Interleukin-17 in acute myeloid leukemia

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Abstract

There are several reports that angiogenesis plays important roles in hematological malignancies including acute myeloid leukemia (AML). Human interleukin-17 (IL-17) is a proinflammatory cytokine produced by activated CD4 T cells. IL-17 plays a potential role in T cell mediated angiogenesis. The role of IL-17 in pathologic angiogenesis has not been evaluated yet. The aim of the study was to determine plasma level of IL-17 in patients with AML. IL-17 levels were measured by ELISA in plasma samples taken from 68 adult patients with AML before chemotherapy was administered. In addition 20 out of 68 patients were reanalysed after achieving complete remission (CR). Ten samples from healthy volunteers were evaluated as the control. In this study we have demonstrated that serum level of IL-17 is not elevated in AML patients. These results suggest that angiogenesis in AML is not mediated by CD4 T cells. To our knowledge this is the first report about IL-17 serum level in acute leukemias. We are currently evaluating IL-17 levels in others haematological malignancies.

Keywords: interleukin 17 • angiogenesis • acute myeloid leukemia

Introduction

Angiogenesis refers to the formation of new capillaries from preexisting vessels. There are several reports that angiogenesis plays important roles in hematological malignancies including acute myeloid leukemia (AML). The initiation of angiogenesis and the switch to the angiogenic phenotype requires a change between proangiogenic factors and angiogenic inhibitors [1, 2]. Human inter-

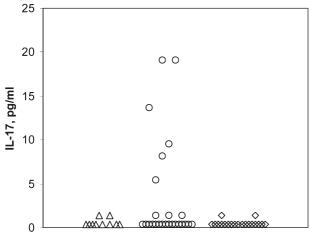
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leukin-17 (IL-17) is proinflammatory cytokine produced by activated CD4 T cells. IL-17 has several biologic acitvities such as induction of secretion of interleukin-6, interleukin-8, prostaglandin E_2 , some adhesion molecules (i.e. ICAM) and tumor necrosis factor alfa (TNF α). It also acts as a stimulatory hematopoietic cytokine by expanding myeloid progenitors and initiating proliferation of mature neutrophils. IL-17 plays a potential role in T cell mediated angiogenesis [3–5]. The role of IL-17 in pathologic angiogenesis has not been evaluated yet. The aim of the study was to determine plasma level of IL-17 in patients with AML.

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 \triangle controls \bigcirc AML at diagnosis \diamond AML, CR

Fig. 1 Serum levels of interleukin-17 in acute myeloid leukemia (AML) at diagnosis, AML in complete remission and in the control.

Material and methods

Plasma samples from 68 adult patients (28 females and 40 males, median age 42 years, range 21-83 years) with AML referred to our institution was taken before chemotherapy was administered. In addition 20 out of 68 patient were analyzed again after achieving complete remission. IL-17 levels were measured by enzyme linked immunoassay - ELISA (R&D Systems, USA) following the manufacturer instruction. Analyses and calibrations were carried out in duplicate, intra- and interassay variations were within the range given by the manufacturer. Minimum detectable level of IL-17 was less than 15 pg/ml.

Ten samples from healthy volunteers (4 females and 6 males median age 40 years; range 35 - 60 years) were evaluated as the control. The data were analyzed using Mann-Whitney U test.

Results

IL-17 was detected in 9 out of 68 AML patients at diagnosis, 2 out of 20 in AML in CR and 2 out of 10 in control group. In all patients IL-17 level was below 20 pg/ml.

There were no statistical differences in IL-17 levels between groups of AML patients (at diagnosis and in CR) versus control.

Results are shown in Fig. 1.

Discussion

IL-17 belongs to a class of indirect angiogenic factors which stimulate angiogenesis in vivo but have no mitogenic activity for endothelial cells in vitro. IL-17 enhances tumor microvessel density, induces formation of new capillary blood vessels in rat cornea and increases proangiogenic factors (i.e. vascular endothelial growth factor - VEGF, basic fibroblasts growth factor - bFGF) production [5]. Many authors reported increased angiogenesis in AML. There are many techniques of the assessment of angiogenesis in hematological malignancies. One of them is measurement of serum level of angiogenic cytokines. Elevated serum level of various proangiogenic factors including but not limited to VEGF, bFGF and TNF α in addition to the increased vascularity have been reported in acute leukemias. Angiogenic factors can be produced by T cells, monocytes, neutrophils, platelets or megakaryocytes. Leukemia cells are also able to secrete angiogenic factors, which in turn stimulate the development of new vessels [2, 6, 7].

In our study we have demonstrated that serum level of IL-17 is not elevated in AML patients. These results suggest that angiogenesis in AML is not mediated by T cells. On the other hand, di Raimondo et al. observed higher levels of angiogenic factors in bone marrow than in peripheral blood in multiple myeloma [8]. To our knowledge this is the first report about IL-17 serum level in acute leukemias. We are currently evaluating IL-17 levels in others haematological malignancies.

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