Blastic NK cell lymphomas are rare hematopoietic malignancies characterized by a frequent skin involvement, an evolution toward leukemia, and a rapid aggressive course with bone marrow infiltration. In contrast to myeloid/NK cell acute leukemia, CD4⁺CD56⁺ malignancies usually lack the expression of conventional myeloid and lymphoid T and B cell markers (Bagot et al., 1998; Petrella et al., 1999; Chaperot et al., 2001). Several recent studies reported phenotypic and functional similarities between these CD4⁺CD56⁺ leukemic cells and a subtype of dendritic cells (DC), the so-called plasmacytoid DC or type 2 dendritic cells (DC2) (Petrella et al., 1999; Chaperot et al., 2001). Tumor cells and DC2 both express CD4 and CD56 antigens (Cella et al., 1999; Chaperot et al., 2001). When stimulated by IL-3 or CD40 ligand, DC2 and CD4⁺CD56⁺ tumor cells both differentiated into mature DC and promote T-helper response (Chaperot et al., 2001). DC2 seems to be specialized in human anti-viral immunity producing high amounts of type I interferon (IFN-α and β) upon viral infection (Cella et al., 1999). Similarly, CD4⁺CD56⁺ blastic cells produce IFN-α in response to virus (Chaperot et al., 2001). CD101 is a human leukocyte cell surface molecule, initially defined by two different monoclonal antibodies (MoAb): BA27 and BB27 (Boumsell et al., 1997). In normal individuals, it is expressed by a minor subset of circulating T lymphocytes, by intestinal mucosal T lymphocytes, and by a major DC subset including DC2 (Petrella et al., 2002). CD101 antigen plays a major role in the activation of T lymphocytes by DC (Bagot et al., 1997). Although some reported that CD101 ligation on T cells inhibits IL-2 production by activated T cells (Soares et al., 1998), others indicated an inhibition of the T cell proliferation via IL-10 secretion by cutaneous DC (Bouloc et al., 2000). Here, we focused on the expression of CD101 molecules on CD4⁺CD56⁺ blastic cells.

The study was conducted according to the Declaration of Helsinki Principles. After informed consent and approval by an ethics committee of the Paris XII University, the identification of CD101 expression was carried out in 17 patients with CD4⁺CD56⁺ malignancy by immunohistochemistry using the anti-CD101 MoAb BC27 previously described by Boumsell et al. (1997). We used the streptavidin/biotin alkaline phosphatase method previously described on frozen cutaneous section (Bouloc et al., 2000) as BC27 MoAb did not give significant staining on paraffin-embedded section. Next, flow cytometry analysis was performed, using a PC5-conjugated anti-CD4 MoAb (Coulter Immunotech, Marseille, France), a PE-conjugated anti-CD56 MoAb (Coulter Immunotech), or the anti-CD101/BC27 MoAb produced locally (Inserm U448, Créteil, France), on the peripheral blood mononuclear cells (PBMC). Stained cells were analyzed using a single argon flow cytometer analyzer (Epics XL, Beckman-Coulter, Miami, Florida).

**Figure 1**

Expression of CD101 by the CD4⁺CD56⁺ tumor lymphocytes. (a) Cryostat tumor section, immunostaining with the CD101 antibody. (b) Immunofluorescence analysis of circulating lymphocytes: cells were stained either with anti-CD101 monoclonal antibodies (MoAb) followed by FITC-conjugated isotype-specific goat anti-mouse second reagent, PC5-conjugated anti-CD4 MoAb or with PE-conjugated anti-CD56 MoAb. Shaded histogram corresponds to irrelevant IgG1 MoAb control staining. Stained cells were analyzed using a single argon flow cytometer analyzer (Epics XL, Beckman-Coulter, Miami, Florida).

Abbreviations: DC, dendritic cells; DC2, type 2 dendritic cells; IFN, interferon; MoAb, monoclonal antibodies; PBMC, peripheral blood mononuclear cells.
blood mononuclear cells (PBMC) in one of the patients with tumor blood involvement.

In 13 patients (76%), CD101-stained cells with blastic morphology were present in the cutaneous infiltrate (Fig 1a). No correlation was found with the evolution, the localization, or the dissemination of the disease. In the analyzed blood sample, 90% of PBMC, corresponding to circulating tumor cells, expressed CD101, CD4, and CD56 antigens. The profile of CD101 antibody binding to CD4+CD56+ cells corresponded to a weak homogeneous expression by the malignant cell population (Fig 1b). It should be noted that three-color flow cytometry analysis was performed and revealed that as expected circulating cells coexpressed CD4, CD56, and CD101 molecules (data not shown). We show that CD4+CD56+ tumor cells co-express the CD101 marker. It further supports the identity between DC2 and CD4+CD56+ tumor cells. Moreover, CD101 could represent a useful tool for the diagnosis of the CD4+CD56+ blastic tumors. In the near future it will be important to determine the role of CD101 in the pathogenesis of this tumor, as it is tempting to speculate that CD101 could promote the progression of the disease by inducing a tumor-specific tolerance by inhibiting reactive T cell proliferation via IL-10 secretion (Bouloc et al, 2000).

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LETTER TO THE EDITOR