Primary cutaneous large cell lymphoma CD30+: a case-based review

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Summary

CD30+ primary cutaneous lymphoproliferative disorders (LPD) are clinically and pathologically heterogeneous entities. They include primary cutaneous anaplastic large cell lymphoma (PC-ALCL), borderline cases and lymphomatoid papulosis (LyP).

In PCALCL > 75% of the tumor cells express CD30 antigen; it is the second most common form of cutaneous T-cell lymphoma (CTCL) and more often affects older males.

We report a case of 85-year-old man with a 2-month history of severe itching, eczematous lesions of the trunk, unresponsive to topical application of steroids (Figure 1 a).

Blood parameters showed neutrophilic leukocytosis and IgE increase; chest radiography, thyroid and abdomen ultrasonography showed no pathological findings.

Physical examination revealed an asymptomatic ulcerated lesion of at least 7 cm diameter localized at right parietal region of the scalp, behind the ear (Figure 1 b). There was no cervical, axillary, or inguinal lymphadenopathy, neither hepatosplenomegaly.

Then, a skin biopsy was performed. It revealed a dermal infiltrate composed of anaplastic large cells, with-
out involvement of the hair follicles. These cells exhibited T phenotype CD45-, CD3+, CD2-, CD5-, CD4+, CD8-, CD20-, CD30++, CD15-, MUM1++, TIA1+/-, ALK-, granzyme+/-, perforin- (Figure 2).

All of these histological features raised three different diagnostic hypotheses: 1. skin involvement by a systemic anaplastic large cell lymphoma ALK negative; 2. primary cutaneous anaplastic large cell lymphoma CD30+; 3. large cell transformation identified during the progression of mycosis fungoides (MF).

Therefore skin biopsy of an eczematous patch was performed. It showed a superficial, dermal infiltrate composed of small cells, without epidermotropism, with T phenotype CD3, CD2, CD5 and CD7 positive, without co-expression of cytotoxic molecules (granzyme, perforin, TIA1) or CD30; the molecular study didn’t shown a monoclonal rearrangement of TCR. This allowed us to exclude the hypothesis of a MF progression.

Bone marrow cytomorphologic examination and total body CT-scan was performed in order to exclude extra-cutaneous involvement.

A diagnosis of primary cutaneous anaplastic large cell lymphoma CD30+ was carried out, according to WHO-EORTC criteria (2).

The lesion was surgically excised and then treated with radiotherapy (Figure 3).

The skin itching was treated with systemic corticosteroid and antihistaminic therapy, and with a daily use of moisturizing cream. This therapeutic strategy led to a significant improvement and the patient remains under follow-up.

Discussion

Mycosis fungoides, a cutaneous T-cell lymphoma, is a subgroup of non-Hodgkin’s lymphomas, characterized by skin infiltration and occasionally systemic involvement (4). CD30+ large transformation of MF is well described in literature (5, 6).

Primary cutaneous anaplastic large-cell lymphomas (PC-ALCL) belong to the CD30+ T-cell lymphoproliferative disorders and they usually affects older patients (2, 7). Male:female ratio is 3:1, with a median age of 55 years at the time of diagnosis (7, 8).

PC-ALCL often appears with a solitary or grouped, rapidly growing and ulcerating large tumors or thick plaques. Rarely, the disease occurs with multifocal lesions. Spontaneous complete or partial regression of the tumor is reported in up to 44% of the patients (9). Histological examination is the first step in the diagnostic work-up of clinically suspected CD30+ lymphoma.
proliferative disorders. The histopathology of CTCLs consists of diffuse non-epidermotropic infiltrates with cohesive sheets of large CD30+ tumor cells. Typically, the tumor cells show a typical aspect, with round, oval, or irregularly shaped nuclei and prominent and eosinophilic nucleoli as well as abundant cytoplasm (2). Immunohistochemistry plays a pivotal role by revealing the presence of CD30+ large pleomorphic or
anaplastic T cells. PC-ALCL is defined by CD30 expression of at least 75% of the tumor cells (10). With respect to the immunophenotype, the tumor cells generally express a CD4+ T-cell phenotype with variable loss of pan-T-cell antigens, such as CD2, CD3, and CD5. CD15 is usually negative, but the cutaneous lymphocyte antigen is positive. In contrast to the primary nodal CD30-positive lymphoma, C-ALCL generally does not express the epithelial membrane antigen (EMA) and anaplastic lymphoma kinase (ALK) (11). Systemic lymphomas frequently express ALK+ cells (12), but some ALK+ primary cutaneous ALCL cases have been reported (13).

PC-ALCL prognosis is good; the neoplasm has an indolent behavior with five-years survival rates range of 76-96%, but cutaneous relapse is frequent (39%) (7, 14).

A presentation with multifocal skin lesions, extensive single limb involvement and head or neck lesions are recognized as unfavorable prognostic factors in PC-ALCL (14-18).

Lee et al. have recently suggested that the extent of the lesion is a prognostic factor and it also correlates with relapse rate. Finally, the extent was more important than other features such as anatomical site or number of skin lesions (19).

The treatment of PC-ALCL with diffuse skin lesions or extracutaneous spread often needs chemotherapy, with frequent relapses. The CD30 directed antibody-drug brentuximab vedotin has appeared as a promising alternative treatment for advanced PC-ALCL (20).

PC-ALCL must be distinguished from the potentially malignant or progressive entities that occur with overlapping clinical and pathological features.

In our patient, histopathological examination revealed the CD30+ T-cell lymphoproliferative nature, but further biopsies and imaging techniques were needed to exclude other CD30+ cutaneous lesions and a systemic involvement.

In conclusion, the diagnosis of PC-ALCL could be difficult without a multidisciplinary approach; the correlation of clinical findings with histopathology and immunophatology is essential for the correct management (21).

References

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