plaque psoriasis, suggesting the need to inform these individuals regarding risks and possible preventive measures, as currently practiced for patients with more common and generalized forms of psoriasis.

METHODS

Study design

This study was reviewed and approved by our institutional review board (0781-17-TLV) in accordance with the principles of the Declaration of Helsinki.

The medical charts of all patients treated for PaPP with topical psoralen and ultraviolet A (PUVA) from 2009 to 2017 were reviewed. All patients were naive to any form of systemic treatments. A total of 170 patients with PaPP were identified. Patients without a clear diagnosis of PaPP as defined by at least 1 dermatologist were excluded from the study (as well as patients with palmoplantar pustular psoriasis).

Each patient with PaPP was matched with up to 5 healthy individuals according to sex and age (±1 year). The healthy individuals were identified through the Tel-Aviv Medical Center Inflammation Survey, a long-term, ongoing cardiovascular cohort study evaluating 20,000 apparently healthy working adults.[5-8] This large cohort comprises individuals who attended the Tel-Aviv Medical Center for routine annual checkups (including a physician's interview and examination, blood and urine tests, and an exercise stress test). Individuals who had psoriasis or any other skin diseases were excluded from the control group in this study.

The presence or absence of each comorbid condition analyzed was determined based on the manual review of each patient's medical chart. In addition, a telephone survey was used to verify patients' history and complete missing data. The data collected included sex, age, age at psoriasis onset, presence of disseminated plaques, number of PUVA treatments, medications, family history of psoriasis, smoking and presence of comorbid diseases (psoriatic arthritis [PsA], hypertension [HTN], diabetes mellitus [DM], CVD [cardiovascular disease], mood disorder [MD], inflammatory bowel disease [IBD], and dyslipidemia). Afterward, we compared the prevalence of comorbid diseases among patients with PaPP to that among control group that was administered a screening questionnaire.

Affected status definitions

We documented the presence of comorbid conditions at any time during the follow-up period.

Patients were classified as having PaPP (plaque psoriasis evident predominantly in the palmoplantar areas, involving a body surface area of less than 5% outside the palmoplantar region) if they had ever received a diagnostic code for palmoplantar psoriasis from a dermatologist. Patients were categorized as affected with PsA, CVD, DM, HTN, MD, dyslipidemia, or IBD based on chart review, diagnostic codes, and/or the results of a telephone survey. Control individuals were categorized based on the results of a questionnaire they were administered.

CVD encompassed the following diagnoses: stable angina, unstable angina, myocardial infarction, ischemic heart disease, cardiac insufficiency, or having post–percutaneous coronary intervention status. MD was identified based on diagnostic codes, a history positive for major depression and/or stress disorders, and/or prescription for antidepression medications.

Statistical analysis

Categorical variables are reported as prevalence and percentage. Age is reported as mean and standard deviation. The chi-square test was used to compare categorical variables between the 2 groups of patients. The independent-samples *t* test was used to compare age between the groups. Univariate logistic regression was used to describe the crude odds ratio (OR), and multivariate logistic regression was applied to evaluate the association after controlling for age and sex. Patients in the groups were matched according to their sex and age (±1 year). Conditional logistic regression was used to evaluate the associations after matching. All statistical tests

Abbreviations used:

CI: confidence interval
CVD: cardiovascular disease
DM: diabetes mellitus
HTN: hypertension
IBD: inflammatory bowel disease
MD: mood disorders
OR: odds ratio
PaPP: palmoplantar plaque psoriasis
PsA: psoriatic arthritis
PUVA: psoralen and ultraviolet A

were 2 tailed, and a *P* value of less than .05 was considered statistically significant. SPSS software was used for all statistical analysis (SPSS Statistics, version 25; IBM, Armonk, NY).

RESULTS

Cohorts

We identified 170 patients who were treated with PUVA for PaPP at the Tel Aviv medical center's phototherapy unit from 2009 to 2017. In all patients, psoriasis manifested predominantly with hyperkeratotic plaques over the palms and soles. Among the patients, 52% of men and 61.5% of women had plaques exclusively on their palms and soles; the rest had extrapalmoplantar lesions involving less than 5% of the body surface. All patients were either in complete or near-complete remission at their last documented PUVA therapy.

Patients with PaPP were matched with up to 5 control individuals based on sex and age (±1 year).

Seven patients with PaPP could not be matched because of their ages (9, 16, 79, 84, 85, and 97 years) and were excluded from the study. Therefore, the psoriasis patient group consisted of 163 patients, and the control group consisted of 781 matched individuals.

The average age was 55.5 ± 14 years, and the male-to-female ratio was 0.47 to 0.53. In the control group, the male-to-female ratio was 0.47 to 0.53, and the average age was 55 ± 14 years (Table I).

Comorbidities in PaPP

Patients with palmoplantar psoriasis had an increased risk of being affected with DM, CVD, and MD after adjustment for age and sex: 14.1% of the patients with psoriasis and 5.9% of the control individuals had DM (OR, 2.296; 95% confidence interval [CI], 1.384-3.809); 13.5% of the patients with psoriasis and 7.4% of the control individuals had CVD (OR, 1.797; 95% CI 1.097-2.942), and 23.9% of the patients with psoriasis and 3.8% of the control individuals were found to have an MD (OR, 6.232; 95% CI, 3.869-10.036) (Fig 1, *A*). No report of suicide attempt was recorded.

Table I. Patient group characteristics

Parameters	Values
Age, y, mean (SD)	55 (15)
Women, n (%)	9 (53.5)
Men, n (%)	79 (46.5)
First-degree relative with psoriasis, n (%)	30 (18)
Average age at PaPP onset, y, mean (SD)	44 (18)
Average number of PUVA treatments, women/men	29/38.5
Acitretin treatment in women/men, n (%)	30 (33)/40 (51)
Extrapalmoplantar involvement in women/men, n (%)	36 (39)/41 (48)

PaPP, Palmoplantar plaque psoriasis; *PUVA*, psoralen and ultraviolet A; *SD*, standard deviation.

PsA, HTN, and dyslipidemia occurred at a higher prevalence among patients with PaPP compared to control individuals, but the differences were not statistically significant (Fig 1, *B*). Surprisingly, IBD, which has been repeatedly shown to be more prevalent among patients with psoriasis vulgaris than in the general population,[9] was not associated with PaPP (OR, 0.708; 95% CI, 0.317-1.580) (Table II).

DISCUSSION

Evidence supporting the association between psoriasis and extracutaneous conditions is accumulating.[10] The co-occurrence of psoriasis and comorbid conditions may be accounted for by intersecting or overlapping pathomechanisms.[11-24] Obesity has been shown to precede the onset of psoriasis and associated disorders and may possibly trigger them.[25,26]

However, little is currently known about the prevalence of these comorbidities and defined minor psoriasis subsets such as PaPP. Here, we show a strong association between PaPP and DM, CVD, and, most remarkably, MD. PsA, dyslipidemia, and HTN, but not IBD, were also encountered more frequently among patients with PaPP then control individuals.

Taken altogether, our data demarcate an overlapping (but not identical) group of conditions associated with PaPP and psoriasis vulgaris. Of note, these observations are, to some extent, surprising given the fact that our patients with PaPP, based on their Psoriasis Area and Severity Index scores, were not severely affected, although comorbidities have been largely reported in patients with psoriasis who have extensive disease (Psoriasis Area and Severity Index, >10) that often requires hospital admissions.[27,28] We cannot exclude the possibility that plantar involvement may have resulted in decreased exercise, which may have contributed to CVD-associated morbidity.

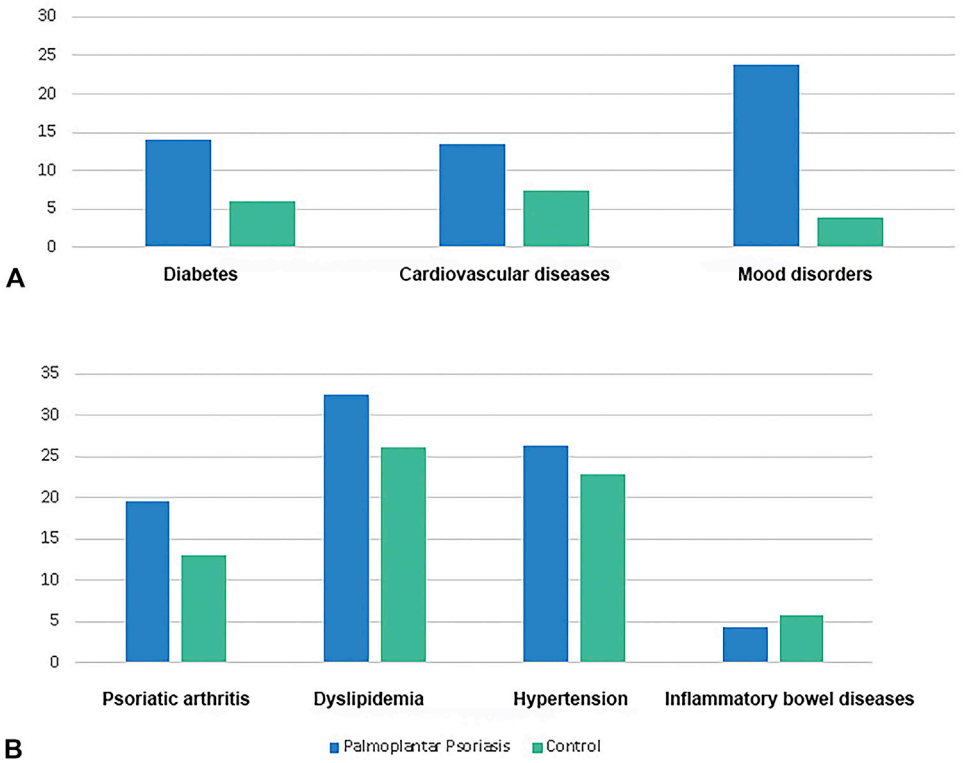

Fig 1. Comorbidities associated with palmoplantar plaque psoriasis. **A**, Significantly associated comorbidities. **B**, Other comorbidities.

Table II. Prevalence of comorbidities

Comorbidity	Palmoplantar, %	Control, %	*P* value	OR (95% CI)
DM	14.1	5.9	.001	2.296 (1.384-3.809)
CVD	13.5	7.4	.02	1.797 (1.097-2.942)
MD	23.9	3.8	<.001	6.232 (3.869-10.036)
PsA	19.6	13.1	.08	1.423 (0.953-2.124)
DL	32.5	26.1	.17	1.236 (0.913-1.672)
HTN	26.4	22.8	.49	1.125 (0.805-1.572)
IBD	4.3	5.8	.40	0.708 (0.317-1.58)

CI, Confidence interval; *CVD*, cardiovascular disease; *DL*, dyslipidemia; *DM*, diabetes mellitus; *HTN*, hypertension; *IBD*, inflammatory bowel diseases; *MD*, mood disorders; *OR*, odds ratio; *PsA*, psoriatic arthritis.

The strong magnitude of the association identified between PaPP and MD was surprising and needs to be validated in confirmatory studies. Previous reports indicated that the OR for MD in psoriasis vulgaris ranges from 1 to 3.[29-31] The fact that PaPP, which is characterized by a very limited degree of skin involvement, confers such a high risk for MD may be accounted for by the deep impact that palm involvement may have on personal and occupational functioning as well as social interactions.

The retrospective nature of this study and the relatively small study size sample clearly point to the need to confirm the present data in a prospective manner.

In summary, we show here that PaPP is associated with an overlapping set of conditions previously shown to be prevalent in patients with generalized psoriasis. The recommendations issued in this regard for patients with plaque type generalized psoriasis should therefore be considered as relevant to patients with limited PaPP as well.[10]

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