ORIGINAL ARTICLE

Quality of life and comorbidities in palmoplantar pustulosis – a cross-sectional study on 102 patients

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Abstract

Background Association of palmoplantar pustulosis (PPP) with metabolic and autoimmune diseases has been reported in mostly small case series or anecdotal cases.

Objective To assess health-related quality of life and prevalence of comorbidities in a large cohort of PPP patients.

Methods We conducted a cross-sectional study on patients with either active or past PPP. Disease severity was measured by the Palmoplantar Pustulosis Area and Severity Index (ppPASI). Quality of life was assessed by the Dermatology Life Quality Index (DLQI). Comorbidities were evaluated by medical history, blood examination, stool testing for Helicobacter pylori antigen and screening tools for depression and psoriatic arthritis.

Results A total of 102 patients (87 women, 15 men) with a mean age of 52.6 ± 14.1 years were evaluated. The mean DLQI was 7 ± 6. Comorbidities were frequent and consisted of hypercholesterolaemia (38%), hypertension (32%), obesity (27%), metabolic syndrome (26%), depression (24%), diabetes (19%), autoimmune thyroiditis (16%) and psoriatic arthritis (16%).

Conclusion Patients with PPP have an impaired quality of life and a broad range of comorbidities. Contrary to other reports, our investigation failed to show an association between PPP and coeliac disease or H. pylori infection.

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Introduction

Palmoplantar pustulosis (PPP) is a chronic relapsing skin disorder with eruption of sterile pustules on palms and/or soles. 90% of patients with PPP are women, and 95% are smokers.[1] Immunoreactivity of PPP sera with the endothelium in non-cutaneous tissues such as the parathyroid and thyroid gland indicates that PPP may be a systemic disease and prompts the search for comorbidities.[2] An association of PPP with autoimmune thyroiditis,[3] depression,[4] diabetes,[4] coeliac disease,[5] contact allergy to dental fillings,[6] dental infections,[7] tonsillitis[8] and Helicobacter pylori[9] has been reported in mostly small case series or anecdotal cases.

Studies on the quality of life in PPP patients are sparse. Palmoplantar psoriasis was shown to be associated with a greater impairment of health-related quality of life than moderate-to-severe plaque psoriasis.[10]

The aim of the present cross-sectional study was to assess the impact of PPP on the patients' health-related quality of life and the prevalence of comorbidities as well as the role of chronic infections in a cohort of 102 Austrian patients.

Materials and methods

We conducted a cross-sectional study. The charts from all PPP patients who were referred to our psoriasis outpatient clinic between 2003 and 2013 were reviewed. Palmoplantar pustulosis was diagnosed on clinical grounds. In doubtful cases, a biopsy for histopathological examination was performed. Patients in whom the diagnosis of PPP could not be established with certainty were excluded from the study. One hundred and sixty patients were eligible for enrolment in the study, of these, 58 patients were lost to follow or declined to participate. Patients were included in the study from May 2014 until June 2015. The

study was approved by our institutional review board and was conducted in accordance with the declaration of Helsinki. Informed consent was obtained from all patients. The Palmoplantar Pustulosis Area and Severity Index (ppPASI) was used to assess PPP severity in patients with active disease. The ppPASI assesses erythema (E), pustules (P) and desquamation (D) on a scale between 0 and 4 (0 = absent, 1 = mild, 2 = moderate, 3 = severe and 4 = very severe) and the extent of the affection (A) of the palms and/or soles on a scale between 0 and 6 (0 = absent, 1 = 1–9%, 2 = 10–29%, 3 = 30–49%, 4 = 50–69%, 5 = 70–89% and 6 = 90–100%). The ppPASI for one hand is calculated by the formula (E+P+D)(A)(0.2), maximum score 14.4. The ppPASI for one foot is calculated by the formula (E+P+D)(A)(0.3), maximum score 21.6.

All patients with active disease were asked to fill out the Dermatology Life Quality Index (DLQI, score 0–30; 0–1 no impairment, 2–5 small impairment, 6–10 moderate impairment, 11–20 severe impairment and 21–30 very severe impairment). Screening tools for psoriatic arthritis (Psoriasis Epidemiology Screening Tool, PEST, cut-off score ≥3) and depression (Patient Health Questionnaire-9, PHQ-9, cut-off score ≥10) were also handed out to the patients. A positive PEST result prompted referral to rheumatology for further investigation. The PHQ-9 questionnaire has a sensitivity of 86.1% and a specificity of 78.4% to detect a major depressive disorder.[11] In addition, the patients were asked about their medical history with special attention to arthritis, thyreopathy, hypertension, hyperlipidemia, diabetes, autoimmune diseases and smoking habits (pack years; packs smoked per day multiplied by years as a smoker). Waist and hip size were measured, and blood was drawn for complete blood count, blood chemistry including alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transpeptidase (GGT), fasting glucose, glycated haemoglobin (HbA1c), lipids, thyroid stimulating hormone (TSH), free thyroxine (FT4), free tri-iodothyronine (FT3), thyroglobulin (TGB), thyroperoxidase (TPO) and TSH-receptor-antibodies (ab), antinuclear antibodies (ANA), antigliadin antibodies (AGA) and antitissue transglutaminase antibodies (tTG). Stool was collected for Helicobacter pylori antigen testing using an amplified immunoassay.

Hypercholesterolaemia was defined as a total cholesterol of ≥240 mg/dL or the intake of lipid-lowering drugs. Metabolic syndrome was diagnosed on the basis of the updated 2001 National Cholesterol Education Program ATP III Guidelines.[12] For quantitative data (e.g. pack years, BMI), descriptive statistics are reported as mean ± standard deviation (SD) if data were normally distributed and as median (first quartile; third quartile) (Q1;Q3) in case of a skewed distribution. Categorical data (e.g. sex, smoking status) are reported as absolute frequency (per cent). For comorbidities, percentages with 95% Agresti–Coull Confidence intervals are reported.

Correlation between different variables was analysed by Spearman correlation. Adjustment for multiple testing was made by Bonferroni correction. Spearman correlation coefficients (Spearman's rho, rs) and adjusted *P*-values are reported.

To compare the proportion of comorbidities (e.g. diabetes, thyroid disorders) between men (n = 15) and women (n = 87) the Chi-squared test or the Fisher's exact test in case of an expected cell count <5 was applied.

All statistical analyses were performed with the software SAS 9.4 (SAS Institute, Cary, NC, USA). *P*-values below 0.05 were considered as statistically significant.

Results

One hundred and two PPP patients (87 women, 15 men) with a mean age of 52.6 ± 14.1 years were enrolled.

Twenty-three patients were in remission (mean time 4.5 years ± 3.8) at the time of examination, of these five (21,7%) were still on continuous systemic treatment (fumaric acid esters = three, adalimumab = one, cyclosporin = one). Of the 78 patients with active disease, 12 (15,4%) had systemic treatments (fumaric acid esters = nine, methotrexate = three, secukinumab = one, acitretin = one), seven (9%) were treated with oral photochemotherapy and the remaining patients with topical corticosteroids.

The mean age at disease onset was 42.1 ± 14.1 years and did not differ significantly between men and women (43 ± 14.4 and 41.9 ± 14.1). The median disease duration was 5.8 (Q1 2.2; Q 3 13.8) years. 71% of the patients were active smokers with a mean number of pack years of 23.9 ± 15.7. Daily alcohol consumption was reported by 5% of the patients, 12% consumed alcohol one to three times weekly, 46% occasionally and 37% were non-drinkers. A positive family history for psoriasis was present in 27%, psoriatic nail changes in 43% and extrapalmoplantar lesions in 19% of the patients.

The mean ppPASI of patients with active disease was 8.9 ± 6.2. Palms and soles were affected in 55.7% of the patients, 32.9% had only lesions on the soles and 11.4% only on the palms.

Quality of life

Pain or itching of the hands was present in 46.2% and 51.9% of patients, respectively, and pain during walking was reported by 25% of the patients.

The mean DLQI score was 7 ± 6 with 24.7% having a moderate and 27.3% a severe or very severe impairment of their quality of life. A significant correlation was found between ppPASI and DLQI (rs = 0.34, P = 0.046, n = 77).

Comorbidities

Antigen testing for Helicobacter pylori was positive in 18% (15/84) of the patients, more than half of them (8 of 15) had inactive disease.

A wide range of comorbidities was found in our patient cohort without significant differences between men and women. PPP patients in our study were most commonly affected by (per cent [95% CI]) hypercholesterolaemia (38 [29; 47]%), hypertension (32 [24; 42]%), obesity (27 [19; 36]%), metabolic syndrome (26 [18; 35]%), depression (24 [16; 34]%), autoimmune disease (20 [13; 28]%), diabetes (19 [12; 27]%) and psoriatic arthritis 16% [9.7; 26.3]. About 95% of patients with major depression had active PPP.

Only 10% of the patients had elevated liver enzymes. The mean values for aspartate aminotransferase (AST), alanine aminotransferase (ALT) and gamma-glutamyl transpeptidase (GGT) were 23,6 ± 8,5, 24,3 ± 13 and 28,5 ± 31, respectively.

Psoriatic arthritis and other autoimmune diseases

Regarding psoriatic arthritis, 11 patients had a known psoriatic arthritis, and two patients were revealed by PEST screening and subsequent rheumatologic evaluation ($n = 79$). One patient each had rheumatoid arthritis and SAPHO syndrome.

With respect to other autoimmune diseases, 16 patients had thyroid autoantibodies (nine without prior history), three patients inflammatory bowel disease, two patients multiple sclerosis and one patient Sjögrens disease (Table 1).

Coeliac disease

Antigliadin antibodies were detected in 11 patients, but none had tissue transglutaminase antibodies. One patient with diagnosed coeliac disease adhered to strict gluten-free diet and therefore had negative autoantibodies against gliadin, endomysium and tissue transglutaminase.

Correlation analysis

No significant correlation was found by Spearman analysis between ppPASI and sex, BMI, cigarette smoking, positive Helicobacter pylori antigen stool test, depression, arthritis or thyroid antibodies.

Table 1 Data on demographics, medical history, clinical and laboratory variables

Variables	$n = 102$*
Age (years), mean ± SD	52.6 ± 14.1
Age (years) at disease onset, mean ± SD	42 ± 14
Sex ratio (men / women)	15 / 87 (14.7/85.3)
ppPASI, mean ± SD ($n = 79$)	8.9 ± 6.2
DLQI, mean ± SD ($n = 77$)	7 ± 6
Smoking habits: current / former / never	72 / 24 / 6 (70.6 / 23.5 / 5.9)
Pack years, mean ± SD ($n = 99$)	23 ± 18.5
Positive family history of psoriasis	27 (26.5)
Extrapalmoplantar plaques	19 (18.6)
Nail involvement	44 (43.1)
BMI, mean ± SD	26.9 ± 4.9
Helicobacter pylori antigen in the stool ($n = 84$)	15 (17.9)
PEST screening ($n = 72$):	
Negative (score < 3)	55 (76.4)
Positive (score ≥ 3)	17 (23.6)
Arthritis ($n = 79$):	
Psoriatic arthritis	13 (16.5)
Rheumatoid arthritis	1 (1.3)
SAPHO syndrome	1 (1.3)
Other autoimmune diseases ($n = 99$)	20 (20.2)†
Thyroid autoantibodies‡	16
TPO-ab	12
TG-ab	8
TSH-receptor-ab	5
Inflammatory bowel disease	3
Crohn disease	2
Ulcerative colitis	1
Coeliac disease	1
Multiple sclerosis	2
Sjögrens syndrome	1

*If not indicated otherwise.
†Three patients had >1 autoimmune disease.
‡Ten patients had two thyroid antibodies.

Discussion

A few studies on PPP have been performed in the past that focused on selected comorbidities such as coeliac disease,[5] thyroid disorders,[3] diabetes and depression.[4] In the present study, we sought to accrue more comprehensive data on the epidemiology, quality of life and comorbidities in a large cohort of Austrian patients with PPP.

Onset of PPP at a mean age of 42 years, a pronounced predominance of females and smokers, the presence of extrapalmoplantar psoriatic lesions in about one fifth of the patients and a chronic course of the disease are in agreement with previous studies.

The average DLQI of patients with active disease was 7 which denotes a moderate affection of the patients' health-related quality of life. Of note, one-quarter of the patients had a DLQI of >10 reflecting a large effect on the patients' life. We also found a significant correlation between the ppPASI and the DLQI underlining the direct impact of disease severity on the patients' well-being.

PPP patients in our study were frequently affected by metabolic disorders, hypertension, depression and autoimmune diseases. As our study lacked an age-matched control group, we used the data from the Austrian Health Interview Survey (AHIS) 2014 that included 15 771 participants (6985 men, 8786 women; mean age 48 years) for comparison.[13] As shown in Figure 1, the prevalence of smoking, hypertension, obesity, depression and diabetes was much higher in our patients compared to the Austrian Health Interview Survey.

Depression is a common comorbidity in patients with psoriasis vulgaris.[14] A substantial impact on quality of life has also been demonstrated in patients with PPP with reported

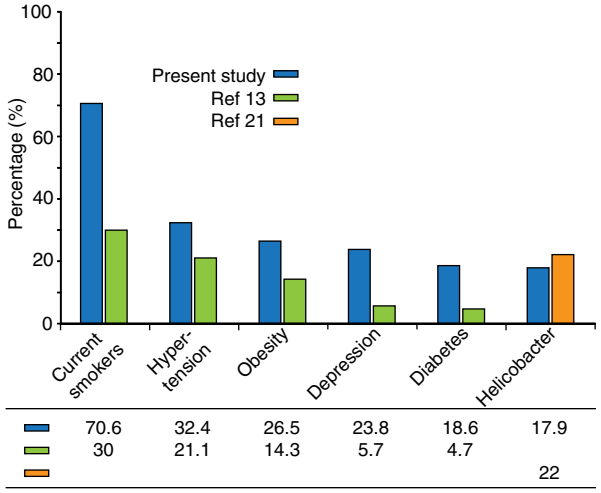

Figure 1 Comparative data on smoking habits and comorbidities.

prevalence rates of depression ranging between 13%[4] and 15%.[5] In our study, we used the PHQ-9 questionnaire to assess depression and found a four times higher prevalence as compared to the general Austrian population (23.8% vs. 5.7%).

Precise data on the association of PPP with Psoriatic arthritis (PsA) are lacking. Previous investigations reported arthritis in 8%[5] or 25.6%[15] and arthralgia in 42%[1] of PPP patients but did not specifically look for PsA. Our study included a validated screening tool for PsA followed by rheumatologic assessment in case of a positive screening result. By using this method, the prevalence of PsA in our patient cohort was 16% [9.7; 26.3], similar to that found in plaque psoriasis (20.5%[16]). However, six of our 17 PEST positive patients were not available for further rheumatologic examination.

Given the fact that most patients are not aware of liver disease and due to lack of imaging studies, liver diseases were not recorded in our sample. However, only 10% showed abnormal liver functional tests in the blood examination.

Autoimmune thyroiditis has been found at an increased rate in patients with PPP (21% reported by Michaelsson *et al.*[5]) In line with older reports, 16% of our patients had thyroid autoantibodies which underlines the necessity to screen PPP patients for latent autoimmune thyroid disease.

In contrast to a previous report from Sweden[5] with coeliac disease in seven of 123 patients (6%), our study did not reveal an association of PPP with coeliac disease. The Swedish study also reported on great improvement following gluten-free diet. In our cohort of PPP patients, only one had known coeliac disease with a high ppPASI (18.9) despite strict adherence to a gluten-free diet. Eleven further patients were found to have antigliadin antibodies, but none of them had tissue transglutaminase antibodies which are currently considered as the gold standard for coeliac disease screening.[17] Consistent with our data, a German study also failed to detect gliadin or tTG antibodies in any of 32 PPP patients.[18] The disparate findings regarding an association between PPP and coeliac disease might be explained in part by geographical, ethnic and dietary differences. A large European screening study for coeliac disease in 29.212 participants has shown a prevalence of 2.4% in Finland as opposed to only 0.3% in Italy and 0.7% in Germany.[19]

Although anecdotal cases of PPP resolution after Helicobacter pylori eradication have been published[9,20] the exact prevalence of Helicobacter pylori in PPP has never been investigated. 18% of our patients had a positive test for Helicobacter pylori antigen in the stool. In a recent Italian investigation that used the 13C-urea breath test, the prevalence of Helicobacter pylori infection was 20.3% in patients with psoriasis vulgaris and 22% in healthy controls, however patients infected by Helicobacter pylori were found to have a higher PASI score.[21] Considering the normal rate of Helicobacter pylori infection in our patient cohort and the lacking correlation with PPP severity, our data do not support a link between Helicobacter pylori infection and PPP.

The major limitation of our study is the lack of an age- and sex-matched control group. For comparison, we resorted to published epidemiological data from healthy Austrian subjects which, however, is hampered by the uneven age and sex distribution and the unusual high proportion of smokers in our study population.

In conclusion, our data show that PPP has a significant impact on the patients' quality of life and is associated with a variety of comorbidities that require early recognition and, if indicated, treatment.

References

1 Eriksson MO, Hagforsen E, Lundin IP, Michaelsson G. Palmoplantar pustulosis: a clinical and immunohistological study. *Br J Dermatol* 1998; **138**: 390–398.
2 Hagforsen E, Hedstrand H, Ronnelid J, Nilsson B, Michaelsson G. Sera from patients with palmoplantar pustulosis show immunoreactivity against endothelial cells. *Acta Derm Venereol* 2007; **87**: 261–263.
3 Rosen K, Lindstedt G, Mobacken H, Nystrom E. Thyroid function in patients with pustulosis palmoplantaris. *J Am Acad Dermatol* 1988; **19**: 1009–1016.
4 Hagforsen E, Michaelsson K, Lundgren E *et al.* Women with palmoplantar pustulosis have disturbed calcium homeostasis and a high prevalence of diabetes mellitus and psychiatric disorders: a case-control study. *Acta Derm Venereol* 2005; **85**: 225–232.
5 Michaelsson G, Kristjansson G, Pihl Lundin I, Hagforsen E. Palmoplantar pustulosis and gluten sensitivity: a study of serum antibodies against gliadin and tissue transglutaminase, the duodenal mucosa and effects of gluten-free diet. *Br J Dermatol* 2007; **156**: 659–666.
6 Yanagi T, Shimizu T, Abe R, Shimizu H. Zinc dental fillings and palmoplantar pustulosis. *Lancet* 2005; **366**: 1050.
7 Kikuchi N, Yamamoto T. Dental infection as a triggering factor in palmoplantar pustulosis. *Acta Derm Venereol* 2013; **93**: 721–722.
8 Takahara M. Clinical outcome of tonsillectomy for palmoplantar pustulosis and etiological relationship between palmoplantar pustulosis and tonsils. *Adv Otorhinolaryngol* 2011; **72**: 86–88.

9 Saez-Rodriguez M, Noda-Cabrera A, Garcia-Bustinduy M *et al.* Palmoplantar pustulosis associated with gastric Helicobacter pylori infection. *Clin Exp Dermatol* 2002; **27**: 720.
10 Chung J, Callis Duffin K, Takeshita J *et al.* Palmoplantar psoriasis is associated with greater impairment of health-related quality of life compared with moderate to severe plaque psoriasis. *J Am Acad Dermatol* 2014; **71**: 623–632.
11 Volker D, Zijlstra-Vlasveld MC, Brouwers EP, Homans WA, Emons WH, van der Feltz-Cornelis CM. Validation of the Patient Health Questionnaire-9 for Major Depressive Disorder in the Occupational Health Setting. *J Occup Rehabil* 2016; **26**: 237–244.
12 Grundy SM, Cleeman JI, Daniels SR *et al.* Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute scientific statement: executive Summary. *Crit Pathw Cardiol* 2005; **4**: 198–203.
13 Klimont J, Baldaszti E. Austrian Health Interview Survey 2014. Main results and methodological documentation. Statistics Austria, Federal Ministry of Health, Vienna, 2015.
14 Cohen BE, Martires KJ, Ho RS. Psoriasis and the Risk of Depression in the US Population: National Health and Nutrition Examination Survey 2009-2012. *JAMA Dermatol* 2016; **152**: 73–79.
15 Brunasso AM, Puntoni M, Aberer W, Delfino C, Fancelli L, Massone C. Clinical and epidemiological comparison of patients affected by palmoplantar plaque psoriasis and palmoplantar pustulosis: a case series study. *Br J Dermatol* 2013; **168**: 1243–1251.
16 Christophers E, Barker JN, Griffiths CE *et al.* The risk of psoriatic arthritis remains constant following initial diagnosis of psoriasis among patients seen in European dermatology clinics. *J Eur Acad Dermatol Venereol* 2010; **24**: 548–554.
17 Dieterich W, Laag E, Schopper H *et al.* Autoantibodies to tissue transglutaminase as predictors of celiac disease. *Gastroenterology* 1998; **115**: 1317–1321.
18 Weisenseel P, Kuznetsov AV, Ruzicka T, Prinz JC. Palmoplantar pustulosis is not inevitably associated with antigliadin antibodies. *Br J Dermatol* 2007; **156**: 1399–1400.
19 Mustalahti K, Catassi C, Reunanen A *et al.* The prevalence of celiac disease in Europe: results of a centralized, international mass screening project. *Ann Med* 2010; **42**: 587–595.
20 Martin Hubner A, Tenbaum SP. Complete remission of palmoplantar psoriasis through Helicobacter pylori eradication: a case report. *Clin Exp Dermatol* 2008; **33**: 339–340.
21 Campanati A, Ganzetti G, Martina E *et al.* Helicobacter pylori infection in psoriasis: results of a clinical study and review of the literature. *Int J Dermatol* 2015; **54**: e109–e114.

