The expression of cell adhesion molecule 1 and its splicing variants in Sézary cells and cell lines from cutaneous T-cell lymphoma

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Short title

CADM1 expression in Sézary syndrome
Abbreviations

cell adhesion molecule-1 (CADM1), tumor suppressor lung cancer-1 (TSLC1), Sézary syndrome (SS), mycosis fungoides (MF), adult T-cell leukemia/lymphoma (ATLL), anaplastic large cell lymphoma (ALCL), C-C chemokine receptor type 4 (CCR4), human T-cell leukemia virus 1 (HTLV-1), peripheral blood mononuclear cell (PBMC), cutaneous T-cell lymphoma (CTCL), diffuse large B-cell lymphoma (DLBCL), enzyme-linked immunosorbent assay (ELISA), reverse transcriptase-polymerase chain reaction (RT-PCR)

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ABSTRACT

Cell adhesion molecule 1 (CADM1) is aberrantly expressed by T-cell neoplasms such as adult T-cell leukemia/lymphoma (ATLL) and mycosis fungoides (MF). We studied the expression of CADM1 and its splicing variants in Sézary syndrome (SS), MF, other cutaneous T-cell lymphoma (CTCL), and cell lines derived from T- and B-cell lymphomas. Soluble CADM1 was measured in the patients’ sera. CADM1+ cells in the blood and skin lesions were examined by flow cytometry and immunostaining, respectively. Soluble CADM1 was measured by ELISA, and the splicing variants of CADMI transcripts were determined by reverse transcriptase-polymerase chain reaction, followed by sequencing. As a result, circulating CADM1+ cells were significantly increased in 7 of 10 patients with SS, ranging from 7.9% to 74.5% of the CD3+CD4+ fractions (median; 33.7%) (cut off value; 6.5%). The percentages of CADM1+ cells were usually less than those of circulating Sézary cells. CADM1 was expressed, to various degrees, in 6 of 9 T-cell lines derived from SS, MF, ATLL, and anaplastic large cell lymphoma (ALCL), but negative in B-cell lymphoma-derived cell lines. CADM1+ cells were present in the skin infiltrates of MF, SS, ATLL, and ALCL. Serum levels of soluble CADM1 were not significantly elevated in SS/MF. Three major splicing variants of CADM1 expressed by neoplastic T cells contained different
combinations of the exons 7, 8, 9 and 11, including a putative oncogenic variant composed of exons 7-8-9-11. In conclusion, CADM1 is frequently expressed in Sézary cells and cell lines from CTCL.

Keywords

CADM1, Mycosis fungoides, Sézary syndrome, splicing variant, T-cell lines,