EUROPEAN HEMATOLOGY ASSOCIATION

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ABSTRACT BOOK

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The European Hematology Association (EHA) promotes excellence in patient care, research and education in hematology.
EHA was founded in June 1992 and today – with over 4000 members from 100 countries – is a consolidated representative of European hematologists.

Our aim

- To become the official European representative of hematology and hematologists – especially where research, education and regulatory issues are concerned – and to become a conduit for European harmonization;
- To promote the creation of a highly attractive market for practitioners and researchers in Europe thus fostering the mobility of hematologists in and to Europe;
- To reach out and offer a platform to countries that wish to further develop excellence in hematology;
- To promote education, training and scientific research in hematology in Europe;
- To exchange and disseminate knowledge and scientific information in the field of hematology.

Our activities

- Organizing an annual scientific and educational congress in a major European city;
- Dissemination of medical research, both basic and clinic, through the Haematologica;
- Collaborating with other leading organizations in the field of hematology and oncology;
- Providing postgraduate education through the annual congress, tutorials and workshops;
- Supporting junior basic and clinical researchers in the development of their careers through the EHA Fellowship Program.
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Acute Myeloid Leukemia 2

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ARA-C SC DURING TREATMENT WITH AZACITIDINE IN ACUTE MYELOID LEUKEMIA SECONDARY TO MYELODYSPLASTIC SYNDROME: A CASE REPORT

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Azacitidine is a hypomethylating agent approved for the treatment of myelodysplastic syndromes (MDS) with Intermediate-2 or high IPPS risk and acute myeloid leukemia with myelodysplasia related changes (AMLWMRC) with blasts from 20 to 30%. We report a 77 years old patient with myelodysplastic syndrome (RAEB-2) IPSS high risk, treated with azacitidine (75 mg/mq day 1-7 every 28 days). At the start of treatment the transfusional dependence was 2 units/month. After 7 cycles, the MDS evolved to AMLWMRC with circulating blasts 35%. The neutrophil granulocytes count was 200/µl, anemia was severe, platlets count was in the normal range.The transfusional dependence increased to 8-9 units/month. Thus we started ARA-C 30 mg sc for 7 consecutive days. After 28 days, the circulating blasts decreased to 2% but the hematological profile didn't improve. So we started again azacitidine with the same schedule. After 1 cycle the neutrophil granulocytes count increased to 1500/µl and the transfusional dependence decreased to 2-3 units/month. The hematological profile is stable after further 2 cycles. The association of ARA-C sc with azacitidine can have a synergistic action to reduce the peripheral blasts count and improve hematological profile.

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METAPLASIA OF IMMATURE CELLS IN BONE MARROW, PANCYTOPENIA AND ELEVATED NSE: A SMALL CELL LUNG CANCER CASE REPORT

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In suspect of hematological malignancies, a 62 years-old woman came to our center and underwent a bone marrow (BM) biopsy. Her clinical presentation included smoke addiction, pancytopenia, fever, hypercalcemia, left hilar adenopathy, an history of chronic obstructive pulmonary disease and breast cancer. A total body CT scan revealed multiple mediastinal and abdominal lymph nodes, brain lesions and a lingula lung mass. Serum neuronal specific enolase (NSE) was 112000 ng/ml and chromogranineA (CgA) was 1055 ng/ml. Due to a worsening clinical status and severe thrombocytopenia, we could not perform a lung biopsy. BM sections revealed a massive infiltration of CD45-/CD34-/CD117+/CD56++/pancytokeratin+ cells; Ki-67 proliferation rate was about 80% and p63 was negative. BM smears showed an immature population with atypical features and large cytoplasm sometimes in syncytium. Flow cytometry on BM revealed a neoplastic population (6,88% of global cells) with an elevated side scatter, negative for CD45 and positive for CD117, CD15 and CD56 antigens. According to oncologist consultant, this was a case of small cell lung cancer (SCLC) at an advanced status with BM carcinomatosis; in this setting, aggressive clinical course and paraneoplastic syndromes at diagnosis are common. The diagnostic challenge relied on morphologic analysis, showing a diffuse infiltration of immature cells with scarce residual hemopoiesis, and on the expression of myeloid antigens (*i.e.* CD15, CD117), suggesting a diagnosis of acute myeloid leukemia (AML). AML can be CD45-negative and this finding does not rule out its diagnosis. CD56 is frequently seen as well. On the other hand, CT scan results and neoplastic markers posed diagnosis of BM carcinomatosis. NSE is frequently elevated in SCLC at diagnosis and linked to advanced disease; CgA levels are also correlated with metastatic disease included BM carcinomatosis; CD56 is found in a variety of cell types and it is quite common in SCLC and correlated with NSE. SCLC is a distinct histological subgroup: it occurs almost exclusively in smokers and is characterized by a high growth fraction and early development of widespread metastases. The hematological morphology and immunophenotype assays potentially guiding to a misdiagnosis of AML need to be carefully interpreted in correlation with other laboratory findings.

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UPREGULATION OF MIR-29A AND GENOMIC DNA HYPERMETHYLATION IN NORMAL KARYOTYPE AML SHOWING DNMT3A MUTATION

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DNMT3A, a member of DNA methyltransferases, is mutated in approximately 22% of *de novo* normal karyotype acute myeloid leukemia (NK-AML) patients leading to adverse overall survival. The highly recurrent mutation in DNMT3A is a "gain of function-like" at codon R882. To indagate about miRNA signature in NK-AML R882-DNMT3A mutated we studied by qRT-PCR the expression of 384 known human miRNA in 9 selected *de novo* AML DNMT3A mutated. We compared miRNA expression data with our previous results obtained in 31 AML DNMT3A wild type (WT) and we focused on a strong up-regulation of miR155, miR29a, miR196b and miR25. We consolidated this data in additional 24 new DNMT3A mutated AML and we confirmed the upregulation of miR29a (fold 289,201; p-value 0,000); miR29a has been demonstrated to directly target 3'UTR of DNMT3A resulting in a global hypomethylation but also directly suppress two major DNA demethylases TET1 and TDG. To understand the pathogenesis of the subgroup of AML DNMT3A mutated and the existing correlation between miR29a and its targets, we evaluated the expression levels of miR29a targets DNMT3A, TET1 and TDG in 43 AML DNMT3A mutated patients and in 43 control group AML DNMT3A WT by qRT-PCR. Results obtained revealed a no significant difference in expression of DNMT3A and of TDG; however we found a significant downregulation of the demethylases TET1 (0,661 fold; p-value 0,039). These data suggest that miR29a acts as a crucial regulator of DNA methylation and probably in presence of DNMT3A activating mutations and TET1 downregulation may cause a perturbation of methylation pattern. We analyzed the methylation status of the genomic DNA of bone marrow cells from 6 AML patients (including 3 DNMT3A-mutated and 3 DNMT3A-WT cases) and from 5 healty donors as control by Methylation Sensitive Arbitrarily Primed-PCR that provides a qualitative estimate of genome-wide DNA methylation. Results showed a global hypermethylation of genome in DNMT3A mutated patients compared to DNMT3A WT group and healthy bone marrow. The performed study increasingly suggests that the DNMT3A gain-of-function mutation, the significant upregulation of miR29a and significant downregulation of demethylase TET1 target gene would contribute to the maintenance of the hypermethylation status of the genome in patients with DNMT3A mutation. This issue may have important implications for treatment and response to hypomethylating drugs in patients affected by alterations in DNMT3A.

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RISK STRATIFICATION OF ACUTE MYELOID LEUKEMIA: A SICILIAN NETWORK FOR INTEGRATIVE ANALYSIS OF MULTIPLE MOLECULAR MARKERS AND KARYOTYPE

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Acute myeloid leukaemia (AML) is a cytogenetically heterogeneous disorder with acquired recurrent chromosomal alterations in about 55% of patients. The remaining normal katyotype AML (NK-AML) are characterized by molecular abnormalities; gene mutations of FLT3, WT1, IDH1, DNMT3A and high expression levels of the BAALC and