ORIGINAL REPORT

From Onset to Outcome: A Long-term Retrospective, Single-centre Study of Guttate Psoriasis from Israel

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Guttate psoriasis is often precipitated by streptococcal infections and is generally regarded as a mild subtype of psoriasis; however, its potential associations with systemic comorbidities are insufficiently explored. In this study, we aimed to evaluate the association of guttate psoriasis with systemic comorbidities such as metabolic syndrome and psoriatic arthritis and identify factors affecting recurrence. In this retrospective single-centre study, we reviewed the data of patients with the first eruption of guttate psoriasis between 1998 and 2020 and at least 4 years of follow-up data. Demographic information and medical data (type of treatment, psoriasis flare-ups, remission of disease and development of metabolic syndrome and/or psoriatic arthritis) were retrieved. Of 395 patients included (mean follow up, 83±34.7 months), 34.9 % experienced at least one recurrence, 14.68 % had multiple recurrences, 5.6 % developed psoriatic arthritis and 8.6 % had metabolic syndrome. Male sex, topical treatment and residual disease were significant risk factors for recurrence. Psoriatic arthritis was strongly associated with multiple recurrences, while a possible association with metabolic syndrome was observed, highlighting the importance of careful long-term monitoring in this population.

Key words: first eruption; guttate psoriasis; metabolic syndrome; phototherapy; psoriatic arthritis; recurrence.

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SIGNIFICANCE

Guttate psoriasis, which is considered a mild subtype of psoriasis, was significantly associated with psoriatic arthritis and showed a possible association with metabolic syndrome, highlighting the importance of careful long-term monitoring.

Psoriasis is an inflammatory skin disease that affects 1–3% of the population worldwide and negatively influences patients' physical, psychological, and social well-being (1–4). The treatment of psoriasis follows a stepwise approach, starting with topical therapies for mild cases, progressing to phototherapy and systemic medications for moderate cases and advancing to biological agents for severe or resistant cases (5, 6).

Guttate psoriasis (GP) is an eruptive clinical variant of psoriasis that is commonly triggered by pharyngitis or other streptococcal or viral infections (including perianal infections) occurring concomitantly or preceding the lesions (7–9). It accounts for up to 30% of psoriasis cases and is more common in children and adolescents (10, 11).

The association between moderate-to-severe psoriasis and metabolic syndrome (MetS) is well documented, with a 20% to 50% prevalence (10, 12, 13). The high risk of myocardial infarction in patients with psoriasis highlights the importance of the early detection of metabolic disorders by dermatologists (13, 14). Approximately 20 % of patients with psoriasis develop psoriatic arthritis (PsA) (15, 16). Although GP is generally believed to have a better prognosis than those of the other types, 25–38.9% of cases may evolve into chronic plaque psoriasis that is mainly influenced by associations with streptococcal infection, among other factors (17–21). Galili et al. (22) reported that male sex, multiple flares, and palmoplantar involvement are predictors of persistence or progression to plaque psoriasis.

Owing to limited data from studies with small sample sizes, retrospective designs, and inconsistent follow-up periods, the clinical course and prognosis of first-episode GP remain poorly understood. Furthermore, critical aspects such as the risk of subsequent eruptions and the potential development of MetS or PsA have not been extensively explored. Therefore, in this study, we aimed to investigate the long-term outcomes of patients with a first GP eruption, focusing on the development of systemic comorbidities including MetS and PsA as well as clinical and demographic risk factors for GP recurrence.

MATERIALS AND METHODS

Study population

This retrospective single-centre study included patients who experienced their first eruption of GP and were

treated at the Tel Hashomer Sheba Medical Center, Tel Aviv University-affiliated Tertiary Care Center, between 1998 and 2020.

Data on demographic information (gender, age), medical history including: hypertension, hyperlipidaemia, ischaemic heart disease, inflammatory bowel disease, indications of streptococcal infection (antistreptolysin O or positive culture), age at disease onset, family history of psoriasis, smoking status, type of initial treatment (topical vs phototherapy), development of psoriasis flare-ups, remission of disease and development of MetS and PsA were obtained from "Chamaeleon" and/or "Magic" databases. Patients diagnosed with the first episode of GP who were followed for a minimum of 4 years were included in the study.

Patients were categorized into three groups to address the study objectives: (1) no recurrence; (2) at least one recurrence; and (3) multiple recurrences (≥2 episodes). Comparisons were made against the no-recurrence group.

Furthermore, we evaluated the time from the initial clinical diagnosis to treatment initiation to determine whether treatment initiation time is associated with subsequent eruptions and/or adverse outcomes such as MetS and PsA.

The study protocol was approved by the Institutional Review Board (IRB) and Ethics Committee of Sheba Medical Center (approval number: SMC-0195–13) and was conducted in accordance with the Helsinki Declaration. Informed consent was waived by the IRB due to the minimal risk posed to participants in this retrospective review.

Statistical analysis

Logistic regression was used to assess the association between guttate psoriasis recurrences and potential risk factors, with appropriate adjustments for multiple comparisons to maintain the integrity of statistical inference. An independent samples *t*-test compared the time from diagnosis to treatment initiation between participants by recurrence status. Pearson correlation evaluated the relationship between time to treatment initiation and the number of recurrences. All statistical tests were two-tailed, with a significance threshold set at α=0.05. Analyses were conducted using R (version 4.1.2) and RStudio (version 1.4).

RESULTS

Patients' demographics

A total of 395 patients with first GP eruption were included. The mean follow-up duration was 83 months (±34.7 months). The mean age at diagnosis was 30.1 years (±15.1 years), and the sample comprised 154 men (38.98%). Among the patients, 65.1 % (257) did not experience recurrence, 34.9 % (138) experienced one or more recurrences, and 14.68 % (58) experienced multiple recurrences (i.e. more than one recurrence).

Evaluation of risk factors for guttate psoriasis recurrences

Tables I and II describe the analyses used to determine the risk factors associated with recurrences. On evaluating risk factors associated with recurrences (Table I), male sex was significantly associated with GP recurrence (OR 1.5; 95% CI 1.01–2.33, p=0.047). Compared to topical therapy, phototherapy was significantly associated with a lower risk for recurrences (OR 0.16, 95% CI 0.06–0.44, p<0.01). Post-treatment residual disease was significantly higher among patients with recurrence (OR 4.17, 95% CI 2.65–6.56, p<0.01).

The mean age was slightly lower in the recurrence group (30.84 vs. 31.83 years), but the difference was not statistically significant (p=0.27). Smoking was more prevalent in the recurrence group (18.8% vs. 10.5%), although the difference was not statistically significant (p=0.258). Patient's family history of psoriasis showed no significant differences between

Table I. Univariate analysis of significant risk factors associated with recurrences

	No recurrence *N*=257	≥1 recurrence *N*=138	OR	CI 95%	*p*-value
Sex (%)					
Males	35.4	45.6	1.5	1.01–2.33	0.047
Females	64.6	54.4	0.5	0.42–0.99	
Treatment at first eruption (%)					
Topical	0.4	5	1		<0.01
Phototherapy	99.2	94.2	0.16	0.06–0.44	
Not available	0.4	0.8			
Residual disease (%)					
Yes	37.3	70.2	4.17	2.65–6.56	<0.01
No	61	27.5	0.23	0.15–0.37	
Not available	1.7	2.3			
Arthritis (%)					
Yes	2.3	11.6	2.77	1.03–7.44	0.043
No	31.5	56.5	0.36	0.13–0.97	
Not available	66.2	31.9			

p-values <0.05 indicate statistical significance. CI: confidence interval; OR: odds ratio.

Table II. Univariate analysis of significant risk factors associated with multiple recurrences

	No recurrence *N*=257	≥2 recurrences *N*=58	OR	Ci 95%	*p*-value
Treatment at first eruption (%)					
Topical	0.4	12.1	3.1	1.72–4	0.03
Phototherapy	99.2	87.9	0.15	0.05–0.45	
Not available	0.4	0			
Residual disease (%)					
Yes	37.3	76.8	4.82	2.49–9.32	<0.01
No	61	23.2	0.32	0.10–0.40	
Not available	1.7				
Arthritis (%)					
Yes	2.3	12	5.7	1.24–12.3	<0.01
No	31.5	58.6	1.3	0.78–2.2	
Not available	66.2	29.4			

p-values <0.05 indicate statistical significance. CI: confidence interval; OR: odds ratio.

the groups. Comorbidities, including hypertension, hyperlipidaemia, ischaemic heart disease, inflammatory bowel disease, and diabetes mellitus, were more common in the recurrence group, but the differences were not significant. Streptococcal pharyngitis was more frequent in the recurrence group (52.2% vs. 38.9%); however, the difference between groups was not statistically significant (p=0.26).

On evaluating risk factors associated with multiple recurrences (Table II), topical treatment at the first eruption was significantly associated with multiple recurrences compared to phototherapy (OR 3.1, 95% CI 1.72–4, p=0.03). Additionally, the presence of residual disease was significantly associated with multiple recurrences (OR 4.82, 95% CI 2.49–9.32, p<0.01). The proportion of male sex in the multiple recurrences group was higher compared to that in the non-recurrence group (44.8% vs 35.4%); however, this difference was not statistically significant (OR 1.45, CI 0.81–2.50, p=0.218). Smoking was also more common among those with multiple recurrences, but this association was not significant (OR 1.33, CI 0.72–2.33, p=0.081).

Association of psoriatic arthritis and metabolic syndrome with guttate psoriasis recurrences

Of the 395 patients with the first GP eruption, 5.6 % developed PsA and 8.6 % developed MetS. PsA was significantly associated with GP recurrences (OR=2.77, 95% CI 1.03–7.44, p=0.043); Table I. Similarly, PsA was significantly associated with multiple GP recurrences (OR 5.7, 95% CI 1.24–12.3, p<0.01); Table II. MetS was not significantly associated with GP recurrences.

Analysis of time from clinical diagnosis to treatment initiation

Time from clinical diagnosis to treatment initiation was not significantly different between those with a recurrence (mean 72.2 days) and those with multiple recurrences (mean 99.8 days), (p=0.798). Pearson correlation analysis was used to examine the relationship between the time from disease onset to treatment initiation and number of recurrences, and no significant correlation was found (p=0.622).

DISCUSSION

Psoriasis, particularly GP, presents a unique clinical challenge due to its variable course. This study aimed to investigate the long-term outcomes of patients experiencing their first episode of GP, with a focus on the development of systemic comorbidities such as MetS and PsA and risk factors for GP recurrences.

We found that 34.9% of the 395 patients experienced recurrence, a proportion that aligns with that in previous studies (22).

Male sex was a potential risk factor for recurrence. Additionally, we observed a significant association between phototherapy and a reduced risk of recurrence, although this finding should be interpreted cautiously, as it may have been partly influenced by baseline disease severity. The presence of residual disease after initial treatment was strongly associated with a higher likelihood of recurrence.

Regarding comorbidities, PsA was significantly associated with recurrence risk, whereas MetS was not. Notably, previous studies have suggested an association between PsA and MetS (23). Thus, although we did not establish a direct link between GP and MetS in our study, the observed association between GP and PsA may indirectly point toward a possible underlying connection with MetS that warrants further investigation. Taken together, these findings contribute to a better understanding of prognostic factors and potential long-term management of patients with GP.

Our study contributes to the understanding of GP outcomes and recurrence patterns by providing additional insights that align and contrast with the existing literature. Iskandar et al. (11) conducted a systematic review on psoriasis incidence and prevalence and noted significant variations based on age and sex, with male sex being a potential risk factor in certain

populations. This aligns with our finding that male sex was a potential risk factor for recurrence.

Svedbom et al. (17) examined the long-term outcomes of new-onset psoriasis vulgaris and emphasized the complexity of disease progression particularly in comorbidities such as PsA. Our findings extend the prognostic landscape by demonstrating a significant association between PsA and GP recurrence.

Naldi et al. (18) identified several risk factors for acute GP, including family history, stress and recent infections. Although our study did not focus on these specific triggers, the recurrence patterns observed in our study could have been influenced by similar factors; however, they were not the primary focus of our investigation.

Galili et al. (22) observed long-term outcomes in patients with new-onset GP and highlighted disease persistence and recurrence, particularly in those with specific risk factors such as male sex and multiple flares. These findings align with our results, which show that GP can persist or evolve into chronic forms. However, our study expands on Galili et al..'s study (22) by including a larger sample and specifically analysing the risk of developing MetS and PsA. This additional focus aimed to provide a more comprehensive understanding of the long-term complications associated with GP.

Furthermore, we found no significant difference in the time from diagnosis to treatment initiation according to GP recurrence status. The lack of association between time to treatment and recurrence suggests that other factors, such as sex, disease severity, or therapeutic response, may have a more substantial impact on long-term outcomes.

Overall, our study complements the existing research and offers new insights into the recurrence and long-term outcomes of GP, particularly in younger populations.

Limitations and future directions

This study had several limitations. The retrospective nature of the analysis and reliance on medical records from a single centre may have introduced selection bias and limited the generalizability of the findings. Additionally, although extensive, the follow-up period may not capture all cases of MetS or PsA that develop later in the disease course. Future prospective studies with longer follow-up periods are required to fully elucidate the association between GP and these comorbidities. Further research should also explore the underlying mechanisms driving the progression to further psoriatic eruptions, with a focus on the role of residual diseases, initial treatment selection and the immune pathways involved. Understanding these mechanisms may enable the development of targeted therapies aimed at preventing disease progression. Larger multicentre studies with multivariable analysis (including age, baseline severity, follow-up duration, treatment selection) are needed to further clarify the clinical course of GP

Conclusion

Our study provides valuable insights into the long-term outcomes of patients experiencing their first episode of GP. Male sex, initial topical treatment selection and residual disease emerged as the key risk factors for recurrence, whereas phototherapy was associated with a reduced risk of further eruptions. The significant association between GP and PsA highlights the importance of careful long-term monitoring in this population. Although MetS did not show a significant association with disease recurrence, further research with larger, multicentre cohorts to robustly assess MetS in guttate psoriasis is needed to explore the long-term implications in patients with GP. These findings underscore the importance of individualized treatment strategies and close follow-up to optimize outcomes in patients with this challenging subtype of psoriasis.

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Data availability statement: The data that supports the findings of this study are available from the corresponding author, Riad Kassem, upon reasonable request.

IRB approval status: The study protocol was approved by the Institutional Review Board (IRB) and Ethics Committee of Sheba Medical Center (approval number: SMC-0195–13) and was conducted in accordance with the Helsinki Declaration. The requirement for informed consent was waived by the IRB due to the minimal risk posed to participants in this retrospective study.

The authors have no conflicts of interest to declare.

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