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Primary cutaneous diffuse large B-cell lymphoma, leg type: case report

Linfoma cutâneo difuso de grandes células B, tipo perna: relato de caso

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ABSTRACT

The report describes the clinic of an aggressive non-Hodgkin lymphoma, primary cutaneous diffuse large-B cell lymphoma, leg type (PCDLBCL-LT), and shows its relevance for addressing the case of a rare lymphoma, with complex diagnosis and, in most cases, late as there are few studies reported on the subject. Since it is an aggressive pathology, it is essential to have the dissemination of knowledge to assist in the early diagnosis of the disease and, consequently, in the choice of a more effective treatment. Therefore, we seek to demonstrate the main clinical characteristics, as well as the diagnostic approach, staging, and the symptomatic and specific treatment of PCDLBCL-LT.

Key words: non-Hodgkin lymphoma; large B-cell lymphoma; immunohistochemistry.

RESUMO

Este trabalho descreve a clínica de um agressivo linfoma não Hodgkin extranodal, o linfoma cutâneo difuso de grandes células B, tipo perna (LCDCBTP) e mostra sua relevância ao abordar o caso de um linfoma raro, com diagnóstico complexo e, na maioria das vezes, tardio devido aos raros estudos sobre o assunto. Por ser uma patologia agressiva, é primordial haver maior difusão de conhecimento para auxiliar no diagnóstico precoce da doença e, consequentemente, na escolha de um tratamento mais eficaz. Portanto, buscamos demonstrar as principais características clínicas, bem como a abordagem diagnóstica, o estadiamento e o tratamento sintomático e específico do LCDCBTP.

Unitermos: *linfoma não Hodgkin; linfoma de grandes células B; imuno-histoquímica.*

RESUMEN

Este trabajo describe la clínica de un linfoma no Hodgkin extranodal agresivo, el linfoma cutáneo difuso de células B grandes, tipo pierna (LCDCGTP), y muestra su relevancia en abordar el caso de un linfoma raro, de diagnóstico complejo y, en la mayor parte de las veces, tardío ante la carencia de estudios sobre el asunto. Por ser una enfermedad agresiva, debe existir una mayor difusión de conocimiento para ayudar a su diagnóstico precoz y, consecuentemente, la selección de un tratamiento más eficaz. Por lo tanto, buscamos demostrar las principales características clínicas, así como el abordaje diagnóstico, la estadificación y el tratamiento sintomático y específico del LCDCGTP.

Palabras clave: *linfoma no Hodgkin; linfoma de células B grandes; inmunohistoquímica.*

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INTRODUCTION

Lymphomas are malignant neoplasms that develop from the clonal expansion of cells of the lymphoreticular system: B, T, and natural killer. They can be classified as Hodgkin's and non-Hodgkin's lymphomas[1]. Approximately 25% of non-Hodgkins lymphomas will affect an extranodal site with nosystemic involvement. The skin is the second most affected primary extranodal site – second only to the gastrointestinal tract – and is called cutaneous lymphoma. These lymphomas can be from T or B cells. Annually, their incidence in the United States is 1/100,000 inhabitants; from this total, 75% are T cells, with a predilection for male. Primary cutaneous B-cell lymphomas (CBCL) represent about 20%-25% of all primary cutaneous lymphomas and are more common among female[2].

CBCL are a heterogeneous group that has three main subtypes according to the World Health Organization-European Organization for Research and Treatment of Cancer (WHO-EORTC): primary cutaneous marginal zone B-cell lymphoma; primary cutaneous centrofollicular lymphoma; primary cutaneous diffuse large B-cell lymphoma, leg type (PCDLBCL-LT). This represents 4% of all cutaneous lymphoma[1, 2].

METHODOLOGY

We report a case that occurred at the Dr. Munir Raffur Municipal Hospital, Volta Redonda, Rio de Janeiro, Brazil. For theoretical support, ebooks, articles from online platforms, searches in the US National Library of Medicine National Institutes of Health (PubMed)/Medline, Tripdatabase, and in the Scientific Eletronic Library Online (Scielo) were used, based on the descriptors consulted in the health sciences Descriptors (DeCS) and in the Medical subject headings (MeSH): diffuse large B-cell lymphoma and non-Hodgkin lymphoma, under a historical cut from 2006 to 2019.

CASE REPORT

Female patient, 84 years old, Caucasian, born in Volta Redonda, Rio de Janeiro state was attended at the emergency room due to intense pain in the left lower limb associated with nodular skin manifestations. The physical examination showed infiltrative nodular lesions with suggestive lymphatic pathway, phlogistic signs and spontaneous leakage of fluid, similar to lymph (**Figures 1** and **2**). Biopsy of the lesion was performed with histopathological and immunohistochemical study, according to the WHO-EORTC protocol (2015), in addition to computed tomography (CT) of the chest, abdomen and pelvis for staging.

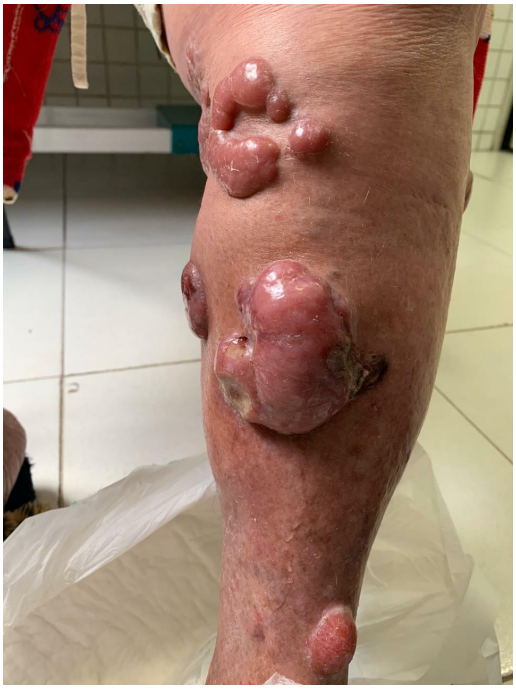

FIGURE 1 – *Nodular skin lesions in the lower limb, suggesting a lymphatic pathway*

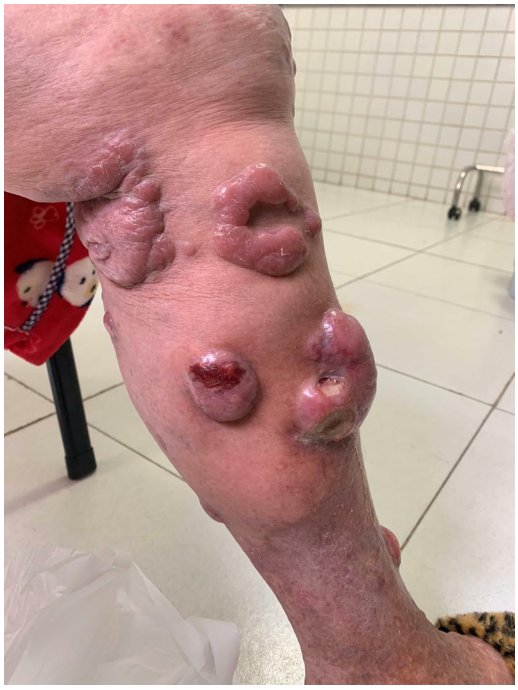

FIGURE 2 – *Nodular skin lesions in the lower limb, suggesting a lymphatic pathway*

Skin lesion biopsy

Histopathological study of skin lesion

• Macroscopy: skin flap demonstrated cuneiform measuring 0.9 × 0.3 cm of brownish surface.

• Microscopy: hyperplasia of the epidermis, excessive papillary dermis, and extensive infiltrate of atypical lymphocytes in the reticular and deep dermis, amid rounded, small structures, distributed in the cell matrix, compatible with atypical cutaneous lymphocyte infiltration/lymphoma (**Figures 3** and **4**).

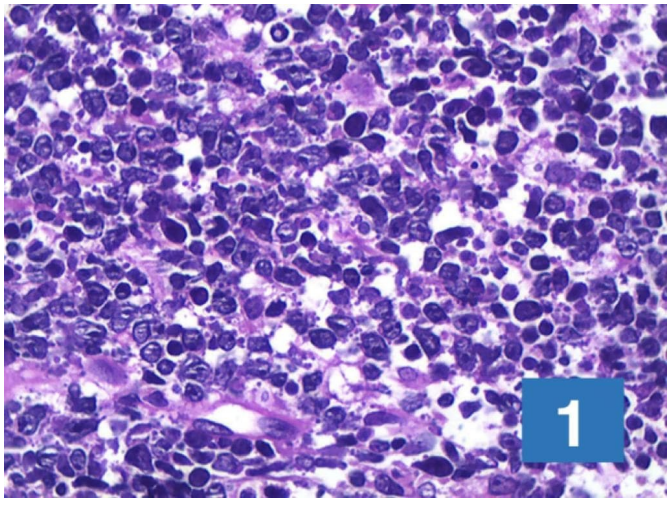

FIGURE 3 – *Skin sections showing epidermal hyperplasia, swollen papillary dermis, and extensive infiltration by atypical lymphocytes in the reticular and deep dermis, amid rounded and small structures distributed in the extracellular dermis. 40× lens*

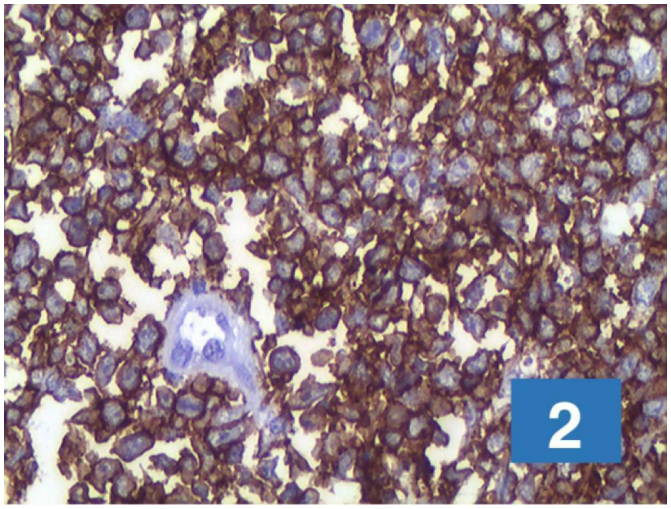

FIGURE 4 – *Skin sections showing epidermal hyperplasia, swollen papillary dermis, and extensive infiltration by atypical lymphocytes in the reticular and deep dermis, amid rounded and small structures distributed in the extracellular dermis. 40× lens*

Immunohistochemical study of skin lesion

• Method: antigenic heating recovery; amplification by polymerization; revealed with diaminobenzidine (DAB); tests with positive control.

• Markers: CD20+, CD79a+, Bcl-2+, Bcl-6-, and CD10- (**Table 1**).

• Conclusion: immunohistochemical panel associated with histological aspects of B-cell non-Hodgkin lymphoma with high proliferative index in skin.

TABLE 1 – Immunohistochemical panel associated with histological aspects of B-cell non-Hodgkin lymphoma with high proliferative index in skin

Marker	Expression
AE1/AE3	Negative (positive internal control in epithelium)
Bcl-2	Positive
Bcl-6	Negative
CD10	Negative (positive internal control)
CD20 (pan-B)	Diffusely positive (Figure 2)
CD23	Negative
CD3 (pan-T)	Negative (positive internal control)
CD5	Negative (positive internal control)
Cyclin D1	Negative (positive internal control)
c-Myc	Positive in 50% of cells
Ki-67	Positive in 95% of cells
MUM-1	Partial positive
TdT	Negative

Bone marrow biopsy

Anatomopathological study of bone marrow

• Macroscopy: brownish cylindrical tissue formation measuring 0.8 × 0.3 cm.

• Microscopy: slight increase bone marrow cellularity, showing focal lymphoid aggregates.

Immunohistochemical study of bone marrow

Cellularity is slightly increased for the patient's age and there is a predominance of the granulocytic series (myeloperoxidase +). There are sparse interstitial T lymphocytes (CD3+). The woven reticulin is preserved. There is no evidence of neoplasia infiltration in the sample.

Chest CT report

No evidence of enlarged mediastinal lymph node, cardiomegaly areas, and presence of bilateral pleuroparenchymal interface irregularity. Other structures with no changes.

Abdominal CT report

Preserved structures; absence of enlarged lymph nodes.

CT report of the pelvis

Enlarged lymph node in superficial inguinal chains, in greater number and volume on the left, the largest measuring 3.3 cm.

DISCUSSION

Manifestations

In this case report, the diagnosis of PCDLBCL-LT was established. The patient had infiltrative nodular lesions in the left lower limb, limited to the skin and rapidly progressing, with phlogistic signs, with no pruritus, and spontaneous lymph-like fluid leakage (Figure 2).

Diagnosis

As the lesions were restricted to the skin over a period of six months, the lymphoma of this patient was classified as primary[1-3].

In the morphology of PCDLBCL-LT, a dense infiltrating pattern of large cells is commonly found in the dermis and subcutaneous tissue, separated from the dermis by a narrow band of collagen named the Grenz zone. Usually, this infiltrate tends to be more intense in the diffuse dermis, known as the bottom-heavy pattern. Regarding the immunohistochemistry, CD20+, CD79a+, Bcl-2+, and Bcl-6+ are positive; CD10-, occasionally is. These findings are suggestive of PCDLBCL-LT[1-3].

The importance of correlating anamnesis and a thorough physical examination is emphasized in order to evaluate probable differential diagnoses, such as systemic lymphoma, primary cutaneous follicle center lymphoma, cutaneous lymphoma marginal zone, cutaneous T-cell lymphoma, among others[2].

Staging

The tests required for staging skin lymphoma are different from those requested for mycosis fungoides and Sézary syndrome: i) laboratory tests – complete blood count, lactate dehydrogenase (LDH), and test for human immunodeficiency virus (HIV); ii) imaging exams – contrast CT or positron emission CT (PET-CT) from the chest, abdomen and pelvis; iii) aspirate and bone marrow biopsy.

Lymphoma classification is performed by the TNM classification system from the EORTC/International Society for Cutaneous Lymphomas (ISCL) for primary cutaneous lymphomas other than mycosis fungoides or Sézary syndrome[4].

The primary tumor (T) refers to how much the skin is affected by the lymphoma (**Table 2**); regional lymph nodes (N) are classified according to the affected lymph nodes (**Table 3**); finally, distant metastasis (M) indicates whether the disease has spread to other organs (**Table 4**)[4]. Therefore, our patient staging was T2cN1M0.

TABLE 2 – Classification of the tumor according to the EORTC/ISCL for primary cutaneous lymphomas other than mycosis fungoides and Sézary syndrome

Tumor	
T1	One skin lesion only: **T1a.** the lesion size is up to 5 cm in diameter **T1b.** the lesion size is greater than 5 cm in diameter
T2	Two or more skin lesions. They can be in a single region of the body or in a nearby region: **T2a.** all skin lesions can be placed within a 15 cm diameter circle **T2b.** the circle necessary to circulate all lesions is between 15 and 30 cm in diameter **T2c.** the circle necessary to circulate all skin lesions is greater than 30 cm in diameter
T3	Skin lesions in different regions of the body or in at least three different regions: **T3a.** there are many lesions involving two regions of the body, distant from each other **T3b.** there are many lesions involving three or more regions of the body

Source: American Cancer Society.

EORTC/ISCL: European Organization for Research and Treatment of Cancer/International Society for Cutaneous Lymphomas.

TABLE 3 – Classification of the lymph node according to the EORTC/ISCL for primary cutaneous lymphomas other than mycosis fungoides and Sézary syndrome

Regional lymph nodes	
N0	No lymph nodes affected or contains lymphoma cells
N1	Presence of lymphoma cells in the drainage area of the affected area
N2	One of the following conditions is true: at least two groups of lymph nodes contain lymphoma cells, or there are lymphoma cells in lymph nodes that do not drain areas that contain lymphoma
N3	Presence of lymphoma cells in the chest or abdomen

Source: American Cancer Society.

EORTC/ISCL: European Organization for Research and Treatment of Cancer/International Society for Cutaneous Lymphomas.

TABLE 4 – Classification of metastasis according to the EORTC/ISCL for primary cutaneous lymphomas other than mycosis fungoides and Sézary syndrome

Distant metastasis	
M0	Absence of lymphoma outside the skin or lymph nodes
M1	Presence of distant metastasis

Source: American Cancer Society.

EORTC/ISCL: European Organization for Research and Treatment of Cancer/International Society for Cutaneous Lymphomas.

Treatment

As it is a rare entity, the literature is still scarce about the therapeutic approach for the PCDLBCL-LT; only bases in retrospective studies are available.

Treatment is carried out with chemotherapy, usually six cycles of R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone), associated or not with the involved-field radiotherapy[1, 2].

Prognosis

PCDLBCL-LT, unlike other cutaneous lymphomas, presents aggressive behavior, frequent relapses and a high tendency for systemic dissemination, in addition to a five-year survival in approximately 41%-66% of cases[2]. There is no prognostic difference in relation to the location of involvement, however, the presence of multiple lesions was considered a significant adverse effect[2].

CONCLUSION

PCDLBCL-LT is a rare disease, so its diagnosis is difficult and often late. It has aggressive behavior, which can drastically affect the patient's quality of life.

This case report aims to expand knowledge about this lymphoma, so that more professionals may add this pathology to their list of differential diagnoses, seeking to improve their prognosis.

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