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CLINICOPATHOLOGICAL CORRELATES OF PLASMA CELLS CD56 (NCAM) EXPRESSION IN MULTIPLE MYELOMA

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It was shown that absence of CD56 on malignant plasma cells (PCs) is hallmark of plasma cell leukemia (PCL), special subset of multiple myeloma (MM) (Leukemia 1998; 12: 1977) and may play role in pathogenesis of central nervous system MM (Br J Haematol 2005; 129: 539). There was also found that expression of CD56 correlates with presence of osteolysis in MM and distinguishes MM from MGUS and lymphomas with plasmacytoid differentiation (Am J Pathol 2002; 160: 1293). Aim of this study was to evaluate intensity of CD56 expression on bone marrow (BM) myelomatous PCs and to assess clinical correlations. The study group consisted of 186 MM patients (100M 86F, median age 63, range 32-89yr ;28 at stage I, 43-II, 115 -III; 137 had osteolysis; monoclonal protein IgG was in 118 patients, IgA-45, IgD-1, IgM-2, Bence Jones'18, NS-2) and 16 PCL patients. Controls were 10 healthy subjects. Immunophenotyping was done on freshly collected BM samples using triple staining combination of CD138/CD56/CD38 monoclonal antibodies analysed by flow cytometry (Cytoron Absolute and FACSCalibur-Becton Dickinson). Plasma cells were identified as cells showing high-density expression of CD38 and CD138 (syndecan-1). Antigen expression intensity was calculated as relative fluorescence intensity (RFI) and for direct quantitative analysis the QuantiBRITE test was applied. Mean channels of phycoerythrin fluorescence were defined and antibody bounding capacity (ABC) was then calculated using QuantiCALC software. *Results.* In 128 patients (69%) PCs showed CD56 expression. Out of all CD38++/CD138+ BM cells mean proportion of PCs with CD56 expression, was 83±20%, median 93%. RFI values ranged from 7,6 to 27,4 in particular patients (18,0±4,5, median 17,8) and the number of CD56 binding sites (ABC) on MM plasma cells ranged from 2255 to 58469 (14199±15038, median 8866). A correlation was found between RFI and ABC values (r=0,76; p<0,001)). In 58 MM patients considered as CD56 negative myeloma mean proportion of all BM CD38++ cells with CD56 expression was 4,8±4,2%, median 3,5%. A correlation was found between proportion of all BM CD38++ cells with CD56 expression and ABC (r=0,60) and RFI (r=0,62) indices (p<0,001). Normal PCs did not express CD56. Osteolytic lesions were found in 80% of CD56+ MM patients and in 60% of patients with CD56 negative myeloma. When comparing other clinical and biological disease characteristics e.g. monoclonal protein isotype, b2M, LDH, stage of disease, calcium, creatinine, response to chemotherapy, survival time of CD56 positive and CD56 negative cases, no significant differences were found. Of 16 PCL cases 8 showed CD56 expression on PCs in BM and on those in peripheral blood. *Conclusions.* In two thirds of MM patients malignant PCs show CD56 expression. Intensity of CD56 expression on PCs varies among particular CD56 positive MM patients. There is relationship between proportion of BM CD56 positive PCs and density (ABC) and intensity (RFI) of expression of this molecule. In half of PCL cases leukemic PCs show CD56 expression.

Myeloma and other monoclonal gammopathies II

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FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY IN MULTIPLE MYELOMA, SOLITARY PLASMOCYTOMA AND MONOCLONAL GAMMAPATHY OF UNKNOWN SIGNIFICANCE

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The aim of our study was to evaluate the role of fluorine-18 fluorodeoxyglucose positron emission tomography (FDG-PET) in plasma cell malignancies. A total of 49 pacients were enrolled including 13 patients with newly diagnosed multiple myeloma (MM) and negative bone radiographs, four patients with solitary plasmocytoma, 26 patients with MM in remission but with suspected relapse, and six patients with monoclonal gammopathy of unknown significance (MGUS) with suspected progression to MM or with suspected other malignancy. FDG-PET results were verified by conventional imaging methods, including plain radiographs, magnetic resonance imaging (MRI) and computer tomography (CT). Focally increased FDG uptake was observed in three (23%) of 11 newly diagnosed myeloma patients with negative bone radiographs. The findings were all confirmed by CT or MRI. FDG-PET was negative in two patients with newly diagnosed MM, negative bone radiographs, and without focal infiltration on MRI but with anemia, high monoclonal imunoglobulin and high bone marrow infiltration by plasmocytes. In all other cases FDG-PET negativity in asymptomatic myeloma was associated with favorable prognosis; these patients are without progression after the median follow-up of 14 months. Focally increased tracer uptake was found in five of 26 patients with MM in remission. In four cases it was due to MM relapse, in one case due to ovarian carcinoma. Only in one patient FDG-PET failed to recognize extraosseal progression. Of the 20 patients who had negative FDG-PET scans, only one relapsed 12 months after FDG-PET examination; the remaining 19 patients are without progression with the median follow-up of 15 months. FDG-PET was positive in two of six patients with MGUS. In one case a thyroid carcinoma was later detected, in the other an intestinal tumor was found. We conclude that FDG PET might contribute to initial staging of MM patients with negative bone radiographs and is useful for the follow-up of patients in remission especially in non-secretory MM and in patients with large plasmocytoma (>5 cm) after radiochemotherapy.

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TREATMENT WITH BENDAMUSTINE, THALIDOMIDE AND PREDNISOLONE IN ADVANCED MYELOMA PATIENTS: RESULTS OF A PHASE I CLINICAL TRIAL.

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Thalidomide is an active single agent in advanced relapsed or refractory multiple myeloma (MM). Combination of low dose thalidomide with bendamustine and prednisolone might be a way to maintain efficacy of the drug without dose limiting toxicity (DLT). The treatment consists of a fixed dose of bendamustine (60 mg/qm) day 1, 8, and 15 and prednisolone (100 mg) day 1, 8, 15, and 22. At the same time, thalidomide was given in patients cohorts with escalating doses, starting with 50 mg to a maximum of 200 mg daily. 8 patients (4 after conventional chemotherapy and 4 after APBSCT) were enrolled at each dose level. Cycles were repeated every 28 days for a minimum of 2 and a maximum of 10 cycles until a maximal response was achieved, a DLT or a disease progression were observed. 23 patients (8 in the first dose level with 50 mg thalidomide, 8 in the second dose level with 100 mg and 7 patients in the third dose level with 200 mg) are enrolled until now. The number of prior treatment regimens was 2 or more in all patients. 6 patients were refractory for the last treatment. Median age was 67 years (range: 40-78). All patients completed 2 cycles of BPT-treatment and were hence evaluable. Response was assessed using EBMT criteria modified to include near complete remission (nCR) and very good partial remission (VGPR). 21 of 23 patients responded after at least 2 cycles of chemotherapy with 3 CR, 5 VGPR, 11 PR and 2 MR. 2 patients had stable disease. With a median follow up of twelfe months, EFS and OS at twelfe months were 47% and 87%, respectively. Most common site