ORIGINAL REPORT

An Exploratory Study to Identify Factors Associated with Recurrence of Generalized Pustular Psoriasis Flares in Adult Patients in Japan

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Generalized pustular psoriasis (GPP) is a rare, systemic inflammatory disease characterized by a heterogeneous and often unpredictable clinical course involving chronic symptoms and recurrent flares. Due to the rarity of GPP, our understanding of factors associated with flare recurrence remains unclear. Using an existing data set of adult patients with GPP in Japan, we performed univariate and multivariate analyses to investigate potential factors related to GPP flare recurrence, including patient demographics, treatment and severity of baseline flare. In total, 150 patients with a baseline flare were included in this analysis; 27.3% (*n*=41) experienced flare recurrence during the follow-up period (mean duration: 4.16 years). For the overall population, 56.0% of patients were male (*n*=84), the mean age at baseline was 55.5 years, and the mean body mass index was 24.3 kg/m². Based on the Cox proportional hazards model, comorbid diabetes mellitus, a fever of ≥38.5°C at baseline flare, experience of flare(s) prior to baseline and certain respiratory infections were associated with a higher risk of flare recurrence, similar to previously published findings. These results could help identify patients at risk of GPP flares; however, clinically applicable prediction of GPP flares requires further research in a wider population.

Key words: Diabetes mellitus; Fever; Infections; Psoriasis; Risk factors; Symptom flare up.

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SIGNIFICANCE

By analysing a population of adult patients with GPP in Japan, this study highlights several factors that could help physicians better manage and monitor patients with GPP who are potentially at higher risk of experiencing recurrence of GPP flares. These factors include a diagnosis of diabetes mellitus, high fever (≥38.5°C) at baseline flare, previous flare experience and certain respiratory infections. These results could help improve patient care for those affected by GPP, a rare and unpredictable disease with potentially fatal outcomes.

Generalized pustular psoriasis (GPP) is a rare, systemic inflammatory skin disease with a reported prevalence of 7.5–15 patients per million people in Japan (1–3). The clinical course of GPP is unpredictable and heterogeneous, characterized by chronic symptoms and recurrent, painful flares of macroscopically visible, sterile pustules on a background of erythema (2, 4–9). During a flare, patients with GPP can also present with systemic symptoms such as fever, arthralgia and fatigue (2, 4–6, 10); flare-related systemic complications may become life-threatening, most commonly from sepsis/septic shock and cardiovascular complications (11, 12). In addition to their significant clinical burden, GPP flares are associated with a considerable impact on patients' quality of life (13–15), as well as increased healthcare resource utilization compared with the general population or patients with plaque psoriasis (16–18). Furthermore, patients with GPP often present with multiple comorbidities, such as hypertension, diabetes mellitus and obesity (18–20), which further contribute to the overall disease burden on patients and healthcare systems.

While some patients may experience multiple flares per year, others may only experience a flare once every few years. Intra-patient variability is also observed regarding the extent, severity and characteristics of flares (7, 21). The unpredictability of GPP is also reflected by the wide variation of flare triggers reported in the literature, including infections, medication withdrawal, stress, menstruation and pregnancy (9, 13,

14, 21). However, identifiable triggers are not always reported; the proportion of patients with unknown triggers is estimated to be 15–62% (10). Even in larger-scale studies of patients with GPP, patterns of flare triggers are heterogeneous (1, 14, 20, 22, 23).

In summary, the rarity and heterogeneity of GPP mean that our understanding of GPP flare triggers and the factors related to flare recurrence remains limited. This study aimed to identify factors related to flare recurrence, which may in turn facilitate tailored management strategies for patients who are more at risk of experiencing a flare.

METHODS

A retrospective, longitudinal, medical chart review of patients with GPP in Japan was conducted in 2023 to describe patient characteristics, treatment patterns, and the frequency and severity of GPP flares (24). The present analysis was carried out via secondary use of the existing data from this study, which included the medical records of patients with a documented history of GPP as the primary data source and the clinical survey form submitted annually to the Ministry of Health, Labour and Welfare as the secondary data source (24, 25). Patients were included if they were diagnosed with GPP (based on the 2006 Japanese Dermatological Association diagnostic criteria) within 10 years of the approval of the study protocol by the Ethics Review Committee (Table SI) and had medical records for ≥6 months of continuous observation (Fig. S1). Patients with baseline GPP flares were investigated for recurrence of flares during the follow-up period (refer to Supplemental Material for details on the definition and time frame of flare recurrence). Several potential factors related to recurrence of GPP flares were investigated, including patient demographics, severity of the baseline flare, types of treatment, previous experience of flares before baseline and time-dependent covariates (e.g. infections during the follow-up period). Univariate and multivariate time-to-event analyses using the Cox proportional hazards model were performed to identify factors associated with recurrence of GPP flares. Covariates for the multivariate analyses were determined based on the univariate analyses and medical experts' recommendations, focusing on patient demographics and minimizing the inclusion of time-dependent variables. Variables with a *p*-value of <0.1 from univariate analyses were included in the multivariate analysis.

Statistical analysis

The hazard ratio (HR), 95% confidence interval (CI) and *p*-values were calculated to estimate the relationship between GPP flare recurrence and covariates. *p*-values of <0.05 were considered statistically significant (not adjusted for multiplicity).

RESULTS

Patient demographics

A total of 205 patients diagnosed with GPP in Japan were included in the original data set (24), and 150 patients were eligible for inclusion in this analysis (Fig. S2). Of these, 41 patients (27.3%) experienced recurrence of GPP flares during the follow-up period (mean duration of follow-up: 4.16 [standard deviation (SD): 2.56] years). The proportion of male patients was similar between the overall population (84/150; 56.0%) and the population that experienced a recurrence of GPP flare (25/41; 60.0%). The mean (SD) age at baseline was also similar: 55.5 (17.1) years in the overall population and 54.5 (16.7) years in patients with recurrent flares. The mean (SD) body mass index (BMI) at baseline was 24.3 (4.5) kg/m^2 in the overall population and 24.0 (5.0) kg/m^2 in patients with recurrent flares. In the overall population, comorbidities were observed in 106 patients (70.7%), with plaque psoriasis being the most common, reported in 65 patients (43.3%). This pattern was reflected in the recurrent flare population: 30 patients (73.2%) and 20 patients (48.8%) reported comorbidities and plaque psoriasis, respectively. In terms of treatment, a similar proportion of patients received biologics during the follow-up period: 121/150 (80.7%) in the overall population and 36/41 (87.8%) in patients with recurrent flares (Table SII). Retrospective data on GPP-related genetic mutations (*IL36RN* and *CARD14*) was available for 35 patients (23.3%) (Table SIII).

Univariate analyses

In the univariate analyses, no difference was observed in the risk of GPP flare recurrence by patients' sex or age (as a categorical or continuous variable). There was a trend towards a lower risk of flare recurrence for patients with a BMI ≥20 vs those with a BMI <20 (HR: 0.50; 95% CI: 0.23–1.08). However, no trend in flare recurrence was observed when BMI was analysed as a continuous variable, i.e. measured in 1-unit increments (**Table I**). Furthermore, there was no difference observed in the risk of GPP flare recurrence based on the presence or absence of *IL36RN* and *CARD14* mutations, although the number of patients with retrospective genetic testing data available was limited (Table I).

There was no difference in the risk of GPP flare recurrence by psoriasis-related comorbidities (e.g. plaque psoriasis). However, patients with diabetes

Table I. Potential factors associated with flare recurrence: baseline demographics

			Number of patients	Recurrence of GPP flare (%)	Hazard ratio	95% CI		*p*-value*
						Lower	Upper	
Sex	Male		84	25 (29.8)				0.8189
	Female		66	16 (24.2)	0.9290	0.4945	1.7451	
Age (years)	≤57 (median)		79	22 (27.8)				0.6681
	>57 (median)		71	19 (26.8)	1.1440	0.6184	2.1163	
	<65		99	28 (28.3)				0.9590
	≥65		51	13 (25.5)	0.9829	0.5088	1.8987	
	Per 1 year increase		150	41 (27.3)	1.0008	0.9823	1.0197	0.9303
BMI[a] (kg/m^2)	<30		100	26 (26.0)				0.4001
	≥30		14	5 (35.7)	1.5101	0.5782	3.9443	
	<25		70	19 (27.1)				0.8722
	≥25		44	12 (27.3)	1.0611	0.5149	2.1867	
	<20		19	9 (47.4)				0.0788
	≥20		95	22 (23.2)	0.4986	0.2294	1.0835	
	Per 1-unit increase		114	31 (27.2)	0.9830	0.9063	1.0663	0.6797
Presence of GPP-associated genetic mutations[b]	*IL36RN* mutation	Yes	8	2 (25.0)				0.7807
		No	15	4 (26.7)	0.7843	0.1418	4.3374	
	CARD14 mutation	Yes	2	0 (0.0)				0.9986
		No	10	2 (20.0)	>999.9999	<0.0001	–	

*The Cox proportional hazards model was used to calculate the *p*-value (*p*-values of <0.05 were considered statistically significant); [a]Information on BMI was available for 114 patients, of whom 31 (27.2%) experienced a flare recurrence; [b]Data derived retrospectively from patients with genetic test results.
BMI:body mass index; CI:confidence interval; GPP:generalized pustular psoriasis.

mellitus or immunological disorders exhibited a significantly higher risk of flare recurrence (HR: 2.89 [95% CI: 1.44–5.81] and 8.49 [95% CI: 2.00–36.05], respectively). Twenty-six patients had concomitant diabetes mellitus, of whom 11 (42.3%) experienced flare recurrence. In contrast, among the 124 patients without concomitant diabetes mellitus, 30 (24.2%) experienced flare recurrence. The number of patients with comorbid immunological disorders was very limited in this population (*n*=2); both patients had rheumatoid arthritis and were treated with topical corticosteroids (**Table II**).

The severity of the baseline flare was confirmed by the Data Review Committee based on the Japanese Dermatological Association criteria (26) – a 17-point numerical score for classifying the severity of GPP as mild (0–6), moderate (7–10), or severe (11–17) based on skin and systemic symptoms and laboratory findings. Among these criteria, high fever (≥38.5°C) was identified as a potential factor associated with a significantly increased risk of flare recurrence. Recurrence of GPP flares was observed in 8/25 patients (32.0%) with a high fever of ≥38.5°C, 23/61 patients (37.7%) with a mild fever between 37°C and <38.5°C (HR: 0.79; 95% CI: 0.35–1.78), and 9/58 patients (15.5%) with a temperature of <37°C (HR: 0.28; 95% CI: 0.11–0.74) (**Table III**).

There was no significant difference in the risk of flare recurrence associated with any type of medication use, either up to 2 months after the onset of the baseline flare or during the follow-up period (**Table IV**). Among patients who received biologics within 2 months of baseline flare onset, the class of biologics – such as

Table II. Potential factors associated with flare recurrence: comorbidities

		Number of patients	Recurrence of GPP flare (%)	Hazard ratio	95% CI		*p*-value*
					Lower	Upper	
Plaque psoriasis	No	85	21 (24.7)				0.8186
	Yes	65	20 (30.8)	1.0748	0.5805	1.9900	
Psoriasis arthritis	No	111	27 (24.3)				0.3718
	Yes	39	14 (35.9)	1.3428	0.7032	2.5642	
Erythrodermic psoriasis	No	149	41 (27.5)				0.9892
	Yes	1	0 (0.0)	<0.0001	<0.0001	–	
Focal infection	No	140	37 (26.4)				0.1725
	Yes	10	4 (40.0)	2.0629	0.7288	5.8387	
Immunological disorders[a]	No	148	39 (26.4)				0.0037
	Yes	2	2 (100.0)	8.4949	2.0016	36.0539	
Renal and urinary tract disorders	No	129	36 (27.9)				0.8848
	Yes	21	5 (23.8)	0.9332	0.3659	2.3800	
Diabetes mellitus	No	124	30 (24.2)				0.0029
	Yes	26	11 (42.3)	2.8879	1.4356	5.8093	
Cardiovascular disorders	No	137	38 (27.7)				0.7729
	Yes	13	3 (23.1)	0.8404	0.2581	2.7369	
Malignancy	No	145	40 (27.6)				0.6205
	Yes	5	1 (20.0)	0.6055	0.0831	4.4119	

*The Cox proportional hazards model was used to calculate the *p*-value (*p*-values of <0.05 were considered statistically significant); [a]Rheumatoid arthritis (both patients were treated with topical corticosteroids).
CI:confidence interval; GPP:generalized pustular psoriasis.

Table III. Potential factors associated with flare recurrence: symptoms and findings at baseline

			Number of patients	Recurrence of GPP flare (%)	Hazard ratio	95% CI		*p*-value*
						Lower	Upper	
Evaluation of skin symptoms[a]	Erythema area (overall)	≥75%	70	18 (25.7)				0.6618
		≥25 to <75%	52	15 (28.8)	1.1909	0.5983	2.3701	
		<25%	21	5 (23.8)	0.7445	0.2737	2.0252	
		None	0					
	Erythema area with pustules	≥50%	27	6 (22.2)				0.4428
		≥10 to <50%	68	22 (32.4)	1.6921	0.6853	4.1780	
		<10%	32	7 (21.9)	1.2229	0.4096	3.6508	
		None	13	3 (23.1)	0.7583	0.1877	3.0632	
	Area of oedema	≥50%	21	6 (28.6)				0.7661
		≥10 to <50%	55	18 (32.7)	1.1057	0.4351	2.8098	
		<10%	22	3 (13.6)	0.6432	0.1604	2.5801	
		None	23	7 (30.4)	0.7780	0.2532	2.3911	
Systemic symptoms and laboratory findings[a]	Fever (℃)	≥38.5	25	8 (32.0)				0.0136
		≥37 to <38.5	61	23 (37.7)	0.7895	0.3495	1.7835	
		<37	58	9 (15.5)	0.2793	0.1060	0.7359	
	White blood cell (/μL)	≥15,000	41	10 (24.4)				0.7765
		≥10,000 to <15,000	52	15 (28.8)	1.2667	0.5683	2.8235	
		<10,000	54	15 (27.8)	1.0063	0.4510	2.2451	
	C-reactive protein (mg/dL)	≥7.0	50	13 (26.0)				0.9890
		≥0.3 to <7.0	69	19 (27.5)	0.9503	0.4687	1.9266	
		<0.3	28	8 (28.6)	0.9525	0.3943	2.3009	
	Serum albumin (g/dL)	<3.0	37	7 (18.9)				0.2312
		≥3.0 to <3.8	40	15 (37.5)	1.7867	0.7256	4.3993	
		≥3.8	65	16 (24.6)	1.0174	0.4159	2.4890	
GPP severity classification (based on JDA criteria)[b]		Mild (0–6)	25	8 (32.0)				0.4138
		Moderate (7–10)	31	6 (19.4)	0.6300	0.2176	1.8240	
		Severe (11–17)	58	18 (31.0)	1.1795	0.5077	2.7400	
Severity of baseline GPP flare (confirmed by the Data Review Committee)		Mild	22	9 (40.9)				0.0661
		Moderate	44	6 (13.6)	0.3459	0.1227	0.9751	
		Severe	84	26 (31.0)	0.9577	0.4437	2.0669	
Experience of flare before baseline[a]		No	96	22 (22.9)				0.0348
		Yes	42	17 (40.5)	1.9793	1.0500	3.7308	

[a]Excluding unknown values; *The Cox proportional hazards model was used to calculate the *p*-value (*p*-values of <0.05 were considered statistically significant); [b]Analysis by GPP severity at baseline (confirmed by the Data Review Committee) was performed on the patient population for whom the severity of baseline GPP flare was grouped based on the sum of the scores of skin symptoms (0–9) and the scores of systemic symptoms and laboratory findings (0–8), excluding patients for whom any of the scores were unknown.
CI:confidence interval; GPP:generalized pustular psoriasis; JDA:Japanese Dermatological Association.

Table IV. Potential factors associated with flare recurrence: types of treatment

			Number of patients	Recurrence of GPP flare (%)	Hazard ratio	95% CI		*p*-value*
						Lower	Upper	
Treatment for GPP up to 2 months after the onset of the baseline flare	Biologics[a]	No	85	29 (34.1)				0.0837
		Yes	65	12 (18.5)	0.5509	0.2804	1.0826	
	Non-biologic systemic therapy (Category 1)[b]	No	59	18 (30.5)				0.5801
		Yes	91	23 (25.3)	0.8401	0.4532	1.5574	
	Non-biologic systemic therapy (Category 2)[c]	No	61	19 (31.1)				0.4479
		Yes	89	22 (24.7)	0.7883	0.4265	1.4570	
	Systemic steroids	No	126	35 (27.8)				0.7553
		Yes	24	6 (25.0)	1.1486	0.4805	2.7454	
	Granulocyte and monocyte adsorption apheresis	No	122	33 (27.0)				0.2492
		Yes	28	8 (28.6)	1.5862	0.7237	3.4766	
Treatment during follow-up period[d]	Systemic steroids	No	–	–				0.6224
		Yes	–	–	0.8234	0.3800	1.7842	
	Antibacterial drugs	No	–	–				0.5231
		Yes	–	–	1.2642	0.6156	2.5959	
	Topical steroids[e] (strongest)	No	–	–				0.7933
		Yes	–	–	1.0928	0.5626	2.1228	

*The Cox proportional hazards model was used (*p*-values of <0.05 were considered statistically significant); [a]Biologics comprised TNF inhibitors (adalimumab, certolizumab pegol and infliximab); IL-17 inhibitors (brodalumab, ixekizumab and secukinumab); IL-23 inhibitors (guselkumab and risankizumab); and IL-12/23 inhibitor (ustekinumab); [b]Category 1 included cyclosporine MEPC, etretinate, methotrexate, apremilast, sulfasalazine and azathioprine; [c]Category 2 included cyclosporine MEPC, etretinate and methotrexate; [d]From the date of onset of the baseline GPP flare to the date of GPP flare recurrence, or to the end of the follow-up period for patients without recurrence of GPP flares; the Cox proportional hazards model with time-dependent covariates was used to calculate the *p*-values, [e]Including steroids for the scalp.
CI:confidence interval; GPP:generalized pustular psoriasis.

tumour necrosis factor inhibitors, interleukin (IL)-17, IL-23 or IL-12/23 inhibitors – was not associated with a significant difference in the risk of flare recurrence (Table SIV). Of the 41 patients who experienced GPP flare recurrence, none of the 9 patients with a mild baseline flare received biologics, whereas 4/6 patients (66.7%) with a moderate baseline flare and 17/26 patients (65.4%) with a severe baseline flare received biologics (Table SV).

Data on infections were collected from the date of onset of the baseline GPP flare to the date of flare recurrence, or to the end of the follow-up period for patients who did not experience flare recurrence. In the univariate analysis for infections that occurred in ≥2 patients within this time frame, nasopharyngitis (HR: 3.68; 95% CI: 1.43–9.46) and pneumonia (HR: 3.34; 95% CI: 1.17–9.57) were identified as factors associated with a significantly higher risk of flare recurrence (**Table V**).

Table V. Potential factors associated with flare recurrence: infections during follow-up

Infection and infestation*	Case (n=150)	Hazard ratio	95% CI		p-value†
			Lower	Upper	
Nasopharyngitis	11 (7.3%)	3.6783	1.4299	9.4623	0.0069
Pneumonia	8 (5.3%)	3.3408	1.1661	9.5714	0.0247
Tinea pedis	7 (4.7%)	2.2157	0.5133	9.5649	0.2863
Cellulitis	6 (4.0%)	0.6787	0.0920	5.0044	0.7038
Dermatophytosis of nail	4 (2.7%)	<0.0001	<0.0001	–	0.9904
Herpes zoster	3 (2.0%)	<0.0001	<0.0001	–	0.9889
Oral herpes	3 (2.0%)	<0.0001	<0.0001	–	0.9908
Herpes simplex	2 (1.3%)	<0.0001	<0.0001	–	0.9899
Oral candidiasis	2 (1.3%)	1.5931	0.2142	11.8483	0.6492
Otitis media	2 (1.3%)	<0.0001	<0.0001	–	0.9912
Periodontitis	2 (1.3%)	<0.0001	<0.0001	–	0.9891
Pulmonary tuberculosis	2 (1.3%)	3.0971	0.4131	23.2210	0.2714
Sepsis	2 (1.3%)	1.2634	0.1732	9.2160	0.8176
Tonsillitis	2 (1.3%)	4.6893	0.6299	34.9104	0.1314
Viral infection	2 (1.3%)	2.2559	0.3009	16.9136	0.4287
Tinea versicolor	2 (1.3%)	<0.0001	<0.0001	–	0.9898
Candida infection	2 (1.3%)	5.8551	0.7567	45.3059	0.0905

*Data on infections were collected from the date of onset of the baseline GPP flare to the date of recurrence of a GPP flare, or to the end of the follow-up (for patients without flare recurrence); †The Cox proportional hazards model with time-dependent covariates was used (p-values of <0.05 were considered statistically significant).
CI:confidence interval; GPP:generalized pustular psoriasis.

Multivariate analysis

Based on the univariate analyses and clinical experience from the medical experts, potential factors associated with recurrence of GPP flares included comorbid diabetes mellitus, experience of GPP flare(s) before baseline, and fever of ≥38.5°C at baseline flare. Multivariate analysis identified diabetes mellitus (HR: 5.10; 95% CI: 1.84–14.19) and experience of GPP flare(s) before baseline (HR: 2.87; 95% CI: 1.32–6.26) as factors related to recurrence of GPP flares (**Table VI**; refer to Table SVI for the full results of the multivariate analysis).

DISCUSSION

This large-scale analysis of over 150 patients with GPP in Japan supports previous findings on the association between patient characteristics and GPP flare recurrence. For example, Ohn et al. identified diabetes mellitus as a predictor of patients with GPP requiring admission to the intensive care unit (27). Interestingly, higher levels of IL-36α and/or IL-36γ have been observed in the serum of patients with diabetes mellitus compared with individuals without (28, 29). As IL-36 cytokines are considered key mediators of inflammation in GPP (30), this inflammatory status in patients with diabetes mellitus may have contributed to the observed increased risk of GPP flares. The presence of high fever, reflecting severe systemic inflammation, was also associated with an increased risk of GPP flare recurrence in our analysis. A fever of >38.5°C during a GPP flare may increase the risk of flare recurrence, according to a predictive model developed by Xu et al. (31). With the exception of fever, we did not observe a link between the severity of the baseline flare and the risk of flare recurrence. Severity of the baseline flare was based on skin symptoms (e.g. surface area of erythema) and systemic inflammation as assessed by fever and certain laboratory findings (e.g. white blood cell count) (26). It is likely that temperature was recorded more frequently than laboratory tests, and therefore fever may be a more sensitive and reliable measure of flare severity. However, practices for recording temperature may have varied across participating centres (e.g. using the highest recorded value vs an average of multiple readings). In addition, the reason why the risk of flare recurrence was not lower in patients who experienced a mild flare at baseline may be because biologics were not prescribed for these patients. Consistent with our analysis, previous studies have found that infections are a trigger for GPP flares (9, 13, 14, 21).

There was no association between the presence of concomitant plaque psoriasis and the risk of GPP flare recurrence in this study. However, a population-based, retrospective cohort study by Choon et al. observed

Table VI. Potential factors associated with flare recurrence: multivariate analysis

		Hazard ratio	95% CI		p-value*
			Lower	Upper	
Diabetes mellitus	No				0.0018
	Yes	5.1045	1.8361	14.1910	
Experienced GPP flare before baseline	No				0.0080
	Yes	2.8714	1.3176	6.2575	

*The Cox proportional hazards model was used to calculate the p-value for covariates or time-dependent covariates (p-values of <0.05 were considered statistically significant).
CI:confidence interval; GPP:generalized pustular psoriasis.

that GPP patients without concomitant plaque psoriasis experience more flares compared with those with plaque psoriasis (32). A possible explanation for this difference in results is that 80% of the patients in our analysis were receiving biologics in specialized centres, whereas Choon et al. utilized electronic health records from primary and secondary care settings (32). Therefore, the presence or absence of plaque psoriasis may not have had much impact on the risk of flare recurrence.

There were some limitations to our study. Some of the subgroups analysed (e.g. patients with certain comorbidities) may have been too small to identify the factors related to flare recurrence risk. Additionally, due to the retrospective nature of the study, the length of the follow-up period depended on when patients were enrolled in the original data set (24), resulting in a biased distribution that could have affected the analyses. Furthermore, certain variables could have changed over time and failed to be captured. For instance, information on infections during the follow-up period was collected from medical chart review; therefore, mild or potential infections may not have been reported.

The original data set mainly included patients who were diagnosed in medical institutions that specialized in psoriasis. Therefore, the generalizability of the study results may be limited to patients who were diagnosed with the von Zumbusch subtype of GPP and treated in such institutions. In order to minimize the impact of this bias, the locations of the facilities where patients' medical records were reviewed and extracted from in the original study were dispersed throughout Japan (24).

In conclusion, this study of adult patients with GPP in Japan suggests that the presence of comorbid diabetes mellitus, high fever at baseline flare, experience of flare(s) prior to baseline and certain infections may be risk factors for GPP flare recurrence. These insights could aid physicians in identifying patients with GPP who are at higher risk of experiencing a flare, thus requiring careful monitoring and management to control their disease. Further research is needed to achieve clinically applicable predictions of GPP flares.

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