Introduction

Leukemia arises from the clonal expansion of immature hematopoietic cells blocked at a particular stage of development. Early attempts to classify acute leukemias by morphologic characteristics on Romanowsky-stained bone marrow smears had a limited clinical impact, often failing to distinguish acute lymphocytic leukemia (ALL) from acute myelocytic leukemia (AML). The French-American-British (FAB) classification system distinguishes three major morphologic subtypes of ALL (L1 – L2 – L 3) and eight subtypes of AML (M0 - M1 - M2 - M3 - M4 - M5 - M6 - M7) ***(Pui et al. 1995)***.

Acute myeloid leukemia (AML) is a frequent hematological neoplasm in adults and although a considerable progress in the treatment of the disease has been made, the majority of the patients die ***(Weidmann et al. 1997)***.

The diagnosis of acute leukemias requires a multi-parametric approach in order to apply risk-adapted therapeutic protocols and appreciate the potential outcome of any given patient ***(Bene et al. 1999)***.

The role of cytokines in tumor regression is now well established. The major limitation of the clinical use of cytokines is the lack of a simple and effective protocol for the local and sustained delivery of cytokines to the tumor medium ***(Kuriakose et al. 2000)***.

Cytokines are involved in hematopoiesis by regulating proliferation, differentiation and cellular functions of various lineages of hematopoietic cells. There is an increasing range of clinical conditions in which cytokines are involved as therapeutic agents ***(Rubak 1996)***.

Fas (Apo-1 / CD95) is a cell membrane receptor involved in apoptotic cell death. Soluble variant forms (sFas) lacking the transmembrane domain due to alternative splicing have been identified. Up-regulation of sFas expression is reportedly implicated in prereceptorial blockage of Fas-induced apoptosis in a dose-dependent manner ***(Inaba et al. 1999).*** It is suggested that, blockade of Fas-signaling by soluble Fas may be a mechanism leading to apoptosis resistance in leukemia ***(Liu et al. 2002).***

Aim of the work

The aim of present work is to:

1- Study some cytokines (interleukin 6, interleukin 8, tumor necrosis factor alpha) and soluble Fas (sFas) as an indicator for apoptosis in acute myeloid leukemia, whether there are differences in these cytokines and sFas in different FAB subtypes, and their impact on the outcome of AML patients regarding the response to chemotherapy.

2- Evaluate the changes in these cytokines, sFas, and hematological parameters before and after chemotherapy and their predictor value for response to chemotherapy.

Cytokines with immuno-stimulating effects have the capacity to induce tumor immunity in animal models, whereas, some cytokines interfere with tumor growth based on their angiostatic effects. Despite these capabilities, cytokines such as tumor necrosis factor (TNF), interleukin 1 (IL-1) and interleukin 2 (IL-2) have had limited clinical efficacy and many undesirable side effects ***(Oppenheim et al. 1997)***. Interleukin 6 (IL-6) and its soluble receptor have been shown to have diverse effects on blast cell growth in acute myeloblastic leukemia ***(Saily et al. 1998)***.

Interleukin 8 (IL-8), a member of the family of small inducible cytokines, is mainly known for its striking neutrophil-activating properties. In leukemic cells expressing the IL-8 receptor, IL-8 induces cytosolic free calcium changes, indicating activation of the classical signaling pathway. These results suggest that IL-8 may have biologic activities in hematopoiesis ***(Tobler et al. 1993)***.

Hematopoietic cells require certain cytokines including colony stimulating factor (CSF) and interleukins to maintain viability. Without these cytokines the program of apoptotic cell death is activated. Cells from much myeloid leukemias require cytokines for viability, and apoptosis is activated in these leukemic cells after cytokine withdrawal resulting in reduced leukemogenicity ***(Lotem and Sachs 1996)***.

Tumor growth is the net result of cell proliferation and cell loss, apoptosis is the most significant component of the continuous cell loss in most tumors. The higher thc malignancy grades the higher the percentage of apoptotic cells ***(Korkolopolou et al. 1998)***.