Abstract

This PhD thesis consists in two major parts, a general and a personal contributions one.

The general part has three subchapters. In the first subchapter I briefly presented the genetic (cytogenetic and molecular) aberrations in malignant hemopathies. The second subchapter focuses on the clinical and paraclinical aspects of different malignant hemopathies. Within the third subchapter I included a brief description of the new treatment for malignant hemopathies.

At the beginning of the personal part I underline the purpose and the objectives of the study:

The main objectives were to assess the importance of cytogenetical aberrations in the diagnosis and prognosis of malignant hemopathies and to monitorise the cytogenetic response to Imatinib therapy, to confirm the remission or the relapse in malignant hemopathies, and to establish the impact of cytogenetic analysis before and after stem cell transplantation in malignant hematologic diseases in Tg.Mureş.

Between January 2006 and July 2009 we received for chromosomal analysis 225 samples of bone marrow and/or peripheral blood from patients with malignant hemopathies from Hematology Clinics Tg. Mures. The karyotypes of patients between ages of 2 and 80 years, 36 with acute lymphoblastic leukemia (ALL), 34 with acute myeloid leukemia (AML), 7 with biphenotypic acute leukemia, 10 with secondary acute leukemia, 52 with chronic myeloid leukemia (CML), 15 with chronic myeloproliferative disorders, 25 with myelodysplastic syndrome (MDS), 37 with chronic lymphocytic leukemia (CLL), and 9 with malignant lymphoma were analyzed. We carried out the
bone marrow and/or peripheral blood culture according to standard methods. We successfully analyzed the leukemic karyotype of 80% of cases and identified 65% cases with chromosomal abnormalities.

In this study, in ALL the most frequent chromosomal abnormality was hyperdiploidy and we found only three cases of Philadelphia chromosome. The most frequent clonal karyotype alteration in AML was hyperdiploidy, detected in 28% of AML cases, while metaphases with structural abnormalities were found in 22% of cases. I identified clonal aberrations in 62.5% of SMD cases, only two with 7q deletion and one with i(17q). Chromosomal abnormalities were detected in 66% of patients with CML. The Ph chromosome frequency at the moment of diagnosis in CML was 87%. We had one case with double Ph+, one patients with i(17q) and only one case with inv(16). Clonal cytogenetic abnormalities were detected in 12 (38%) patients with CLL. An abnormal clone carrying t(7q;14q) was detected in one patient with CLL. I found deletions at 13q onlz in one case even it is the most common genetic abnormality in CLL. In this study the most frequently observed chromosome abnormalities in CLL are numerical aberrations, mainly +21, +12 and +X. Abnormal clones were detected in 66% of cases of acute biphenotypic leukemia. In our study the most frequent abnormality was hyperdiploidy. These findings are similar to the results obtained in other studies using a similar approach. Cytogenetic abnormalities were detected in 71% of cases with secondary acute leukemia, the most frequent abnormality was involving chromosome 7.

The main conclusions are:

- Karyotyping or classical cytogenetic analysis is still the standard method for demonstrating chromosomal aberrations.
- Our results confirm the importance of the classical cytogenetic investigation in acute leukemia, especially with regard to the prognostic value of the structural and numerical anomalies found.
- Performing classic cytogenetics both at diagnosis and during the course of the CML is important for detecting the presence of Philadelphia chromosome and/or the development of additional chromosome changes before and during therapy, with prognostic and, consequently, therapeutic implications.
- However, only standard cytogenetics enable the detection of additional cytogenetic abnormalities which, when found at the time of diagnosis, might predict a shorter
• Chromosomal changes in the biphenotypic acute leukemia, chronic myeloproliferative disorders and in malignant lymphoma are not specific, but their presence at least confirms the diagnosis of a malignant hematopoietic disorder and contributes additional aspects to differential diagnosis.

• Patients with secondary leukemia often express complex chromosome abnormalities with adverse prognosis.

• The cytogenetic analyse is an important part of the protocol of investigation of patients with hematological malignant diseases.