(46,XX(18)/45,X0(7)). The patient was conditioned with the classical BuCy regimen and rescued with 5.8 million/kg of body weight allogeneic CD34+ peripheral blood stem-cells. He received IV cyclosporine and four doses of methotrexate as GVHD prophylaxis, but on day +11 he manifested a hyperacute cutaneous and oral mucosa GVHD grade II. On day+16 the patient engrafted the WBC completely, while platelets engrafted on day +70. One month later he manifested a profound thrombotic thrombocytopenic purpura. Cytogenetic analyses of the patient revealed the complete donor karyotype 46,XX/45,X0 two times after transplantation. Chimerism study was 99.5% of donor type. On day +97 he manifested an extensive chronic cutaneous GVHD grade III, with conjunctival and oral involvement. The post-transplant course was further complicated by the development of diabetes mellitus, severe osteoporosis with a pathologic smash of the L2 vertebra and CMV reactivation. Nineteen months later, the patient is in fairly good general condition. He has limited cutaneous GVHD, suffering mainly from his orthopedic problem. Summary/Conclusions. Our patient manifested osteoporosis, diabetes mellitus and conjunctival defect after SCT from a mosaicic TS. Osteoporosis is a rare phenomenon in male patients after SCT, while it is very common in adults with TS who show a reduction in bone mass and an increased risk of fractures. Diabetes mellitus and ophthalmic disorders are also uncommon after SCT. On the contrary, diabetes mellitus is 2-4 times more frequent in TS compared with the general population. Osteoporosis problems are seen in 65% of women with TS. As it is has been accepted, dosage of specific genes located on X chromosome in X0 cells are responsible for such abnormalities in TS. Therefore, the X0 cells could have pathologic consequences in the recipient, especially under immunologic stress.

1467
LEVELS OF METALLOPROTEINASE-9 (MMP-9) IN PATIENTS WITH POLYCYTHEMIA VERA


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Chronic myeloproliferative disorders are characterized by the progressive remodeling of the bone marrow stroma during angiogenesis and the fibrotic tissue deposition. Angiogenesis shares common mechanistic steps between the cells and the extracellular matrix including proteolysis. The family of metalloproteinases (MMPs) and their inhibitors play a serious role in this proteolysis and their balance determines whether the tissue remodeling goes to breakdown or increased fibrosis. Matrix metalloproteinase-9 (MMP-9) is produced in haematopoietic tissue by monocytes and mature granulocytes and is stored in the gelatinase granules while pro-MMP-9 is also stored in platelets and acts as an endogenous angiogenic factor. In order to investigate the role of MMP-9 as an angiogenic factor in Polycythemia Vera (PV) and to evaluate the role of MMP-9 in the tissue remodeling process we determined by sensitive LDH release assay, serum levels of MMP-9 in 38 polycythemic patients. A total of 38 patients with PV (18 males and 20 females) with a mean age of 56.1±15.54 (m ± SD) year (range 24-81) were included. Twenty five patients were managed with phlebotomy, four received hydroxyurea, eight were managed with hydroxyurea and phlebotomy and one was treated with interferon. Three had clinically detected spleen enlargement. The control group consisted of 16 healthy subjects (mean age 55.3±6 years). The age difference between the two groups was not statistically significant (p=0.82). Serum levels of total MMP-9 were measured by a commercial quantitative sandwich enzyme immunoassay. Serum MMP-9 concentrations did not differ among polycythemic patients and the control group (316±249 pg/ml and 446.2±290.3 pg/ml, respectively, p=0.08). In the patient group and in the control group we found no statistically significant correlation between serum MMP-9 levels and platelet count, haematocrit, WBC count and age. No difference was found between patients on different therapeutic regimens. In conclusion the present report demonstrates no difference among polycythemic patients and healthy individuals in concern to MMP-9 serum levels in a large group of patients. Future studies are needed to investigate whether serum markers for collagen metabolism reflect the disturbed balance of matrix synthesis and proteolytic degradation that exists in neangiogenesis that characterizes polycythemia vera and myeloproliferative disorders.

1468
ELEVATED TNF-α AND LDH WITHOUT DISTURBANCE IN PARARTHROME ASSOCIATED WITH DIFFUSE OSTEOLOGIC LESIONS IN LEUKEMIC TRANSFORMATION OF MYELOFIBROSIS

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Backgrounds. Myelofibrosis is a clonal myeloproliferative disorder characterized by splenomegaly, abnormal deposition of collagen in the bone marrow, extramedullary haematopoiesis, dacrocytosis and leukoerythroblastic blood smear. The pathogenesis and course of the disease is mediated by complex network of several cytokines. These cytokines mainly include transforming growth factor α, basic fibroblast growth factor, vascular endothelial growth factor, platelet factor 4, calmodulin and tumor necrosis factor α. Aims. Based on role cytokines in myelofibrosis, we present an atypical case of leukaemic transformation in myelofibrosis associated with diffuse osteolytic lesions and extremely elevated sera TNF-α and LDH without disturbance in parathormone in a 49-year-old female that firstly developed malaise and abdominal pain at first visit. Results. The laboratory analyses showed decrease in heimocyte count, increase of platelets and presence of erythroblast and dacrocytes in peripheral blood. Cytological examination disclosed hypocellularity with the presence of all cell lines without increased blasts. Bone marrow biopsy disclosed hypocellularity, presence of all cell lineage and bone marrow reticulin and collagen fibrosis. A diagnosis of myelofibrosis was established. After 5 years, her condition deteriorated with malaise and bone pain. Physical examination showed pallor skin and mucous membranes with enlarged spleen 270 mm in diameter. The laboratory analyses showed Hb of 54 g/l, WBC of 8.0×10/L, platelets of 122×10/L, with myeloblasts 39%, myelocytes 7%, metamyelocytes 1%, bands 6% segmented neutrophils 16%, eosinophils 1%, lymphocytes 22%, monoocytes 6%, and 15 erythroblasts/100 leukocytes. The biochemical analyses showed extremely elevated sera LDH activity (1339 U/L). Bone marrow aspirate was hypocellular with 72% of blasts mostly with characteristics of myeloblasts and more than 20% of monoblastic type. Cytochemical staining with myeloperoxidase showed that 30% of blasts were positive, and 25% of blasts were α-naphthol-esterase positive. The cytological finding was in accordance with FAB M4 type of acute leukemia. The immunophenotyping of the peripheral blood cells expressed HLA-DR (74.9%), CD34 (77.9%), CD13 (60.3%), CD33 (42.6%), CD14 (59.8%), CD4 (42.4%) markers. Cyto genetic examination of bone marrow cells showed inversion of chromosome 16 (46XX, inv(16)(p13q22)). RT-PCR studies/MYH11 fusion gene confirmed cytogenetic finding and revealed the CBF transcript. PCR analysis disclosed the presence of FLT3 Asp835 mutation. Retrospective analyses of extracted DNA from bone marrow histologic specimen at the time of diagnosis, showed that there no presence of FLT3 mutations. X-ray showed the presence of diffuse osteolytic lesions in the pelvis, long bones as well as in vertebrae. As the global bone destruction was documented diffusely increased accumulation of the radiopharma. The values of parathormone in the sera and supernatants of cultured blast cells were normal. TNF-α determined by sensitive LDH release assay, was extremely increased (1421 pg/ml) in comparison to control values of 700 pg/ml. Summary / Conclusions. We postulated that elevated TNF-α can be reason for lytic bone lesions, accompanied with high sera LDH activity indicating high bone turnover. Also continuously elevated TNF-α can contribute for developing of the leukemia growth in this patient, as endogenous promoter.
report of IHS patient diagnosed in 1998. Serious organ damage developed at 2 years and required treatment initiation. Corticoids were quite ineffective as well as cyclosporin A was. Cyto genetic examination of bone marrow cells revealed in 49% of examined metaphases karyotype 45,X,-Y. Fluorescence in situ hybridization (FISH)-based strategy was used to detect F/P in bone marrow cells. Using bacterial artificial chromosome (BAC) probes fusion of F/P was not revealed. Considering the strong patient ineffective, disease progression, and hematopoiesis finding imatinib treatment was started. Imatinib in dose of 100 mg daily was administered despite the F/P negativity. Results. Eosinophils fully disappeared after 6 days of the therapy. Complete hematologic remission was achieved after 2 weeks. Cyto genetic response was assessed after 3 months of treatment. Conclusions. The case of IHS/CEI patient presenting with the karyotype 45, X,-Y, F/P-negative but imatinib-sensitive has not been published yet. Identification of imatinib-sensitive target structure responsible for the disease development is a challenge to future research.

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**1470 MIXED IMMUNODEFICIENCY, ATYICAL MYCOBACTERIA AND MYELOFIBROSIS**

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**Background and Aims.** Myelofibrosis can be idiopathic (a chronic myeloproliferative syndrome) or secondary to many kinds of insults, as a reaction to malignancy, infections, endocrinopathies, auto-immune diseases and granulomatous disease. Pancytopenia and hepatosplenomegaly are frequent, and only reversible when the secondary injury can be treated. The authors present a case of myelofibrosis diagnosed in an 11 months old boy; later it was discovered to be secondary to atypical mycobacteria and quadruple antibacterial therapy for one year reversed the clinical status. Results. The decreasing of aggregation response (16 cases in all after conductors used) was not accompanied by statistically significant changes in other examinations of platelet function tests. Moreover, there were no observed statistically significant changes in repeated examinations after six month of the treatment. There was an even no correlation between functional examination of the platelets and clinical symptoms of the disease. Conclusion. Functional disorder of the platelets seems to be the part of clinical findings of the disease, but does not correspond with biological activity of the disease or with clinical symptoms and/or with the answer to the therapy. Although, the treatment (especially with acid acetylsalicylic-ASA) can widely modify platelet function, it was not even observed to be significantly different in our ASA-treated vs. ASA-untreated patients.

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**1471 PLATELET FUNCTION EXAMINATION IN ESSENTIAL THROMBOCYTHEMIA**

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**Background.** Basic diagnosis of essential thrombocythemia is proved by estimation of elevated platelets count and corresponding findings of activated megakaryopoiesis in bone marrow with contemporaneous inclu sion of their reactive changes. The therapy is mainly focused on correction of high platelets count in the blood. The treatment is different in young and elderly patients, in cardiovascular or thrombotic risk and non-risk patients. However, the treatment influences not only the count, but also the function of platelets and so can lead to influencing of clinical symptoms. The function of platelets is not currently investigated before drug administration and in the course of the treatment. Aim of the study was to evaluate clinical and laboratory importance of platelet functional characteristics in essential thrombocythemia. Methods. 30 patients have been included in our observation and we performed (beside the basic laboratory tests - platelets aggregation according to Born, PFA-100 examination and flow-cytometric estimation of CD36, CD42a, CD61, CD62, CD63 markers). The laboratory testing was done before and six months after the treatment. The platelet aggregation was tested using ADP in two concentrations, colagen and caticion propylgalat as inductors, and three parameters - percentil of aggregation, slope and desaggregation remained. Results. the decreasing of aggregation response and the deviation of aggregation to many kinds of insults, as a reaction to malignancy, infections, endocrinopathies, auto-immune diseases and granulomatous disease. Pancytopenia and hepatosplenomegaly are frequent, and only reversible when the secondary injury can be treated. The authors present a case of myelofibrosis diagnosed in an 11 months old boy; later it was discovered to be secondary to atypical mycobacteria and quadruple antibacterial therapy for one year reversed the clinical status. Results. The decreasing of aggregation response (16 cases in all after conductors used) was not accompanied by statistically significant changes in other examinations of platelet function tests. Moreover, there were no observed statistically significant changes in repeated examinations after six month of the treatment. There was an even no correlation between functional examination of the platelets and clinical symptoms of the disease. Conclusion. Functional disorder of the platelets seems to be the part of clinical findings of the disease, but does not correspond with biological activity of the disease or with clinical symptoms and/or with the answer to the therapy. Although, the treatment (especially with acid acetylsalicylic-ASA) can widely modify platelet function, it was not even observed to be significantly different in our ASA-treated vs. ASA-untreated patients.

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**1472 POLYCYTHEMIA VERA INITIALLY DIAGNOSED AS ESSENTIAL THROMBOCYTHEMIA**

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**Backgrounds.** The differentiated diagnosis as part of the myeloid proliferative chronic disease Ph- remains afterwards difficult, in spite of the differentiation possibilities. The purpose of this study was to evaluate clinical and laboratory importance of platelet functional characteristics in essential thrombocythemia. Methods. 30 patients have been included in our observation and we performed (beside the basic laboratory tests - platelets aggregation according to Born, PFA-100 examination and flow-cytometric estimation of CD36, CD42a, CD61, CD62, CD63 markers). The laboratory testing was done before and six months after the treatment. The platelet aggregation was tested using ADP in two concentrations, colagen and caticion propylgalat as inductors, and three parameters - percentil of aggregation, slope and desaggregation remained. Results. the decreasing of aggregation response (16 cases in all after conductors used) was not accompanied by statistically significant changes in other examinations of platelet function tests. Moreover, there were no observed statistically significant changes in repeated examinations after six month of the treatment. There was an even no correlation between functional examination of the platelets and clinical symptoms of the disease. Conclusion. Functional disorder of the platelets seems to be the part of clinical findings of the disease, but does not correspond with biological activity of the disease or with clinical symptoms and/or with the answer to the therapy. Although, the treatment (especially with acid acetylsalicylic-ASA) can widely modify platelet function, it was not even observed to be significantly different in our ASA-treated vs. ASA-untreated patients.

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