tive characteristics of neoplastic B-CLL cells. The impact of trisomy 12, del(13q), del(17p) and del(11q) was determined by interphase fluorescence in situ hybridization analysis (iFISH) of purified neoplastic B-cells from a series of 180 patients with newly diagnosed B-CLL on the immunophenotype , DNA ploidy status and the proliferative rate of neoplastic B-cells. Half (50%) of all B-CLL cases studied displayed one (40%) or more (10%) of the genetic abnormalities, trisomy 12 and del(13q) being the most frequently detected ones (23% and 21%, respectively), del(17p) and del(11q) being found in 9% and 9.4% of the cases, respectively. Trisomy 12 was associated with a higher frequency of DNA aneuploidy (p=0.012) together with a higher reactivity for CD22, CD27, CD24 and CD79b. The expression of the this latter marker was also higher among cases with 17p- which in turn showed reduced CD11c expression. Cases carrying del(13q) showed a higher expression of CD5, CD43 and CyBCL2, these latter two markers being also brighter among cases with 11q-. Remarkably, none of the chromosomal abnormalities investigated was associated with an increased proliferation of neoplastic B-cell by itself, although B-CLL cases simultaneous showing 13q- and 17p- displayed a higher percentage of S+G2/M-phase tumor cells as compared with individuals carrying either 13q- (p=0.02) alone or cases showing no genetic abnormalities (p=0.03). In summary, our results confirm and extend previous observations about the frequency of trisomy 12, 13q-, 17p- and 11q- in B-CLL patients, where they affect only a variable proportion of all neoplastic cells showing that the abnormalities have a clear impact on the immunophenotypic profile of B-CLL cells; in contrast, the impact of these cytogenetic abnormalities on the proliferative rate of neoplastic B-cells was only noted for cases simultaneously carrying 13q- and 17p-.

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ANGIOGENIC CYTOKINES IN B-CELL CHRONIC LYMPHOCYTIC LEUKEMIA: ASSOCIATION WITH IGVH MUTATION STATUS AND GENETIC ABNORMALITIES

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Backgrounds. B-cell chronic lymphocytic leukemia (B-CLL) is a disease with an extremely variable clinical course. New prognostic factors such as mutation status of immunoglobulin heavy chain variable region (IgVH) or genetic aberrations detected by fluorescent in situ hybridization (FISH) are being increasingly used in order to identify patients with high-risk disease. Several studies have shown that angiogenesis is increased in B-CLL and may potentially help in prognostic assessment of B-CLL patients. *Aims.* To assess relationship between plasma concentrations of vascular endothelial growth factor (VEGF) or basic fibroblast growth factor (bFGF) and IgVH mutational status or genetic aberrations. Methods. We measured VEGF and bFGF using sandwich enzyme-linked immunosorbent assay (ELISA) kits in peripheral blood plasma of 49 patients (males, females, age) with untreated B-CLL and 50 healthy donors. IgVH mutation status was analyzed using cDNA transcribed from B-CLL RNA for touch-down reverse transcriptase polymerase chain reaction (RT-PCR) with degenerate primers for VH1-7 families; IgVH sequences were aligned to the nearest germline using the Ig BLAST database. There were 28 patients with low risk, 17 with intermediate risk and 4 with high-risk disease according to modified Rai staging. Mutated IgVH genes (i.e. more than 2% of somatic mutations) were identified in 23 and unmutated in 26 patients. Genetic abnormalities using fluorescence in situ hybridization (FISH) probes for del 13q, del 11q, del 17p and +12 were investigated in 40 patients. We divided patients according to genetic aberrations into favourable (no abnormality or del 13q, n=25) and unfavourable group (del 11q or +12 or 17p or multiple abnormalities, n=15). Results. There was statistically significant increase of both VEGF (p=0.006) and bFGF (p<0.0001) in patients with B-CLL compared to the control group. Patients with mutated IgVH genes had significantly higher concentrations of bFGF (p=0.0149) but not VEGF (p=0.146) than those with unmutated IgVH. Furthemore, bFGF was significantly higher in both IgVH subgroups (p<0.0001) while VEGF was significantly elevated in IgVH mutated (p=0.0002) but not unmutated patients (p=0.0788). Regarding cytogenetics, significant difference between patients with favourable vs. unfavourable aberrations was neither in VEGF nor bFGF levels (p=0.878 and p=0.494). *Conclusions.* This study confirms that angiogenic activators are elevated in patients with B-CLL. Interestingly, bFGF but not VEGF was significantly higher in patients with mutated IgVH genes in comparison to unmutated IgVH. We did not observe significant difference between low- and high-risk genetic abnormalities. The data must however be interpreted with caution due to relatively low number of patient. Larger study is necessary to perform a more detailed statistical assessment including multivariate analysis.

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CASE REPORT: PLASMA CELL LEUKEMIA SUCESSFULLY TREATED WITH BORTEZOMIB, MELPHALAN, PREDNISONE AND THALIDOMIDE (V-MPT)

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Plasma cell leukemia (PCL) is an aggressive disease defined as circulating peripheral blood plasma cells exceeding 2×10^9/L or 20% of peripheral blood plasma cells (1).The disease can occur as primary disease or as secondary disease evoluted of a Multiple Myeloma . The disease is very aggressive with median overall survival of about seven months for primary and 2 months for secondary plasma cell leukemia (2). This is the report of a 67 year old woman with three years history of MGUS (monoclonal gammopathy of unknown significance) IgG lambda that evolved into Multiple Myeloma stage IIA according to Salmon and Durie (International Scoring System ISS 3). Deletion 13q was present in FISH-Analysis. She was treated with induction chemotherapy (3 cycles of Vincristine, Doxorubicine and Dexamethasone (VAD)), stem cell mobilisation with IEV (Ifosfamide, Epirubicine, Etoposide) and double autologous transplantation after conditioning with Melphalan 140mg/m^2. After the second autologous transplantation the patient remained in partial remission showing a small monoclonal component in the serum for seven months when the patient presented at the day hospital with diffuse effusions. Peripheral blood showed 19×10^9/L white blood cells, 8.9 g/dL of hemoglobin and 16×10^9/L platelets with a differential leukocyte count of 50% neutrophils, 22% lymphocytes, 4% monocytes and 24% plasmacells. Flow cytometric analysis confirmed the presence of 36% plasmacells as shown by the expression of CD138$^+$. All of them had an aberrant antigen expression (CD138$^+$/CD19$^-$/CD56$^-$). Further the patient had acute renal failure with a creatinine-level of 4.1g/dl. The monoclonal component had risen to 5g /l. Bone marrow aspiration was not possible (punctio sicca) and histological examination showed an almost complete infiltration of the bone marrow by clonal plasmacells of intermediate differentiation. The patient was initially treated with dexamethasone 40 mg/die on days 1-4, 9-12 and 17-20 for two cycles with reduction of plasmacellinfiltration in the bone marrow to 50% of all nucleated cells. After clearance of plasmacells in the peripheral blood smear cerebrospinal fluid was analysed and the presence of plasmacells was excluded by morphological examination and by flow cytometry. After the two cycles of Dexamethasone-monotherapy a combination chemotherapy including bortezomib (1.3 m^2 on days 1, 4, 8,1 1), thalidomide (50 mg/die), melphalan (0.4mg/kg on days 1-5) and prednisone (40 mg/m^2 on days 1-5) (3) was started. After three of four cycles (recycling every 35 days) the patient had a normal peripheral blood count and the monoclonal component in the peripheral blood disappeared while immunofixation remained positive (near complete Remission nCR) A maintenance therapy with daily thalidomide (50mg/die) and dexamethasone (40 mg/die days 1-4 to recycle every 28 days) was initiated and eleven months after diagnosis of plasmacell leukaemia the patient is still in nCR without significant side effects. Combination therapy including bortezomib, thalidomide, melphalan and prednisone should be considered as effective and save treatment of plasmacell leukemia.

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MAINTENANCE WITH VERY LOW DOSE THALIDOMIDE AFTER AUTO-SCT IN MULTIPLE MYELOMA: LOW TOXICITY AND IMPROVED OUTCOME

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High dose therapy with single or double transplantation (auto-SCT) has improved prognosis of multiple myeloma (MM). New drugs are