AML 06

SELECTION OF A METASTATIC MASTOCYTOMA P 815 VARIANT AND CHARACTERIZATION OF ITS GANGLIOSIDE PATTERN

G. Bandlow, R. Härtl, K. Ritter, B. Gröner

In vitro cultured Mastocytoma P 815 cells were injected into DBA/2 mice either i.p. or into a tail vain. After intravenious injection tumour cells predominantly proliferated in the liver. The liver was broken up and the released Mastocytoma cells were now transplanted and further passaged i.p. After several passages the volume of tumour ascites gradually decreased whereas the rate of tumour proliferation increased. This selected tumour cell variant could also be differentiated from the original primary tumour line using histological, immune histological and electronmicroscopical methods. Both tumour lines differed in vivo in their enzyme pattern in the peripheral blood. The cell surfaces of the two cell lines showed a high content of GSL in the lipid fraction, mainly NANA containing GSL, respectively gangliosides. The gangliosides from Mastocytoma P 815 cells, from liver tissues and from liver infiltrated by tumour cells were analysed by HPTLC. A characteristic pattern was found for liver tissue and Mastocytoma P 815. The infiltrated liver showed a combined pattern of both. Furthermore the ganglioside content was determined in the peripheral blood. Tumour bearing mice showed a higher amount of gangliosides than normal animals. A steady increase of the ganglioside level was observed during tumour growth.

Abtlg. Med. Mikrobiologie, Zentrum für Hygiene und Humangenetik der Universität Göttingen, Kreuzbergring 57, D-3400 Göttingen

AML 07

COMPARISON OF CYTOTOXIC EFFECTS OF 1,2,4-TRIGLYCIDYLURAZOL (TGU) ON MURINE HEMATOPOIETIC PROGENITOR CELLS AND COLONY-FORMING LEUKEMIC CELLS (L1210-CFU) IN VIVO

M.R.Nowrousian, C.Doberauer, R.B.Schilcher, C.G.Schmidt

TGU is a new Triepoxide with antitumoral activity in animal models and in man. In the present study, acute and cumulative effects of the agent on hematopoiesis were investigated in mice by measurements of WBC count and marrow concentrations of pluripotential (CFU-S) and granulocytic (CFU-C) progenitor cells. Antileukemic effects were evaluated in a group of mice bearing diffusion chambers (DCs) with L1210 cells. In these experiments, the activity of TGU was also compared to that of Cyclophosphamide (Cy) and Mafosfamide (Ma), a new Oxazaphosphorine derivative. WBC count and marrow content of CFU-S and CFU-C were found to be reduced much more severely and to recover less rapidly after a single dose of 144 mg/kg than after 36 mg/kg of TGU. Weekly injections of 36 mg/kg of TGU for 4 weeks also appeared to be less myelotoxic than the same total dose when given as a single injection. In mice treated with weekly doses of 36, 72 (=LD10), 108 or 144 mg/kg of TGU for 4 weeks, there appeared to be a dose-related but not cumulative suppression of the WBC count and the marrow CFU-S and CFU-C content during the 4 weeks of treatment. After single equitoxic (1/2LD10) doses of TGU (36 mg/kg), Cy (200 mg/kg) or Ma (200 mg/kg), the total number of L1210 cells and the number of L1210-CFU in DCs were found to be reduced to a higher degree by Cy or Ma than by TGU. In all 3 groups, however, the cells did not recover completely during the 21 days of observation. Results indicate dose-related but not cumulative effects of TGU on hematopoiesis. At equitoxic doses (1/2LD10), TGU seems to have a lower antileukemic effect than Cy or Ma. At this dose level, however, the drug appears to be more toxic to leukemic cells than to normal hematopoietic progenitor cells.

Innere Universitätsklinik und Poliklinik (Tumorforschung), Westdeutsches Tumorzentrum, D-4300 Essen
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AML 08

SEQUENTIAL ANTIBIOTIC CHEMOTHERAPY FOR HIGH RISK NEUTROPENIC PATIENTS

C.U.Anders,H.Höfeler,J.Kemper,K.Höffken and C.G.Schmidt

Infections in neutropenic patients are mostly caused by bacteria. Since the responsible pathogens can rarely be identified upon manifestation of the infection, initial antibiotic therapy has to cover a broad bacterial spectrum. Likewise, regimens for nonresponders to first-line antibiotic therapy should aim at those parts of the spectrum where initial therapy was less effective. We investigated the sequential antibiotic regimen described below during 63 febrile episodes in 38 patients.

Fever 38.5°C: random

Reg.A: azlocillin + netilmycin
Reg.B: cefotaxime + netilmycin

persistent fever for 3 days or relapse

Reg.C: ceftazidime + netilmycin

persistent fever for 3 days or relapse

Reg.D: ceftazidime + vancomycin

In conclusion, regimen A and B are equally effective as initial therapy with response-rates of 72%(A) and 70%(B) respectively. Overall 90% (53/59) of bacterial infections responded to the sequential antibiotic regimens. The presented antibiotic chemotherapy has demonstrated a high efficacy in neutropenic and immunocompromised patients and diminished mortality of severe infections thus allowing intensified cytostatic therapy with calculable risk.

Innere Universitätsklinik und Poliklinik(Tumorforschung), Westdeutsches Tumorzentrum, Hufelandstr.55, D-4300 Essen

AML 09

THERAPY OF INFECTIONS IN NEUTROPENIC CANCER AND LEUKEMIA PATIENTS WITH TICARCILLIN AND CLAVULANIC ACID

H.H. Fülle and K.P. Hellriegel

The main problem in neutropenic patients is prevention and treatment of infections. 55 patients suffering from acute leukemias, malignant lymphomas or solide tumours and infections during the granulocytopenic phase were treated with the combination of 5000 mg ticarcillin and 200 mg clavulanic acid given 3 times daily by intravenous short infusion. Immediately after the occurence of fever of more than 38,5°C on two consecutive measurements the empiric antibiotic treatment was started. The median granulocyte count was 60/µl on the beginning. The clinical and bacteriological examinations documented 13 septicemias, 6 bronchopneumonias and 1 peritonitis. In 35 patients the origin of the fever was unknown. Patients were treated for a median duration of 9 days. 30 patients responded to treatment with ticarcillin and clavulanic acid alone. 25 of these patients were cured despite ongoing neutropenia. Patients getting not free of fever received in most instances amikacin, additionally. Thereby, 8 further patients could be cured and 5 patients improved. Thus, 43 of the 53 evaluable patients responded to the empiric antibiotic combination therapy. 4 patients had side effects: 2 diarrhoe, 1 cutaneous rush and 1 anaphylactoid reaction. In conclusion, the combination of ticarcillin and clavulanic acid is a safe and effective treatment for infections in neutropenic cancer patients. For patients not responding, the addition of an aminoglycoside is recommended.

II. Innere Abteilung des Krankenhauses Moabit, Turmstr. 21, D-1000 Berlin 21