

PRIMARY CUTANEOUS FOLLICLE CENTER LYMPHOMA AND THE HIGH-FREQUENCY ULTRASOUND AS A DIAGNOSTIC TOOL

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ABSTRACT

This case report describes the use of high-frequency ultrasound (HFUS) as a diagnostic tool for cutaneous lymphomas. Cutaneous lymphomas are classified into T-cell and B-cell lymphomas, with B-cell lymphomas characterised by few lesions with rapid growth.

The patient in this case report presented with an intensely vascularized reddish-brown nodule on the left shoulder. HFUS revealed a heterogeneous tumour lesion located in the epidermis and subcutaneous, infiltrating the adjacent muscles with increased vascularization. Computed tomography (CT) confirmed the presence of an expansive lesion. Anatomopathological examination revealed a primary cutaneous follicle center lymphoma. A finding of interest was the presence of the Grenz zone, which was seen on both ultrasound and histopathology.

While HFUS has been used for various dermatological conditions, there is limited data available on its use for skin lymphomas.

This case report highlights the potential use of HFUS as a non-invasive, repeatable, and objective monitoring tool for cutaneous lymphomas.

KEYWORDS: HIGH-FREQUENCY ULTRASOUND; CUTANEOUS LYMPHOMAS; DERMATOLOGICAL ULTRASOUND; SKIN ULTRASOUND

INTRODUCTION

Cutaneous lymphomas are classified according to their cellular origin into T-cell lymphoma and B-cell lymphoma. The annual incidence rate is 0.3 per 100,000 inhabitants. 65% of cases are T-cell, 25% are B-cell, and 10% are true histiocytic lymphomas or other rare types of lymphomas. From a dermatological perspective, B-cell lymphomas are characterized by few lesions, typically nodules or infiltrates, and they tend to exhibit relatively rapid growth.^{1,2}

There are few reports in the literature regarding the diagnosis of cutaneous lymphomas using ultrasound. Our aim with this report is to highlight high-frequency ultrasound as a potential diagnostic and monitoring tool for cutaneous lymphomas.

CASE REPORT

Male patient, 43 years old, construction worker. He denied any comorbidities, continuous medication use, or allergies. No history of smoking, alcohol consumption, or prior skin cancer. He reported having the lesion on his left shoulder for five months. The condition began a year before with the appearance of similar lesions on the right shoulder, anterior chest, and back, all of which spontaneously disappeared within a few months. He experienced a burning sensation and occasional itching in the affected area, with no change in the mobility of the affected shoulder. The patient mentioned recurrent cervical lymphadenopathy during this period. No

weight loss reported, and serologies were negative.

On physical examination, he presented with an intensely vascularized erythematous-brownish nodule, along with some papules on the surface. The lesion measured 22 x 15 cm and was located on the left shoulder. It felt warm, soft, and elastic to the touch (Figure 1). The only notable laboratory findings were elevated inflammatory markers (CRP and ESR), with no other noteworthy abnormalities.



Figure 1: Clinical lesion on the right shoulder with dermoscopy (right).

High-frequency ultrasonography (HFUS) of soft tissues was performed with an 18MHz transducer and showed a heterogeneous tumor lesion located in the epidermis and subcutaneous cellular tissue, infiltrating the adjacent muscles and with increased vascularization at SMI (Superb Micro-vascular Imaging) (Figure 2).



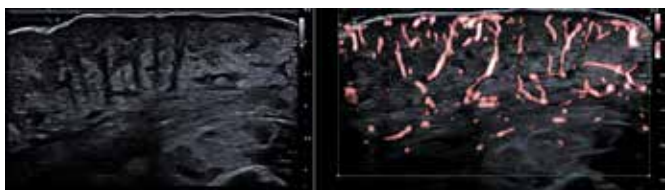


Figure 2: Heterogeneous lesion involving the dermis, subcutaneous tissue, and infiltrating, with increased vascularity on SMI.

The computed tomography (CT) scan revealed an expansive lesion in the right shoulder with soft tissue density and an infiltrative appearance. It was inseparable from the rotator cuff musculature and the deltoid muscle, measuring approximately 13.7 x 12.5 cm. It also showed some hypoattenuating areas suggestive of cystic/necrotic degeneration, along with diffuse lymphadenopathy.

The histopathological examination of the lesion revealed diffuse proliferation of atypical lymphoid cells, without affecting/respecting the epidermis, in addition to details of the inflammatory infiltrate of monomorphic cells, of medium to large size. Immunohistochemistry showed positive CD79 for all cells, B lymphocyte marker and CD10 and Bcl2: markers of systemic centrofollicular lymphoma. (Figure 3).

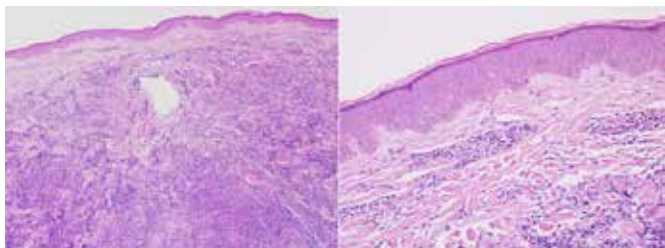


Figure 3: Histological sections of the skin reveal a highly cellular lesion involving the entire dermis and hypodermis, composed of atypical lymphocytes, including centrocytes and centroblasts, with a diffuse pattern of infiltration and rare residual follicular centers. The epidermis and a small portion of the papillary dermis (Grenz zone) are spared (HE, 10x / 40x).

One noteworthy finding in the case was the presence of the Grenz Zone (a spared dermal zone between the epidermis and the tumor) and its ultrasound translation as a hypoechoic band between the epidermis and the affected dermis (Figure 4).

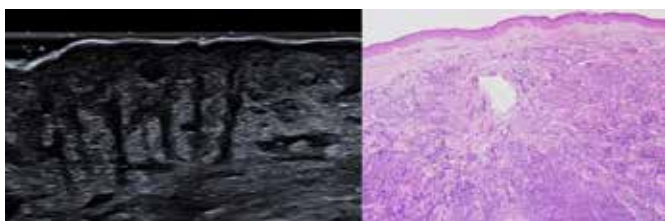


Figure 4: Correlation between ultrasound and histopathology. In both, it is possible to observe the intact epidermis and a zone of uninvolved dermis between the epidermis and the tumor (Grenz Zone).

Diagnosis of large B-cell lymphoma was confirmed, with a centrofollicular phenotype rich in T lymphocytes, with cutaneous infiltration. The patient maintained follow-up with hematology, who began the R-CHOP chemotherapy protocol.

DISCUSSION

The clinical history, physical examination and imaging tests such as HFUS help in the diagnosis of cutaneous lymphomas. Confirmation, however, is essentially obtained through histological and immunohistochemical examinations. Follicular center cells generally express CD20+, CD79a+, BCL-6+ and BCL-2- (possibly with a weak expression of BCL-2 in a minority of B cells), with variable expression of CD43 and CD106^{2,3}. Left untreated, the lesions will enlarge and may become locally aggressive⁴.

Although HFUS has been available since 1979, it is increasingly being used in a growing number of applications, including clinical and experimental dermatology.⁵

HFUS (high-frequency ultrasound) is fast, non-invasive, and reproducible, making it an objective monitoring tool. Furthermore, since ultrasound images allow for quantitative assessment of treatment response, it can be used in numerous skin conditions, including inflammatory conditions (atopic dermatitis, psoriasis); it can also be used to guide therapeutic interventions in various dermatoses. To date, the oncological use of USG-AF has focused primarily on melanoma and non-melanoma skin cancers, with little data available on its use in cutaneous lymphomas⁶.

To our knowledge, the ultrasonographic characteristics of cutaneous lymphomas and their similarity with histology have been little explored, although many articles on dermoscopic characteristics of cutaneous lymphomas have been published in recent years. Recently, ultrasonography has been proposed to monitor response to therapy in mycosis fungoides (a subtype of T lymphomas)⁷.

As ultrasound characteristics, in cutaneous lymphomas of the dermal-epidermal layer, irregularly shaped hypoechoic areas were observed. These gaps presented intralesional vascularization⁸. In the case presented, what drew attention was the presence of preserved epidermis and a strip of normal dermis between the epidermis and the tumor lesion, which is translated into histopathology as the Grenz zone. This finding, in the context of the clinical hypothesis of lymphoma, leads us to think about B-cell lymphomas and not T-cell lymphomas (since the latter group presents as a characteristic epidermotropism, that is, the involvement of the epidermis by lymphocytes T, the discovery of the Grenz zone is not expected).

CONCLUSION

We have a limited arsenal of imaging tests for the diagnostic assistance of cutaneous lymphomas, and HFUS has proven to be an important and useful tool in this role. In this report, we emphasize the potential of high-frequency ultrasound as a diagnostic and monitoring instrument for cutaneous lymphomas. Additionally, we highlight the importance

of the correlation between ultrasound and histopathology to better understand the examination findings, such as the ultrasonographic translation of the Grenz Zone in the presented case.

REFERENCES

- 1) Nunes MC, Morais JCO, Pierro APSM, Coutinho MFV, Morais JCO, Carneiro SCS, Azulay DR. Linfoma cutâneo de células B: relato de caso. *An Bras Dermatol.* 2004; 79: 715-720.
- 2) Arenas CM, Mariño ML, Calderón JE, González MI, Robayo MP. Linfoma cutâneo de células B tipo centro folicular con infiltración a médula ósea: reporte de un caso. *Rev Fac Med.* 2012; 20: 84-89.
- 3) Weba EP, de Lucena BD, Amin GA, Dias Jr LB, Pires CAA. Primary cutaneous follicle center lymphoma. *An Bras Dermatol.* 2017; 92(5): 701-703.
- 4) Willemze R, Jaffe ES, Burg G, et al. WHO-EORTC classification for cutaneous lymphomas. *Blood.* 2005; 105(10): 3768-3785.
- 5) Ballester-Sánchez R, Pons-Llanas O, Llavador-Ros M, et al. Depth determination of skin cancers treated with superficial brachytherapy: ultrasound vs. histopathology. *J Contemp Brachytherapy.* 2015; 6: 356-361.
- 6) Genovese G, Nazzaro G, Alberti Violetti S, Passoni E, Berti E. Rosacea-like cutaneous localization of small lymphocytic lymphoma unmasked by high-frequency-ultrasound. *Skin Res Technol.* 2018; 24(4): 701-703
- 7) Pola ska A, Da czak-Pazdrowska A, Olek-Hrab K, Osmola-Ma kowska A, Bowszyc-Dmochowska M, aba R, Adamski Z. High-frequency ultrasonography New non-invasive method in assessment of skin lymphomas. *Skin Res Technol.* 2018; 24(3): 517-521.
- 8) Alexander H, Miller DL. Determining skin thickness with pulsed ultrasound. *J Invest Dermatol.* 1979; 72: 17-19.
- 9) Pola ska A, Siłny W, Jenerowicz D, Kniola K, Moli ska-Glura M, Da czak-Pazdrowska A. Monitoring of therapy in atopic dermatitis observations with the use of high-frequency ultrasonography. *Skin Res Technol.* 2015; 21: 35-40.