Molecular responses during chemotherapy in acute myeloid leukemias in predicting poor-response to standard chemotherapy.

ABSTRACT

Signal transduction pathways are constitutively expressed in leukaemic cells resulting in aberrant survival of the cells. It is postulated that in cells of chemo-sensitive patients, chemotherapy induces apoptotic signals leading to cell death while survival signals are maintained in cells of chemoresistant patients. There is very little information currently, on the expression of these mediators in patients immediately after chemotherapy initiation. We examined the expression pattern of proinfl ammatory cytokines, signaling molecules of the PI3K and MAPK pathways molecules and death receptor, DR5 on paired samples at diagnosis and during chemotherapy in acute myeloid leukaemia patients treated with cytosine arabinoside and daunorubicin. The results were correlated with remission status one month after chemotherapy. We found that in chemo-sensitive patients, chemotherapy signifi cantly increased the percentage of cases expressing TNF-α ($p=0.025$, $n=9$) and IL-6 ($p=0.002$, $n=11$) compared to chemo-resistant cases. We also observed an increased percentage of chemo-sensitive cases expressing DR5 and phosphorylated p38, and Jnk. Thus, expression of TNF-α, IL-6, DR5, phospho-p38 and phospho-Jnk may regulate cell death in chemo-sensitive cases. In contrast, a signifi cantly higher percentage of chemo-resistant cases expressed phospho-Bad ($p=0.027$, $n=9$). IL-1β and IL-18 were also found to be higher in chemo-resistant cases at diagnosis and during chemotherapy. Thus, expression of various cellular molecules in leukaemic blasts during chemotherapy may be useful in predicting treatment outcome. These cellular molecules may also be potential targets for alternative therapy.

Keyword: Apoptosis; Interleukin; Signal transduction; Treatment response.