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Immunologic disorders of the acute dioxin exposed patient

Amirova Z.K., Kruglov E.A., Loshkina E.A.

Regional Ecological Centré of the Republic Bashkortostan. 147. October Av., 450075, Ufa, Bashkortostan, Russia

Sibiryak S.V., Kurchatova N., Yusopova R.Sh.

Department of immunology and immunopharmocology Russian Eye and Plastic Surgery Centre. 47, Koltzevaya St., 450040, Ufa, Bashkortostan, Russia

1. Introduction

The feature of toxicodynamics of dioxins consists in a disorder of immunologic reactivity related to the intervention of ecotoxicants into the process of maturing, differentiation and proliferation of immunocompetent cells. It is known that the immunotoxicity of dioxins is determined in a great extent by their intensity of metabolic activation on citochrome P 4501 A affected by substancial genetic variations ^{1,2)}.

Just because of this the nature and the extent of disorder of immune status, depending on the peculiarities of toxicokinetics, expecially in the limited selection of contingent discussed, are not always unambiguous and they are exposed to considerable variations 3).

The joint chemical-biological investigations are of special importance, where the parallel evaluation of body burden dioxin content and immunoreactivity state is performed.

2. Objects and methods of investigations

We have performed the selected examination of immune status of a patient N., 54 years old, exposed to superacute dioxin intoxication in 1965-1967, accompanied with a skin manifestation (chloracne).

Mononuclears from the heparinized peripheral blood were separated on the gradient of ficoll-visotrast (Flow Lab.), washed with 0,15 M phospate-buffers salt-solution (pH 7,2), containing 3 mM sodium azid and 0,2 % BSA, and weighed in the same medium. Phenotyping was performed with the help of the indirect immunofluorescent method using the monoclonal antibodies of clones LT (Sorbent) and JCO (Diagnotex). The lymphocytes reactivity to the mitogens - PHA (Flow Lab.), ConA (Flow Lab.) and PWM (Flow Lab.) has been evaluated by the traditional method. The immunoglobulins level in serum was determined according to the Manchini method.

The PCDD/Fs content in the whole blood (40 ml) was determined according to 7 . The sample was spiked with 15 13 C₁₂ - 2,3,7,8-PCDD/Fs. The sample extract clean up was performed by use of standards method on the multilayer silica, carbon and alumina columns.

The $^{13}\text{C}_{12}$ -1,2,3,4-TCDD and $^{13}\text{C}_{12}$ -1,2,3,7,8,9-HxCDD were added as the internal standards to the final extract in 5 μ l of dodecane. All the criteria of US EPA Method 1613 were fulfilled.

The measuring system consisted of VG Autospec-Ultima HRMS and Carlo Erba 8035 GC (MS:SIR, 10000, EI+, 36 ev, reg. 2 ions; GC: I&W Scientific DB-5, 60 m, 0,25 μ m, injection volume - 1 μ l).

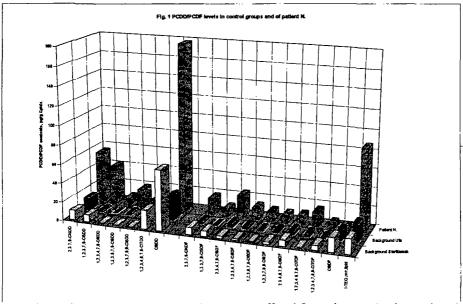
3. Results and Discussions

During 1965-1967 the patient N. was working as an operator on the 2,4,5-T unit (Chimprom, Ufa) and was considered to be a representative of occupationally exposed workers group (about 200 persons) with chloracne.

In 1991 A. Schecter has carried out the inspection of the women, the former workers of that unit and also their children ⁴⁾. The PCDD/Fs level in women blood came up to 280 pg/g lipids (1-TEQ) and the elevated one was discovered for their children (100 pg/g). In the control group (Ufa, n=100) the levels were in the range of 20-23 pg/g lipid ^{5,6)}. These values were lower in comparing to the average values for Europe, but some higher than in the other areas of Russia (St. Petersburg - 17 pg/g, Baikalsk - 18 pg/g) ⁵⁾.

In the man-group of 2,4,5-T unit operators the blood levels of PCDD/Fs was in the range of 60-200 pg/g lipids. For the patient N this level amounted to I-TEQ - 89 pg/g lipids.

The isomeric pattern of this sample in comparison to the background data for Ufa and Sterlitamak (Bashkortostan) is demonstrated on the Fig. 1.



To the medical follow-up moment the patient suffered from the gastric ulcers, chronic cardial ischemia. The complaints typical for immunopathological sundromes have been not brought by the patient. The immunophenotypizing has discovered the following ratio of lymphocyte subpopulations in periphenal blood (%/ abs. value): CD3+ - 73 (1,1); CD4+ - 58 (0,9); CD 8+ - 33 (0,5); CD72+ - 16 (0,2); CD16+ - 28 (0,4); CD25+ - 17 (0,3); HLA-DR-28 (0,4); CD95+ - 38 (0,6). The lymphocyte reactivity to the optimal doses of

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mitogens were following (the stimulation index): for PHA-4; ConA - 1,8; PWM - 4. The level of immunoglobulins in serum was (g/l): IgG - 14; IgM - 2,5; IgM- 1,2.

Thus the patient N. has manifested the disbalance of immunoreactivity, expressed in terms of an increased amount of B- and NK-cells and lymphocytes, bearing the markers of early and late activation in peripheral blood and this is accompanied by the reduced response for the most part to the T-mitogens at relatively high response to mitogen. The alterations described are rather typical for Vietnam war veterans 7 .

4.References

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