A decrease in the psychological burden of HS may improve QoL, although we did not test this. While dermatologists and healthcare providers treating HS can manage psychological aspects of the disease, most lack formal training in psychiatric diagnoses and psychopharmacology. Moreover, patients often refuse psychiatric referral.[7] Screening for psychiatric comorbidities and traits, such as the tendency towards having social anxiety, may help implement effective nonpharmacological and pharmacological interventions.[7] Thus, a multipronged approach to HS treatment, involving both pharmacological and psychosocial interventions, may help decrease HS burden and improve QoL. The use of online support groups may also provide an accessible and effective intervention for patients with HS.[8]

One limitation of the study was its sample size; however, the study was sufficiently powered to find statistically significant differences, indicative of the large effect size that the tendency towards social anxiety has on patients' lives. While there were nonresponders, the comparable demographics of respondents and nonrespondents contribute to the generalizability of the findings.

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Granulomatous slack skin: clinical characteristics, prognosis and response to therapy. A study from the Cutaneous Lymphoma French Study Group

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Dear Editor, Granulomatous slack skin (GSS) is an extremely rare subtype of mycosis fungoides (MF) with characteristic clinicohistological features.[1] Although GSS is classically described as an indolent, slowly progressive disease, its association with second lymphoma was reported in up to 48% of cases in a previous case report and literature review.[2] The effectiveness of several treatments has been described in a few single GSS case reports,[3] but their efficacy varies between reports, and complete response (CR) is exceptional. Consequently, GSS remains poorly understood and there is no consensus on its management. Thus, we conducted a retrospective multicentre study to analyse the clinical characteristics, evolution and response to therapy of GSS. This study was approved by the local institutional review board.

We included all cases ($n = 8$) found in the multicentre Cutaneous Lymphoma French Study Group database from 1998 to 2021. Seven patients (88%) were male and the median age was 29 years (range 22–70) (Table 1). One case has already been published separately.[4] The most frequently affected area was the inguinal folds (75%), but involvement of all body segments was observed (additional figure at https://figshare.com/articles/figure/fig_GSS_bjd_pdf/19945268). The search for a cutaneous T-cell clone was positive in seven cases (88%).

All patients had whole-body imaging for staging, two (25%) had histologically confirmed visceral involvement (stage IVB) and another (13%) had nodal involvement (ISCL-EORTC stage N2). Overall, three patients (38%) had advanced-stage disease (≥ IIB) at diagnosis.

The efficacy of 30 lines of treatments (of 21 different treatments in six different cases) could be characterized. At best,

Table 1 Patients' characteristics and response to therapy

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8
Sex, age (years) at diagnosis	Male, 22	Male, 26	Male, 29	Male, 24	Female, 50	Male, 70	Male, 65	Male, 28
GSS cutaneous site	Axillary folds, upper and lower limbs, trunk, gluteal area	Gluteal area, inguinal folds	Trunk, lower limbs	Inguinal fold[a]	Trunk, inguinal folds	Cervical and gluteal areas, axillary and inguinal folds	Axillary and inguinal folds	Face, axillary and inguinal folds, upper and lower limbs, trunk, gluteal area
BSA involvement[b] (%)	20	20	15–20	3	8	10	10	15
Lymph node biopsy performed	–	+[c]	–	+	+[c]	–	–	–
Visceral involvement[d]	–	+ (liver)	–	–	–	–	–	+[c] (pharynx)
Clonality analysis								
Skin (GSS)	+ (PCR)	+ (PCR)	+ (PCR)	+ (PCR)	+ (HTS)	+ (HTS)	– (PCR)	+ (PCR)
Blood	+ (PCR)	/	/	– (PCR)	/	/	/	– (PCR)
Lymph node	/	/	/	/	+ (HTS)	/	/	/
TNMB at diagnosis	T2bN0M0B0b	T3N3M1B0	T3N0M0Bx	T1N1M0B0	T1N2M0B0	T2N0M0B0	T2N0M0B0	T3NxM1B0
Stage	IB	IVB	IIB	IIA	IIA	IB	IB	IVB
Large-cell transformation[d]	–	+	–	–	–	–	–	–
Line of treatment/ best response								
1	MTX/ SD	PUVA + IFNα/ SD	TCS + topical chlormethine/ NA	Surgery + IFNα/ CR (then relapse)	MTX/ PR	TCS/ SD	TCS + topical chlormethine + MTX/ NA	IFNα/ NA
2	CS + chlorambucil/ SD	IFNγ/ SD	MTX/ NA	BXT + RT/ SD		BXT/ PR		CS/ PR
3	BXT/ SD	Vorinostat + BXT/ PR		MTX/ CR[e]				BXT/ PR
4	Chlormethine/ SD	PUVA/ SD						Romidepsin/ SD
5		IFNα/ PR						MTX/ PR
6		RT/ PR						Surgery/ PR
7		BXT/ PD						Doxorubicin/ NA
8		Gemcitabine/ PR						Gemcitabine/ SD
9		Doxorubicin/ PD						Brentuximab v./ SD
10		Brentuximab v./ PR						Mogamulizumab/ SD
11		aHSCT/ PR						Doxorubicin/ PD
Paraneoplastic events	–	+[f]	–	–	–	–	+[f,g]	+[h]

(continued)

Table 1 (continued)

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8
Other lymphoid malignancy	–	–	–	–	–	–	–	–
Follow-up (years)	4·5	15	12	9	0·5	0	0·5	7
5-year overall survival	+	+	+	+	NA	NA	NA	+
Alive at last follow-up	+	–	–	+	+	NA	+	–

aHSCT, allogeneic haematopoietic stem cell transplantation; Brentuximab v., brentuximab vedotin; BSA, body surface area; BXT, bexarotene; CR, complete response; CS, systemic corticosteroids; GSS, granulomatous slack skin; HTS, high-throughput sequencing; IFN, interferon; MTX, methotrexate; NA, not available/applicable; PCR, polymerase chain reaction; PD, progressive disease; PR, partial response; PUVA, psoralen and ultraviolet A; RT, radiotherapy; SD, stable disease; TCS, topical corticosteroids; TNMB, tumour–nodes–metastasis–blood. [a]Presenting as a single 20-cm long-axis subcutaneous mass. [b]By GSS lesions. [c]Displaying granulomas within the lymphoma infiltrate. [d]Histologically documented. [e]With an ongoing complete response 5 years after cessation of methotrexate (20 mg per week). [f]Venous thromboembolic disease. [g]Haemophagocytic lymphohistiocytosis. [h]Hypercalcaemia.

stable disease (SD) was achieved after 13 of the treatment lines (43%), partial response (PR) after 12 (40%), CR after two (7%) and progressive disease (PD) after three (10%). The treatments assessed in at least two patients were methotrexate (1 SD, 2 PR, 1 CR), bexarotene (2 SD, 1 PR, 1 PD), gemcitabine and brentuximab vedotin (1 SD, 1 PR each) and doxorubicin (2 PD) and brentuximab vedotin (1 SD, 1 PR).

The median follow-up duration was 6 years (range 0–15). One patient (stage IVB) experienced large-cell transformation. Follow-up data were available for seven patients. At the last visit, one patient (14%) was in ongoing CR 5 years after stopping methotrexate and three patients (43%) had controlled disease, including one without treatment. The other three patients (43%) had died (7–15 years after the diagnosis), two related to GSS (the two patients with stage IVB) and one, in the context of loss of follow-up, haemophagocytic lymphohistiocytosis (HLH) and uncontrolled GSS. In these three patients, potential paraneoplastic events were reported: venous thromboembolic disease (two cases), granuloma-mediated hypercalcaemia[4] and HLH. No patient experienced a second lymphoma. The 5-year survival rate was 100%.

We report the largest case series of GSS to date. Our rate of extracutaneous involvement (38%) is higher than previously reported (0%) in a series of four cases,[5] which could be partly explained by the systematic use of whole-body imaging for staging. As extracutaneous involvement has a prognostic value in MF,[1] our findings support the systematic use of whole-body imaging for GSS staging.

GSS treatment is challenging and mostly allows patients to achieve SD or PR. With a response rate of 75%, we identified for the first time the efficacy of methotrexate in a case series of GSS. Methotrexate is known to be an effective drug in MF (overall response rate of 70% among all subtypes taken together),[6] as well as in granulomatous inflammatory skin diseases, such as granuloma annulare.[7] It could thus be effective on both tumoral and granulomatous components.

No patient experienced a second lymphoma despite a median follow-up duration of 6 years, which contrasts with the 48% rate found in a literature review. This could be due to several reasons. Firstly, this previous review included mainly single case reports and was therefore prone to publication bias.[2] Furthermore, a misinterpretation of extracutaneous involvement and/or large-cell transformation of MF is possible, considering the lack of comparative clonality studies between GSS and presumed second lymphoma in these previous case reports. Secondly, as HLH is not a common finding in MF, an undiagnosed second lymphoma associated with HLH seems possible for one patient in the current series.[8]

Although the 5-year survival rate was 100%, three patients eventually died, including two related to GSS (25%), highlighting the fact that lethal forms exist but after a slow initial progression.

To conclude, in this largest series published so far, GSS is characterized by a relatively important frequency of

extracutaneous involvement, a slow but sometimes lethal course with paraneoplastic events, and challenging therapeutic management. Among MF treatments, methotrexate showed the best results.

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Ixekizumab rapidly improves inflammatory markers in patients with generalized pustular psoriasis

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Dear Editor, Generalized pustular psoriasis (GPP) is not only a skin disease but is also associated with systemic inflammation and microvascular hyperpermeability, resulting in fever and oedema. Reflecting this, laboratory data demonstrate elevated inflammatory markers and reduced serum levels of albumin.[1] As GPP is sometimes life threatening, sufficiently strong treatment with a rapid onset of effectiveness is needed, especially in patients with systemic inflammation. Although the effectiveness of ixekizumab for skin manifestations has been demonstrated,[2–4] the rapidity of its effectiveness for systemic inflammation has not been reported yet. Furthermore, to date, data on GPP are limited due to its rarity. We investigated the immediate impact of ixekizumab on systemic inflammation on a daily basis over the first 7 or 14 days in patients with GPP.

Patients with GPP with systemic inflammation treated with a loading dose of 160 mg of ixekizumab in our department from March 2017 to November 2022 were included in this study. We defined systemic inflammation as meeting all of the following criteria: body temperature (BT) $\geq$ 37 °C, white blood cell (WBC) count $\geq 10 \times 10^9$ cells L^{-1}, serum C-reactive protein (CRP) $\geq 0{\cdot}3$ mg dL^{-1} and serum albumin level $< 3{\cdot}8$ g dL^{-1}; and at least one criterion among the following: BT $\geq 38{\cdot}5$ °C, WBC count $\geq 15 \times 10^9$ cells L^{-1}, CRP $\geq 7{\cdot}0$ mg dL^{-1} and albumin $< 3{\cdot}0$ g dL^{-1}, according to the GPP guidelines in Japan.[1] Data were retrospectively collected from patients' charts. Their BT, WBC count, neutrophil count, CRP and serum albumin were evaluated daily until day 7 or 14, relative to the baseline values. As serum albumin was not measured daily in most patients, the mean of 3 days' results was calculated and assessed. This study was approved by the ethics committee of Teikyo University (19-080), and was carried out under the principles of the Declaration of Helsinki.

Nine GPP patients (one female, eight male) with systemic inflammation were analysed (https://doi.org/10.6084/m9.