THE DIAGNOSIS OF THE ANAPLASIC PRIMARY CUTANATE LYMPHOMA WITH THE BIG CELLS – A CHALLENGE

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Summary

Primary cutaneous CD30 lymphoproliferative disorders are the second most common group of cutaneous T-cell lymphomas (CTCLs), accounting for approximately 30% of CTCLs. Patients typically present with an asymptomatic solitary skin nodule that may be ulcerated, present anywhere on the body as a solitary nodule or multifocal nodule. Histologically, large tumor cells with an anaplastic, pleomorphic and immunoblastic cyto-morphology characterize C-ALCL with more than 75% of the tumor cells expressing CD30. C-ALCL has an indolent course with an excellent prognosis (5-year survival rate exceeds 95 %) with good response to treatments such as local radiotherapy, methotrexate or surgery.

We report the case of a 61-year-old man, who presented witha right gluteal ulceration, 4 cm/5 cm in diameter, along with multiple red-violaceous nodules, 1-3cm in diameter, located on the chest and right flank, treated with local antibiotics and local corticosteroids, without an improved outcome.

Key words: *primary cutaneous anaplastic T cell lymphoma, difficult differential diagnosis.*

Received: 10.06.2019 *Accepted: 5.09.2019*

Introduction

Primary cutaneous T cell lymphomas are lymphoproliferative diseases, which express at the time of the evaluation only with cutaneous involvement and no systemic affliction. Since the 2016 WHO revision of the malignant lymphomas, it was established that this group of diseases accompanies not only primary cutaneous large cell anaplastic lymphomas, but also lymphomatoid papulosis and borderline cases. [2]

Median age at presentation is usually greater than 60 years, affecting with a slight predominance the males. [3] The majority of the patients show fast growing asymptomatic tumors, frequently ulcerated, solitary of multifocal, in random stages of evolution, some of them spontaneous healed. [4]

Clinical appearance and evolution of the lesions are decisive criteria in choosing the best-suited therapeutic option, thus the need for and multidisciplinary approach to assure safety to the therapeutic act is highly important. To ensure that, the team is made not only of dermatologists and pathologists but also hematologists and oncologists.

Clinical case

We report the case of a 61-year-old man, who address our dermatology department with an ulceration measuring 4/5 cm in diameter, located on the right gluteal region, which appeared approximately 2 months ago, and also with several other red-coppery nodules, measuring 1-3 cm in diameter, located on the anterior chest wall, on the anterior axillary line and on the right flank. These lesions appeared 2 weeks after the first lesion located on the right gluteal emerged

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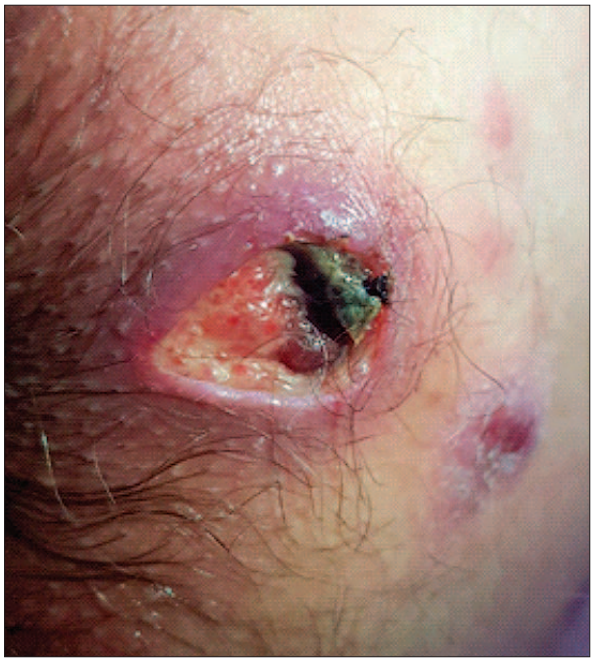

Figure 1. Ulceration with straight margins, and surrounding erythematous-violaceous halo

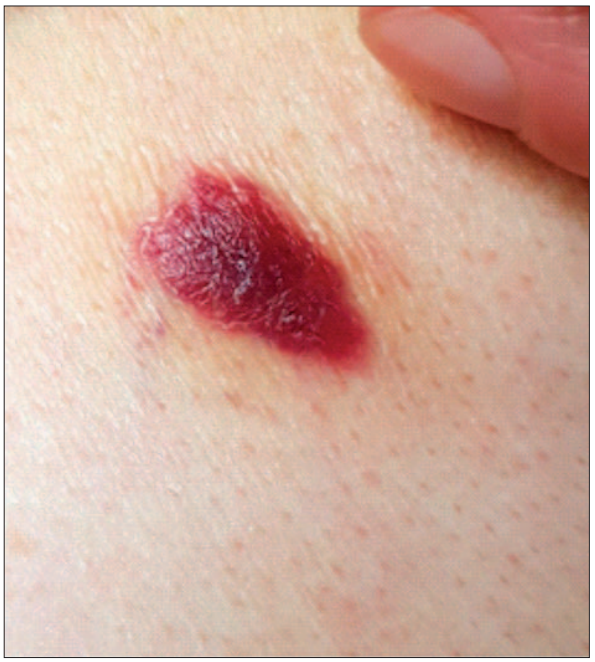

Figure 2. Red-coppery nodule with regular outline and smooth surface

(fig. 1, fig. 2). The patient followed a treatment consisting of local dermatocorticoids and antibiotics, with a slight improvement of the symptomatology. The patient reports thata grey-yellowish material was expressed one month after the red-violaceous painless nodule on the right gluteal region appeared, while he was still following a treatment with systemic antibiotics and antihistaminics recommended after a dermatologic consultation (fig. 3, fig. 4).

The patient's medical records revealed a history of pulmonary tuberculosis treated in 2014. Family history showed a vulgar pemphigus diagnostic for his son, which was successfully treated with methotrexate and corticotherapy, currently being in a remission state.

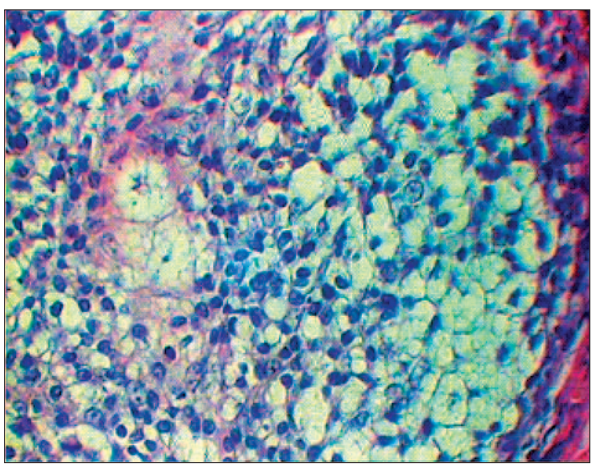

Figure 3. Histopathologic view of the anaplastic cells H & E 100x

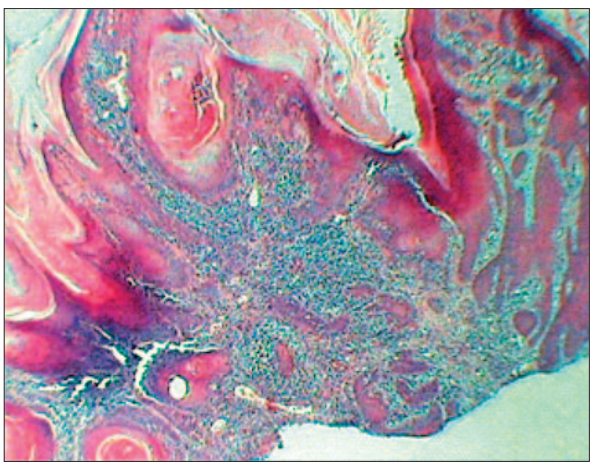

Figure 4. Histopathologic view of the dermal infiltrate. H & E 20x

Clinical examination showed a round ulceration, measuring 4/5 cm in diameter, on the right gluteal region, with well-defined straight margins, surrounded by a red-violaceous halo, with a clean base except one area covered with necrotic detritus, limited on the periphery of the right lesions pole. The patient shows minimal to moderate pain levels. In the infero-lateral margin of the ulcer, there is a red-coppery, round, nodule, measuring 1.5/1 cm in diameter, with well-defined margins, presenting a necrotic crust on the surface covering the center of the lesion. On the anterior chest wall, on the anterior axillary line, the patient presented a red-violaceous round nodule, measuring 2 cm/1 cm in diameter, with well-defined outline, with smooth and shiny surface.

The differential diagnosis was based initially on the clinical aspect and personal medical history and overviewed the possibility of certain diseases like: tertiary syphilis – gumma in the ulceration stage (straight cut margins with clean base, the red-coppery color and months-old evolution), cutaneous tuberculosis – tuberculous gumma (ulceration with irregular margins, base presenting necrotic detritus, months/years old evolution) profound fungal infection (ulcerations associated with multiple fistulous cavities, and of course the cutaneous lymphoma.

Laboratory test results showed slight monocytosis (9.4% ref. 2-8), high VSH levels - 37 (ref. 0-20), slight hypercholesterolemia (201 ref. 0-200) and positive Ac. Anti-HBs with no detectable Ag-HBs, negative cultures for fungi or bacteria from the gathered samples, and lastly, negative serology for syphilis and HIV.

Histopathological examination of the tissue fragments showed a malignant proliferation located in the superficial and profound dermis, around the annexes, the nervous structures and some of the vessels, focally infiltrated, with no signs of necrosis of the wall. This infiltrate was present also in the hypodermis and intra-epithelial, and was composed of medium-large cell with hypertrophic nucleus, with frequent typical and atypical mitoses, abundant, pale eosinophilic cytoplasm (fig. 3, fig. 4).

Immunohistochemistry tests revealed negative CK AE1/AE3 and CK8/18 in the tumoral proliferation – excluding so the epithelial origin of the tumor, negative CD3 cells, positive CD 68 in rare histiocytes, positive CD20 reactive B lymphocytes locally in small groups of but negative overall, CD5 and CD30 cells intensely positive on the majority of the tumoral cells, confirming so the diagnostic of large cell anaplastic lymphoma.

After thorough hematological investigations made at the Coltea Clinical Hospital, no signs of cellular abnormalities were found neither in the peripheral blood nor in the osteomedular sample. Seric protein electrophoresys indicated raised levels of beta 2 fraction 1.1 (0.2-0.5). Computer tomography showed nodular and pseudo-nodular interstitial fibrosis in the superior right lobe and in the Fowler segments, mediastinal, and bilateral pulmonary hilar adenopathies, measuring less than 10 mm each. At that time, the clinical choice resided in temporization of the aggressive systemic treatment and focusing on clinical improvement of the cutaneous lesions following local radiotherapy, with periodic reevaluation of the clinical, histological and imagistic status.

Discussions

Shortly after the discovery of the CD30 antigen almost two decades ago, CD30+ anaplastic large cell lymphoma was first described as a unique entity, currently being classified as part of the primary cutaneous CD30+ lymphoproliferative disorders spectrum, together with lymphomatoid papulosis. Primary cutaneous CD30 lymphoproliferative disorders are the second most common group of cutaneous T-cell lymphomas (CTCLs), after mycosis fungoides and Sezary syndrome, accounting for approximately 30% of CTCLs.[1]

Most frequently, the patient is an older male, over 60 years, presenting for solitary or grouped nodules, typically ulcerated, with evolution ranging from weeks to months, showing in 50% of cases spontaneous resolution. [5] Extensive evaluation is required for excluding systemic involvement and thus arriving to a complete and accurate diagnostic, and for this matter a complete blood work, pulmonary imagistic tests and a bone marrow biopsy and aspirate is recommended.[7]

Excisional biopsy is preferred before incisional or punch biopsy, followed by an immunohistochemical examination. Histopathology shows a rich dermal infiltrate composed of large cells with abundant and pale cytoplasm, with large and pleomorphic nuclei. Immunohistochemistry reveals CD30 positive cell in approximately 75% of the cell population, and negative expression for CD 2, 3, 5 and ALK (anaplastic lymphoma kinase – frequently positive in systemic involvement).[6]

Given the fact that the differential diagnosis of the positive CD30 large cell cutaneous lymphoma is hard to acknowledge only from histologic and immunohistochemistry data, it is important to take into consideration also the clinical appearance and the lesions evolution. Other frequent CD30 positive lymphoproliferative disorders are lymphomatoid papulosis, mycosis fungoid and systemic lymphoma.[1] Lymphoid papulosis manifests with papulonodular lesions, measuring up to 2 cm, presenting spontaneous resolution within 8 weeks – longer than this suggests lymphoma. Transformed mycosis fungoides presents appears at the beginning in form of papules and plaques and systemic lymphoma is ruled out after pulmonary imagistic acquisition, blood tests and immunochemistry – the presence of ALK. Other possible differential diagnosis are HTLV 1 infection and Hodgkin lymphoma.

Regarding the therapeutic approach, solitary localized lesions have a favorable evolution either by using local radiotherapy or surgical excision, low doses of methotrexate (15 mg, once per week, with adjustment based on the clinical .

Bibliography

[1] E. Perry, J. Karajgikar and A. Tabbara, "Primary Cutaneous Anaplastic Large-cell Lymphoma," *American Journal of Clinical Oncolgy* , vol. 36, p. 526–529, 2013.

[2] S. Swerdlow, E. Campo and S. Pilleri, "The 2016 revision of the World HEalth Organization classification of lymphoid neoplasm.," *Blood,* vol. 127, no. 20, p. 2375, 2016.

[3] N. Booken and S. Goerdt, "Clinical spectrum of primary cutaneous CD30-positive anaplastic large cell lymphoma; an analysis of the Mannheim Cutabeous Lymphoma Registry," *Journal oder Deutschen Dermatologischen Gesellschaft,* vol. 10, no. 5, pp. 331-319, 2012.

[4] J. Shehan, A. Kalaaji and S. Markovic, "Management of multifocal primary cutaneous CD30+ anaplastic larege-cell lymphoma.," *Jornal of American Academy of Dermatology,* no. 51, pp. 103-110, 2004.

[5] J. Weaver and A. Mahindra, "Non-mycosis fungoides cutaneous T-cell lymphomaș reclassification according to WHO-EORTC classification," *Journal of Cutaneous Pathology* , vol. 5, no. 37, pp. 516-524, 2010.

[6] "EORTC,ISCL and USCLC consensus recommendations for the treatment of primary cutaneous CD30-positive lymphoproliferative disorders," *Blood,* vol. 15, no. 118, pp. 4024-35, 2011.

[7] S. Yang, P. Khera and C. Wahlgren, "Cutaneous anaplastic large-cell lymphoma should be evaluated for systemic involvment regardless of ALK-1 status "case reports and review literature," *American Journal of Clinical Dermatology,* vol. 12, no. 3, pp. 203-9, 2011.

[8] C. Querfeld, I. Khan and B. Mahon, "Primary cutaneous and systemic anaplastic large cell lymphoma: clinicopathologic aspects and therapeutic options," *Oncology,* vol. 24, p. 574–587, 2010.

[9] M. Honma, M. Hashimoto and T. Iwasaki, "Primary cutaneous anaplastic large cell lymphoma successfully treated with local thermotherapy using pocket hand warmers," *Journal of Dermatology,* vol. 35, p. 748–750., 2008.

[10] M. Kadin, "Current management of primary cutaneous CD30+ T-cell lymphoproliferative disorders," *Oncology,* vol. 9, no. 32, p. 1158–1164, 2009.

Conflict of interest
NONE DECLARED

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