


Research Letter

Assessment of Treatment Response in Cutaneous Lymphomas Using Cutaneous Ultrasound

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To the Editor,

Primary cutaneous lymphomas (PCLs) constitute a heterogeneous group of diseases with distinct clinicopathologic, phenotypic, genetic,

and prognostic characteristics.¹ TNM staging is used for the initial evaluation of PCLs (TNMB in the case of mycosis fungoides [MF] or Sézary syndrome). However, treatment evaluation and follow-up of patients with PCL lack standardization. Clinical tools such as the modified

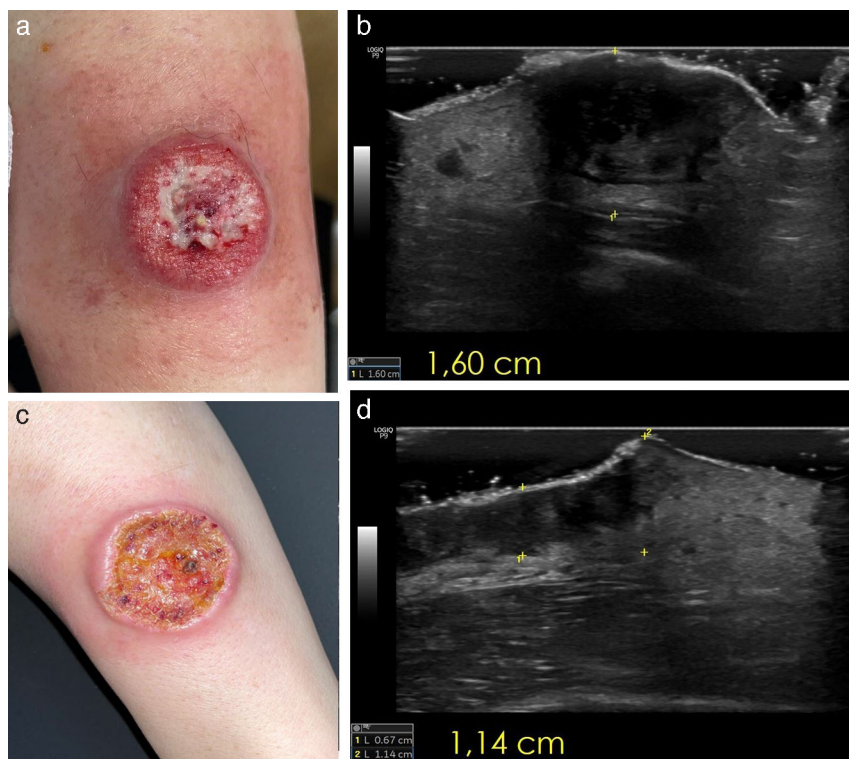


Fig. 1. Clinical and ultrasound appearance of case 1 (A–D) and case 2 (E–H). (A) Ulcerated tumoral lesion on the left arm. (B) Ultrasound appearance of the lesion: poorly demarcated heteroechoic lesion occupying the dermis and subcutis, with a thickness of 1.60 cm. (C) Clinical appearance of the lesion after 6 months. (D) Ultrasound findings after 6 months showing a thinner lesion, 1.14 cm thick. (E) Tumoral lesion on the posterior aspect of the left shoulder. (F) Ultrasound appearance of the lesion: poorly defined heteroechoic lesion occupying the dermis and subcutis, with a thickness of 1.53 cm. (G) Clinical appearance of the lesion after 6 months showing a complete response. (H) Ultrasound findings after 6 months showing a complete response.

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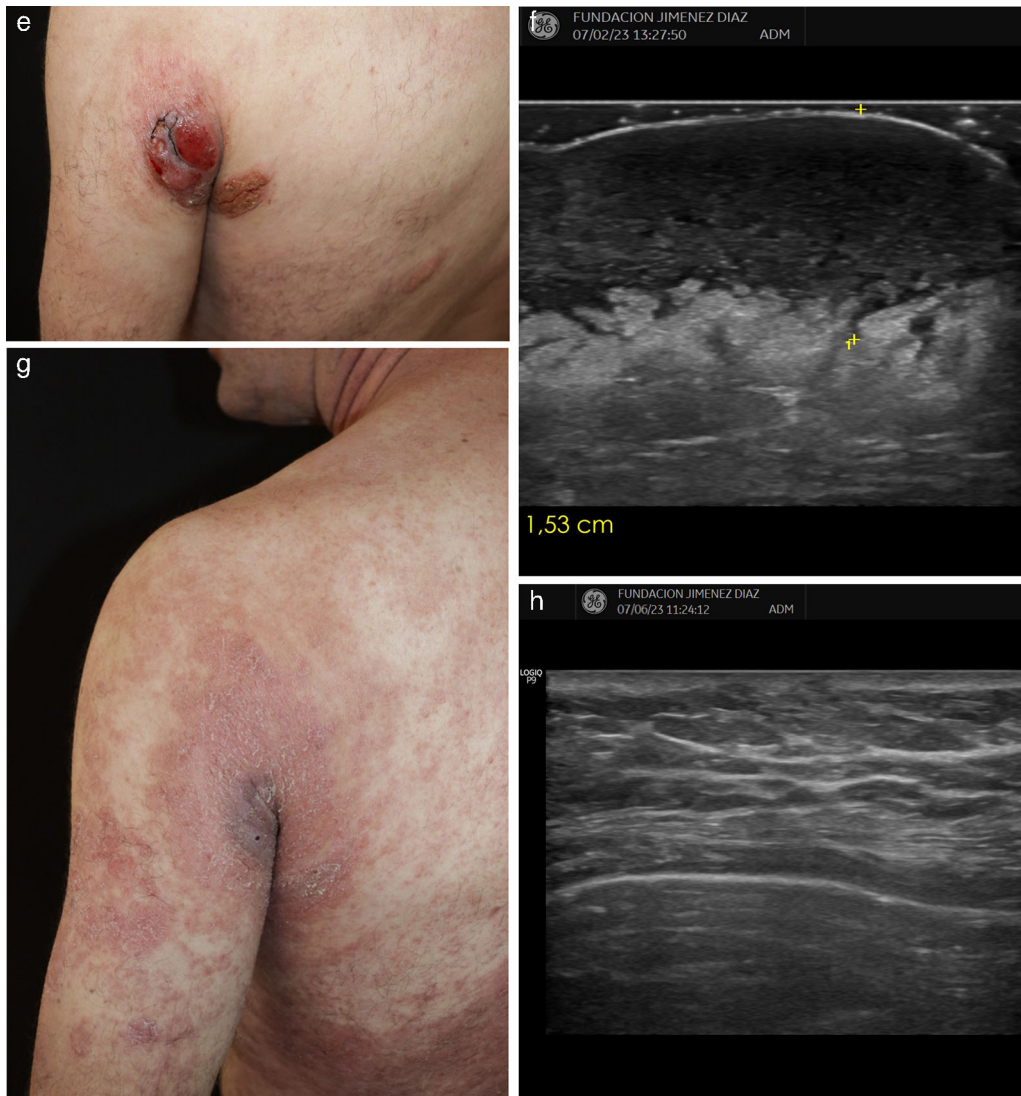


Fig. 1. (Continued)

Severity-Weighted Assessment Tool (mSWAT) are used to monitor patients, but they depend on physician subjectivity.²

Cutaneous ultrasound is increasingly used as a diagnostic tool.^{3,4} In PCLs, characteristic ultrasound patterns have been described in case series.^{5,6}

In addition to primary cutaneous lymphomas, lymphomas originating in lymph nodes may secondarily involve the skin, presenting as leukemia cutis, with considerable variability in clinical presentation.⁷ The ultrasonographic findings of these lesions have been described in several case series in the literature.⁸ However, no clinical scale is available to monitor response to treatment in this type of entity.

We hypothesize that measuring the ultrasound thickness of lymphomas involving the skin—including both primary cutaneous lymphomas and systemic lymphomas with secondary cutaneous involvement—may represent an objective method for assessing response to treatment.

Methods

We conducted a prospective case series including 13 patients with histologically confirmed primary cutaneous lymphoma or systemic lymphoma with cutaneous involvement who presented with nodular or tumoral lesions and were about to start a new treatment.

Ultrasound thickness of the lesions, measured from the epidermis to the deepest point on the ultrasound scan, was assessed at baseline and at 3 and 6 months after starting treatment. A LOGIQ P9 ultrasound scanner with a 6–15-MHz probe was used (Fig. 1).

Response to treatment was classified as follows:

- **100% reduction:** complete response
- **50–99% reduction:** partial response
- **<50% reduction:** stable disease
- **Increase in thickness:** progressive disease.

Results

Patient data are summarized in Table 1. Four patients had MF (3 in the tumor stage and 1 in the plaque stage), 3 patients had follicle center B-cell lymphoma (FCL), 3 patients were diagnosed with marginal zone B-cell lymphoproliferative disorder (MZLPD), 2 patients had CD4+ lymphoproliferative disorder (CD4-LPD), and 1 patient had angioimmunoblastic T-cell lymphoma (AITL) with cutaneous involvement. Treatments administered to each patient are detailed in Table 1.

Table 1
Data collection table including histopathologic diagnosis, baseline ultrasound thickness of the lesion, treatment administered, and ultrasound thickness after 3 and 6 months.

Cases	Diagnosis	Clinical presentation	Basal thickness	Treatment administered	Thickness after 3 months (cm)	Thickness after 6 months (cm)	Response to treatment
Case #1	Mycosis fungoides (tumor stage)	Tumor lesion	1.60 cm	Systemic mogamulizumab (1 mg/kg every 2 weeks) and intralesional pegylated interferon (0.25 mL [45 µg] every week)	1.25	1.14	Stable disease
Case #2	Primary cutaneous CD4 + small/medium T-cell lymphoproliferative disorder	Papule	0.80 cm	1 mL of intralesional triamcinolone acetate 20 mg/mL every 8 weeks	0.40	0.18	Partial response
Case #3	Mycosis fungoides (plaque stage)	Plaque	0.16 cm	Systemic gemcitabine (1000 mg/m ² on days 1 and 8 of each 28-day cycle)	0.32	0.53	Progressive disease
Case #4	Angioimmunoblastic T lymphoma	Subcutaneous nodule	0.66 cm	Biopsy excision and GEMOX chemotherapy (gemcitabine 1000 mg/m ² , oxaliplatin 100 mg/m ² , ondansetron 8 mg, dexamethasone 8 mg every 2 weeks for a total of 6 cycles)	0.00	0.00	Complete response
Case #5	Primary cutaneous marginal zone lymphoproliferative disorder	Subcutaneous nodule	0.72 cm	Intralesional rituximab (1 mL of rituximab 10 mg/mL, every week, up to 3 doses)	0.28	0.00	Complete response
Case #6	Primary cutaneous follicle center lymphoma	Plaque	0.42 cm	1 mL of intralesional triamcinolone acetate 20 mg/mL every 8 weeks	0.41	0.41	Stable disease
Case #7	Primary cutaneous follicle center lymphoma	Subcutaneous nodule	0.78 cm	Intralesional rituximab (1 mL of rituximab 10 mg/mL, every week, up to 3 doses)	0.34	0.00	Complete response
Case #8	Primary cutaneous marginal zone lymphoproliferative disorder	Plaque	0.58 cm	1 mL of intralesional triamcinolone acetate 20 mg/mL every 8 weeks	0.43	0.22	Partial response
Case #9	Mycosis fungoides (tumor stage)	Tuberous lesion	1.53 cm	Systemic gemcitabine (1000 mg/m ² on days 1 and 8 of each 28-day cycle) and intralesional brentuximab (1 mL of brentuximab vedotin 5 mg/mL every 6 weeks for up to 2 doses)	1.26	0.00	Complete response
Case #10	Mycosis fungoides (tumor stage)	Tumor lesion	1.20 cm	Subcutaneous and intralesional pegylated interferon (0.25 mL [45 µg] every week)	1.31	1.49	Progressive disease
Case #11	Primary cutaneous follicle center lymphoma	Plaque	0.62 cm	1 mL of intralesional triamcinolone acetate 20 mg/mL every 8 weeks	0.73	0.85	Progressive disease
Case #12	Primary cutaneous CD4 + small/medium T-cell lymphoproliferative disorder	Plaque	0.33 cm	1 mL of intralesional triamcinolone acetate 20 mg/mL every 8 weeks	0.16	0.00	Complete response
Case #13	Primary cutaneous marginal zone lymphoproliferative disorder	Subcutaneous nodule	0.69 cm	1 mL of intralesional triamcinolone acetate 20 mg/mL every 8 weeks	0.48	0.32	Partial response

Of the 13 patients, 2 (15.4%) presented with stable disease at follow-up visits, 3 (23.1%) showed a partial response, 5 (38.4%) achieved a complete response, and 3 (23.1%) developed progressive disease.

The mean thickness reduction calculated for all patients in the study—considering that some lesions decreased in thickness while others increased—was 0.21 cm at the 3-month follow-up visit and 0.38 cm at the 6-month follow-up visit. The mean thickness reduction between the 3-month and 6-month visits was 0.17 cm.

The lesion pattern in B-mode and vascularization in Doppler mode did not change after treatment, except in cases that showed a complete response.

Discussion

Currently, clinical scales used to monitor treatment response in PCL are subjective and do not account for the size and depth of nodular or tumoral lesions. In systemic lymphomas with skin involvement, there are no standardized clinical scales that allow clinicians to monitor disease status at the cutaneous level.

Furthermore, skin ultrasound, already established in many areas of dermatologic practice,^{3,4} has been used to identify lymphoproliferative diseases affecting the skin.^{5,6}

We consider skin ultrasound to be an effective and minimally invasive diagnostic tool that, when used in conjunction with dermatologic examination, can be very useful in the management of cutaneous lymphoproliferative disorders. In particular, measuring the thickness of tumoral lesions may represent an objective method for determining treatment response and may assist clinicians in deciding whether a change in therapeutic strategy is required. This approach may strengthen the

dermatologist's role in decision-making regarding the clinical management of patients with cutaneous lymphomas.

Conflict of interest

The authors declare that they have no conflict of interest.

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