

Poster Abstracts

Biology of solid tumours & leukaemia

Poster S-I-11

Estimation of hematopoietic progenitor cells in patients with chronic myeloid leukemia with resistance to tyrosine kinase inhibitors

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Introduction

Chronic myeloid leukemia (CML) is a clonal oncological disease associated with the formation of chimeric bcr-abl gene, the product of which is active BCR-ABL tyrosine kinase playing a major role in the pathogenesis of CML. Data obtained in recent years allowed to assume the decisive role not only of hematopoietic stem cells, but also of bone marrow (BM) progenitor cells in both onset and progression of the disease. However, information on the functional characteristics of BM hematopoietic progenitor cells in different CML phases, in terms of therapeutic inhibition of BCR-ABL tyrosine kinase and the resistance to Imatinib, is not sufficient today and some findings are contradictory. Hence, the aim of this investigation was the estimation of BM hematopoietic progenitor cells in patients with CML with the resistance to tyrosine kinase inhibitors, using in vitro cell culture.

Methods

It was expedient to provide morphological and functional analysis of hematopoietic progenitor cells extracted from the BM of 56 patients with CML, using in vitro cultivation in semisolid agar. Colony to cluster ratio (CCR) was calculated as the number of colonies divided by the number of clusters. The changes in functional properties of hematopoietic progenitor cells were analyzed, such as alterations in proliferation potential and the ability to form cell aggregates during the cultivation in CFU assay. We have also performed further cytological and cytochemical assessment of cell aggregates composition and determined the correlation of these indices with CML progression.

Results

The analysis of obtained results has shown the ability of BM hematopoietic progenitor cells in CML to form the colonies in cell culture in vitro and to maintain a long-term suspension culture without the addition of exogenous growth factors, depending on the response to BCR-ABL tyrosine kinase inhibitor. It was found that in BM samples of the patients, who received busulfan before the use of Imatinib, regardless of the number of months of its administration, resistance to the further Imatinib therapy was determined, as well as high colony-forming activity and high proliferative potential of BM progenitor cells.

Conclusion

It was shown that the indices of proliferative potential and cellular composition of colonies, formed during BM progenitor cells cultivation in vitro, can serve not only to assess the state of hematopoietic system at the time of the study, but also to be early predictors of the progression of pathological process.