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Primary Cutaneous CD30+ Large T-Cell Lymphoma with Lymph Node and Cerebral Metastases

Linfoma T de células grandes CD30+ cutáneo primario: presentación de un caso, con metástasis ganglionares y cerebral

To the Editor:

Lymphomas account for a small proportion of skin tumors. Primary cutaneous T-cell lymphoma (CTCL), specifically, accounts for just a small proportion of non-Hodgkin lymphomas, with an incidence of 0.36 cases per 100 000 population per year.¹

CD30⁺ anaplastic large T-cell lymphoma (ALCL), a form of CTCL, is characterized by large atypical lymphocytes with an anaplastic, pleomorphic, or immunoblastic morphology and expression of the CD30 antigen by the majority (>75%) of tumor cells.² In the World Health Organization-European Organization for Research and Treatment of Cancer Classification of Cutaneous Lymphomas, ALCL is included in the subgroup of primary cutaneous CD30⁺ lymphoproliferative disorders within the larger group of T-cell and natural killer cell neoplasms.^{3,4} It responds well to treatment and has a favorable prognosis, unlike the more aggressive primary nodal variant.^{5,6}

We present a rare and aggressive variant of CD30⁺ ALCL in which metastasis to the brain during chemotherapy contributed to the death of the patient.

The patient, an 84-year-old woman, was seen for several violaceous cutaneous tumor lesions, some of which were ulcerated, on the right forearm and upper arm (Figure 1);

the lesions had appeared 2 years earlier. The examination also revealed a considerably enlarged right axillary lymph node that was hard and fixed to the deep layers.

Biopsy showed a tumor occupying the full thickness of the dermis with destruction of the appendages and sparing of the epidermis (Figure 2). The tumor was formed of large atypical cells with marked nuclear pleomorphism, prominent nucleoli (many of which were multiple), and eosinophilic cytoplasm. The mitotic index was high, with as many as 4 mitoses per high-power field; many of the mitoses were atypical.



Figure 1 Erythematous-violaceous tumor lesion, with several ulcerated areas, occupying the lateral aspect of the right forearm and upper arm.

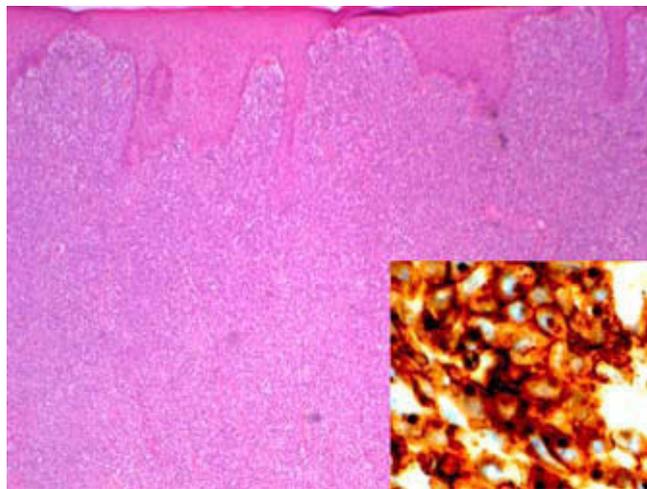


Figure 2 Dermis occupied by an atypical lymphoid proliferation with sparing of the epidermis and destruction of the appendages (hematoxylin-eosin, original magnification, $\times 40$). The insert shows CD30 (ki-1) positivity for over 90% of the tumor cells.



Figure 3 Clinical appearance of patient's arm after 6 cycles of chemotherapy with cyclophosphamide, doxorubicin, vincristine, and prednisone.

The diagnosis was confirmed by the morphologic findings described above and an immunohistochemistry study, which showed positivity for the common leukocyte antigen CD45 as well as for CD30 and CD4 and negativity for keratins (AE1-AE3 and keratins 7 and 20), epithelial membrane antigen (EMA), S100, CD3, CD20, and p80 (ALK1). The study also revealed membrane and paranuclear cytoplasmic positivity for CD30 in over 95% of the cells (Figure 2).

Computed tomography of the chest and abdomen showed enlarged right axillary lymph nodes suggestive of metastasis. Flow cytometry analysis of peripheral blood did not detect circulating atypical lymphocytes.

The patient was started on 6 cycles of chemotherapy with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP), to which she responded well (Figure 3). Six months

later, however, she was readmitted with retroocular pain and diplopia. Magnetic resonance imaging showed a brain lesion in the right temporal lobe that was compatible with lymphoma.

The patient died 6 months after the diagnosis. The immediate cause of death was cardiorespiratory failure, the intermediate cause lymphoma of the brain, and the underlying cause CD30⁺ ALCL.

CD30⁺ ALCL accounts for 30% of all CTCLs and is the most common variant after mycosis fungoides/Sézary syndrome. The prognosis is typically good, with an average 5-year survival rate of 96% to 100%.⁴ It affects both sexes but is more common in men. Clinically, it manifests as a single tumor in the majority of cases, or as grouped or widespread papules, and lesions tend to ulcerate. Twenty percent of patients develop multifocal lesions and 10% develop extracutaneous dissemination with diseased lymph nodes.⁴

In the case reported here, the skin lesions appeared 2 years before the patient was hospitalized but the diseased axillary lymph node was detected just 6 months previously. Although the skin tumor responded favorably to treatment with CHOP, the patient developed a brain metastasis, which ultimately contributed to her death.

It is well known that primary nodal CD30⁺ ALCL has a more aggressive course than the primary cutaneous variant.³ The negative immunohistochemical findings for EMA were compatible with primary cutaneous CD30⁺ ALCL² as, unlike the nodal variant, these tumors very rarely express EMA. p80 (ALK) negativity was also suggestive of a cutaneous origin.² Considering the above, a primary nodal CD30⁺ large-cell lymphoma with secondary cutaneous involvement was ruled out. There were also no clinical or morphologic signs of a history of mycosis fungoides that could have evolved into CD30⁺ ALCL, a situation that is associated with very poor prognosis.²

The prognosis of CD30⁺ ALCL is generally very favorable, with 10-year survival rates of over 90%. Nonetheless, patients with generalized skin lesions, such as ours, appear to have a greater risk of extracutaneous involvement.⁷ In a study by Grange et al⁸ on prognostic factors in cutaneous lymphomas, lesion number and size, histologic type, lactate dehydrogenase levels, and the presence of B symptoms (weight loss, unexplained fever, and night sweats) were all identified as valuable prognostic factors. It should be noted, however, that there is a shortage of studies using uniform criteria in this area. Advanced age is associated with poorer prognosis, which is influenced by the comorbidities typically encountered in elderly patients.

Localized multifocal lesions can be treated with radiotherapy, methotrexate, interferon alone or in association with bexarotene, or CHOP, a chemotherapy regimen which is the current treatment of choice for disseminated lesions.⁴ Several authors have stressed the need for less aggressive treatment of CD30⁺ ALCL in view of the favorable prognosis associated with this type of lymphoma.^{5,9,10} Nonetheless, it should be borne in mind that elderly patients with multiple lesions and lymph node involvement are at greater risk and can develop aggressive tumors, as did our patient who died despite a favorable initial response to 6 cycles of CHOP.

Acknowledgments

We thank Dr Miguel Ángel Marín Cárdenas of the Radiodiagnostic Unit at Hospital Universitario Miguel Servet in Zaragoza, Spain, for providing us with the magnetic resonance imaging report and images.

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Poliosis and Status Epilepticus as the Presentation of Tuberous Sclerosis in an Infant

Poliosis y estatus epiléptico en un lactante como presentación de esclerosis tuberosa

To the Editor:

Tuberous sclerosis (TS) is a neurocutaneous syndrome with an autosomal dominant pattern of inheritance and a high penetrance. It is characterized by the appearance of hamartomatous lesions in several organs,¹ and the most usual clinical signs of this disease are skin lesions, epilepsy, learning difficulties,² and behavioral disorders.

We report the case of a 51-day-old infant, born at term of nonconsanguineous healthy parents after an uncomplicated pregnancy and delivery, who was seen in the pediatric emergency department due to persistent convulsive seizures that had lasted 3 days. Physical examination revealed the presence of lanceolate hypopigmented macules on the limbs and trunk that were 3 to 11 mm in diameter (Figure 1). Of particular interest was the presence of poliosis of the

medial half of the left upper eyelid and a hypopigmented macule at the medial angle of the eye (Figure 2), which were present at birth. The clinical suspicion of tuberous sclerosis led us to perform cerebral magnetic resonance imaging, which revealed multiple cortical tubers (Figure 3), and an



Figure 1 Lanceolate hypopigmented macule on the thigh.