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1162

PROGNOSTIC SIGNIFICANCE OF MINIMAL RESIDUAL DISEASE IN PEDIATRIC PRECURSOR-B ACUTE LYMPHOBLASTIC LEUKEMIA

A Kamel, N El-Sharkawy, E Kandeel, HS Moussa, A El-Haddad
NCI, Cairo University, Cairo, Egypt

Background. Minimal residual disease (MRD) has emerged as the most powerful tool for assessing response to chemotherapy in pediatric precursor B ALL. **Aims.** This study aimed to assess the presence of MRD in relation to other prognostic parameters such as age, gender, CSF status and molecular genetic abnormalities in pediatric precursor-B ALL. In addition, we aimed to clarify the impact of MRD status on disease progression. **Methods.** Bone marrow samples were obtained from 70 newly diagnosed pediatric ALL patients diagnosed in 2008-2011. Immunophenotypic characterization was performed at diagnosis. Cases were followed up for MRD at day 15 (d15) and 42 (d42). Leukemia associated phenotype(s) were identified using the following panels: CD58/CD10/CD34/CD19, CD38/CD10/CD34/CD19 and CD45/NG2/CD19/CD22 as well as any aberrant myeloid (CD13 or CD33) or T markers (CD7, CD2)/CD19/CD34/CD45. The cut off value used for MRD detection was 0. 01%. Patients were treated according to the Egyptian NCI treatment protocol modified from the total therapy study XV. Disease free survival (DFS) was evaluated at 28 months. **Results.** At D15 post-induction MRD was evaluated in 61 patients; 31 had MRD <0. 01, 20 had ≥0. 01<0. 1, 4 had MRD level ≥0. 1<1. 0%, 4 had MRD level > 1% and 2 patients did not achieve complete remission (CR). Associations between MRD at d15 post induction and other clinical and biological risk factors including age, gender, TLC, lymphadenopathy, hepatosplenomegly, cytogenetic molecular studies and DNA index were of no statistical significance. We reported statistically significant association between MRD positivity at d15 post induction and CSF infiltration (P value = 0. 03). The association between MRD, OS, and DFS at 28 months did not reveal statistical significance using different cutoff values of 0. 01 or 0. 1%. A trend of association with poor outcome was demonstrated with 0. 1% cutoff value though not statistically significant. At d42 post-induction MRD was evaluated in 56 patients; 32 had MRD level <0. 01, 19 had ≥0. 01<0. 1 and 4 patients had MRD level ≥0. 1<1. 0% and one patient had a level of > 1%. As with d15, we reported statistically significant association between MRD positivity at d42 post induction and CSF infiltration (P value = 0. 01) Also, significant association was demonstrated between MRD at d42 and molecular genetics; t(12;21) was significantly associated with negative MRD while t(9;22) was significantly associated with positive MRD (p=0. 045). Patients with negative MRD at d42 had significantly better DFS than those with positive MRD (p<0. 0001). No statistically significant association between d42 MRD and other prognostic parameters was encountered. **Summary and Conclusions.** Positive MRD is associated with some other bad prognostic parameters namely CSF infiltration and t(9;22). At day 42, MRD detection by flow cytometric assay using 0. 01% cutoff level is useful in predicting treatment outcome. The proven clinical value of MRD in the plethora of studies would raise a need for changing the current definition of CR, which is still based on the morphologic appearance of BM. Investigation of MRD identifies patients who will experience relapse in spite of a standard morphologic.

1163

PROGNOSTIC ROLE OF BLOOD COAGULATION FACTOR XIIIA EXPRESSION IN ACUTE LYMPHOBLASTIC LEUKEMIA

I Szegedi, L Csáthy, Z Hevessy, J Kappelmayer, C Kiss
University of Debrecen, Debrecen, Hungary

Background. Previously we have identified B-cell progenitor (BCP) lymphoblasts as a new expression site of coagulation factor XIII subunite A (FXIIIA). Detection of FXIIIA in BCP ALL blasts by flow cytometry (FC) can be used for more accurate definition on the leukemia-associated immunophenotype (LAIO) and quantitation of minimal residual disease (MRD). **Aims.** Here we have examined, for the first time, the possible impact of factor XIIIA expression in childhood BCP ALL. **Patients and Methods.** MRD detection was performed using four color FC analysis with a FACSCalibur flow cytometer. Sixty-one leukemic children with a BCP ALL phenotype were treated according to the antileukemic protocol BFM95/BFM ALL-IC 2002 and studied retrospectively. **Results.** Multiparametric data analysis of prognostic factors pointed on the possible role of FXIIIA expression to influence disease outcome. Unfavorable genetic conditions were significantly more frequent among FXIIIA-negative vs positive cases. Distribution of other conventional prognostic factors was similar between the two groups. Three-years overall survival of patients with FXIIIA positive disease (64%) was significantly higher than that of FXIIIA-negative patients (36%). **Conclusions.** Retrospective analysis of a limited number of patients indicated an important prognostic role of FXIIIA expression in childhood BCP ALL. Preliminary data suggest that FXIIIA expression may define a new subgroup of childhood ALL. Granted by TÁMOP-4. 2. 1/B-09/1/KONV-2010-0007 project, supported by the European Union, co-funded by the European-Social Fund.

1164

UTILITY OF A SINGLE MULTIPLEX REVERSE TRANSCRIPTASE POLYMERASE CHAIN REACTION (RT-PCR) ASSAY FOR DETECTION OF THE COMMON CHIMERIC FUSION TRANSCRIPTS IN ACUTE LEUKEMIA PATIENTS FROM NORTH INDIA

N Varma, P Bhatia, J Binota, D Bansal, A Trehan, P Malhotra, S Varma
PGIMER, Chandigarh, India

Background. Cytogenetic and molecular abnormalities identify prognostically relevant subgroups in B-cell acute lymphoblastic leukemia (ALL) and Acute Myeloid Leukemia (AML). Many western studies quote the incidence of these fusion transcripts to be 30-35% in B-ALL and around 40-45% in AML. However the data from Indian Sub-continent is limited. **Aims and Objectives.** The present pilot study was undertaken to detect the incidence of common chimeric fusion transcripts of t(12;21), t(9;22), t(1;19), t(4;11), t(8;21), t(15;17) and t(inv16) in adult and pediatric B-ALL and AML cases using a single Multiplex RT-PCR assay. **Methods.** This prospective study carried out over a period of one year included 95 B- ALL cases and 56 AML cases diagnosed on bone marrow (BM) examination and flowcytometric Immunophenotyping (FCM-IP) analysis. A single Multiplex RT-PCR assay was carried out using primers specific to the fusion transcripts. **Results.** Out of the 95 B-ALL cases enrolled in the study, 56 (59. 0%) were pediatric and 39 (41. 0%) adult cases. A total of 29/95 cases (30. 52%) showed positivity for the various fusion transcripts with 15/56 (26. 8%) pediatric and 14/39 (35. 9%) adult cases. Of the fifteen positive pediatric cases, 9/56 (16. 07%) were positive for TEL-AML1 transcript, 3/56 (5. 35%) for BCR-ABL transcript, 2/56 (3. 5%) for MLL-AF4 transcript and 1/56 (1. 79%) for E2A-PBX transcript. Out of the fourteen positive adult cases, 10/39 (25. 64%) were positive for BCR-ABL transcript, 2/39 (5. 12%) were positive for TEL-AML1 transcript and 1/39 (2. 56%) each for E2A-PBX transcript and MLL-AF4 transcript. Of the total 56 AML cases, 44 (78. 5%) were adult AML cases and 12 (21. 5%) pediatric cases. A total of 27/56 (48%) AML cases showed positivity for various fusion transcripts of which 18/44 (40%) were adult AML cases and 9/12 (75%) pediatric cases. Of the 18 positive adult cases, 8/44 (18%) each were positive for t (8;21) and t (15;17) and 2/44 (4. 5%) for t (inv 16). In the 9 positive pediatric cases, 5/12 (42%) were positive for t (8;21), 2/12 (16%) each for t (15;17) and t (inv 16). **Conclusions.** Our study results show that TEL-AML1 and AML1-ETO transcripts are the most common fusion transcripts seen in pediatric B-ALL & AML cases and BCR-ABL and AML1-ETO & PML-RARA in adult B-ALL & AML cases respectively. The incidence of the above common fusion transcripts in our pilot study is in accordance with that described in western studies. It is important to identify these transcripts as they provide useful prognostic information to the treating clinician.

1165

GERMLINE MUTATIONS IN MRE11/RAD50/NBN COMPLEX GENES IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

M Mosor[1], I Ziólkowska-Suchanek[1], K Nowicka[2], D Januszkiewicz-Lewandowska[3], J Nowak[2]
[1]Institute of Human Genetics, Polish Academy of Sciences, Poznan, Poland
[2]Institute of Human Genetics Polish Academy of Sciences, Poznan, Poland
[3]University of Medical Sciences, Poznan, Poland

Background. The *MRE11*, *RAD50*, and *NBN* genes encode proteins of the MRE11-RAD50-NBN (MRN) complex involved in cellular response to DNA damage and the maintenance of genome stability. In our previous study we showed that the germline I171V mutation in *NBN,* may be considered as a risk factor in the development of childhood acute lymphoblastic leukemia (ALL) and some specific haplotypes of that gene may be associated with childhood leukemia. This finding raises important questions about the role of mutations in others genes of the MRN complex in childhood ALL. **Aims.** The aim of the study was to answer the question whether *MRE11* and *RAD50* alternations have a potential role in childhood acute lymphoblastic leukemia. **Methods.** The aim was carried out by determining the frequency of constitutional mutations and polymorphisms in selected regions of *MRE11*, *RAD50*, and *NBN* in the group of 200 children diagnosed with ALL and treated at the Department of Pediatric Hematology, Oncology and Transplantology Poznan University of Medical Sciences in Poland. We have for the first time made simultaneous