SUPPRESSION OF THE ACTIVITY OF NATURAL KILLER-CELLS IN NMRI MICE BY T-2 TOXIN

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Natural killer (NK) cells play an important role in the immune system of man and animals, especially in the rejection of tumors. As tumor promoting activities of T-2 toxin were described repeatedly (1,2), the effects of T-2 toxin on NK-cell function were examined.

EXPERIMENTAL

Animals: Female NMRI-mice, 4-6 week old.

T-2 toxin treatment: T-2 toxin was provided either as a diet or injected i.p. once (2,5 mg/kg) or threetimes (1.25 mg/kg). The experimental design for the oral administration is shown in Table 1. The NK-tests were carried out on day 8 and day 21.

Table 1: Experimental design for oral T-2 administration

Group	Number of animals	T-2 toxin diet		Toxinfree diet
		mg/kg	days	days
A	35	20	7	14
B	40	10	7	14
C	20	1	7	14
D	20	0	0	21*

* Reduced diet (daily feed intake was equivalent to group B)

Poly I:C treatment: To stimulate the NK-cell acitivity, the animals were treated with poly I:C (100 µg, i.p.) 18 hours before setting up the NK-test.

Determination of NK-cell activity: The acitivity of splenic and peritoneal NK-cells was determined using a 4 h ⁵¹Cr-release assay (3). To demonstrate the NK-nature of the effector cells, 3 mice were treated with rabbit anti-asialo GM₁ (20 ng/mouse).

RESULTS

Treatment of mice with rabbit anti-asialo GM₁ abolished cytotoxicity of the isolated cells, indicating the NK-nature of the effector cells. Repeated i.p. injections of T-2 toxin lead to a marked decrease of the splenic NK-cell activity of poly I:C treated mice (Table 2).

Table 2: NK-cell activity in the spleens after i.p. injection of T-2 toxin.

T-2 toxin treatment		%Specific lysis (effector:target)		
hours*	mg/kg bw	100:1	50:1	25:1
18	2,5	17.5	18.5	9.5
96,48,24	1,25	6.0	7.3	2.7
-	-	24.5	16.8	12.3

*before setting up the NK-test

A 7 day oral intake of T-2 toxin containing diets (1 - 20 mg/kg) resulted in a reduction of the cytotoxicity of poly I:C stimulated splenic and peritoneal NK-cells. The suppression was still detectable after feeding a toxinfree diet for 14 days although at a lower degree (Table 3).

Table 3: Reduction of poly I:C activated splenic and peritoneal NK-cell activity after feeding T-2 toxin containing diets (A-C) or a restricted toxinfree diet (D).

Group	Compartment	%Reduction of NK-cell activity*	
		day 8	day 21
A (20 mg/kg)	spleen	56.4	48.9
	peritoneum	80.5	25.9
B (10 mg/kg)	spleen	51.5	15.0
	peritoneum	44.3	18.9
C (1 mg/kg)	spleen	6.2	18.9
	peritoneum	50.4	0.0
D (0 mg/kg)	spleen	0.0	0.0
	peritoneum	0.0	0.0

* at an effector target ratio of 100:1

CONCLUSIONS

The data confirm that injection as well as oral intake of T-2 toxin lead to a long lasting suppression of splenic and peritoneal NK-cell activity in NMRI mice. This inhibition is due to the toxic effect of T-2 toxin and not caused by reduced feed intake. The suppression of NK-cell functions might be one reason for the carcinogenic and tumor promoting activities of T-2 toxin.

REFERENCES

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