Specific cutaneous infiltrates of chronic lymphocytic leukaemia in primary cutaneous malignant and premalignant epithelial neoplasms

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Introduction
Chronic lymphocytic leukaemia (CLL) is a low-grade lymphoproliferative disease characterized by a clonal proliferation of mature B cells. CLL is the most frequent form of leukaemia and it predominantly affects elderly people. The leukaemic cells are characterized by small diameter, hyperchromatic nuclei and scanty cytoplasm, expressing CD43 and CD5, with variable expression of CD23. The prevalence of cutaneous manifestations in CLL ranges between 4-50% of cases and may represent an initial sign of the disease. 

Patients and methods
A retrospective histopathologic study of peritumoral infiltrates in CLL patients with primary cutaneous malignant or premalignant epithelial neoplasms was performed. The clinical charts of all patients diagnosed of CLL during the period 1996 to 2006 in the Department of Haematology, Hospital del Mar, Barcelona, were reviewed. Patients who have presented basal cell carcinoma, squamous cell carcinoma, Bowen’s disease or actinic keratosis were selected and included in the study. All skin biopsy specimens from the selected patients were blindly evaluated by two independent observers. Following a systematized protocol a hand of histopathological, immunohistochemical and genotypic features was recorded.

Results
Ten patients with primary cutaneous epithelial malignant neoplasms were identified from 145 CLL patients diagnosed in our series. 33 skin lesions from the selected patients were studied. They corresponded to 7 actinic keratosis, 4 Bowen’s disease, 17 squamous cell carcinomas and 5 basal cell carcinomas. The intensity of the leukaemic infiltrates have been reported within the inflammatory infiltrate of cutaneous malignant lesions. Moreover, it is possible that the presence of the leukaemic infiltrate could be related to tumour-associated neovascularization and an increased vascular permeability. However, it should also be noted that the presence of a leukaemic infiltrate surrounding primary epithelial neoplasms does not seem to confer an adverse prognosis.

The presence of specific CLL infiltrates surrounding primary epithelial neoplasms was first described by Smoller and Waniek in 1996 in seven patients. Another study showed specific leukaemic infiltrates in 27% of primary cutaneous epithelial neoplasms removed by Mohs surgery from 55 patients with CLL. These infiltrates can appear surrounding actinic keratosis, Bowen disease and basal cell or squamous cell carcinomas. The pathogenesis of this phenomenon is not clear and multiple hypotheses for this finding have been put forward. It has also been described the infiltration by leukaemic cells in the sites of previous scars, herpes simplex infection, traumas and larva migrans. Occasionally intense specific leukaemic infiltrates have been reported within the inflammatory infiltrate of cutaneous malignant neoplasms in patients with CLL. In such instances the frequency and significance of these observations has not been fully defined.

Discussion
The presence of specific CLL infiltrates surrounding primary epithelial neoplasms was first described by Smoller and Waniek in 1996 in seven patients. Another study showed specific leukaemic infiltrates in 27% of primary cutaneous epithelial neoplasms removed by Mohs surgery from 55 patients with CLL.

The presence of specific cutaneous infiltrates of chronic lymphocytic leukemia has been linked to the pathogenesis of skin lesions in patients with chronic lymphocytic leukemia. The infiltration by leukaemic cells in the sites of previous scars, herpes simplex infection, traumas and larva migrans. Occasionally intense specific leukaemic infiltrates have been reported within the inflammatory infiltrate of cutaneous malignant neoplasms in patients with CLL. In such instances the frequency and significance of these observations has not been fully defined.

References