Tohoku J. Exp. Med., 1990, **161**, 157-158

Short Report

Production of Tumor Necrosis Factor α and Interleukin 1β by Peripheral Blood Mononuclear Cells from Chronic Hepatitis Type C Patients during Interferon Therapy

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UENO, Y., SUZUKI, H., KOBAYASHI, K., MIURA, M. and TOYATA, T. *Production of Tumor Necrosis Factor α and Interleukin 1β by Peripheral Blood Mononuclear Cells from Chronic Hepatitis Type C Patients during Interferon Therapy.* Tohoku J. Exp. Med., 1990, **161** (2), 157-158 —— To elucidate the role of tumor necrosis factor α (TNF-α) and interleukin 1β (IL-1β) in chronic hepatitis type C (CH(C)), TNF α and IL-1β released from peripheral blood mononuclear cells were measured in 6 CH(C) patients before and during interferon therapy. During the therapy, TNF-α levels were significantly high in two patients whose serum ALT levels turned normal, while IL-1β levels did not show significant change. These results suggest that TNF-α takes part in improvement of CH(C). ———— tumor necrosis factor α; interleukin-1β; chronic hepatitis type C; interferon

Tumor necrosis factor α (TNF-α) and interleukin 1β (IL-1β), released mainly from monocytes, are known to have anti-viral effects (Van Damme et al. 1985; Wong and Goeddel 1986), and may contribute to the elimination of hepatitis type B virus from infected hepatocytes with interferon (IFN) therapy (Daniels et al. 1990). But little is known about their significance in chronic hepatitis type C (CH(C)). We aimed here at proving the role of both cytokines in improvement of CH(C) during IFN therapy.

Six patients with chronic hepatitis were recruited and serologically confirmed type C by Ortho HCV kits (Chiron Co., Emeryville, CA, USA). All patients were administrated IFNs according to the three protocols shown in Table 1. Peripheral blood mononuclear cells (PBMC) were obtained before and during IFN therapy, and cultured with 20 μg of lipopolysaccharide (Difco Laboratories, Detroit, MI, USA) (Daniels et al. 1990). The supernatants were harvested after 24 hours' incubation, and stored at -20°C until assay. TNF-α and IL-1β levels were measured by commercial radio-immuno assay kits (Amersham International plc., Little Chalfont, Buckingham Shire, UK).

During IFN treatment, serum ALT levels continuously fell to normal range (less than 30 international units per liter; IU/liter) in two patients. The TNF-α levels in these patients throughout IFN treatment were significantly higher than those in the other 4 patients ($p<0.01$, U-test). In contrast, the IL-1β levels showed no statistical difference

Received May 17, 1990; revision accepted for publication May 31, 1990.

TABLE 1. *Serum alanine aminotransferase levels and TNF-α and IL-1β production by mononuclear cells*

Patients No.	Dose of IFN[a,b] (million units)	ALT level (IU/liter)		Peak TNF-α (fmol/ml)	Peak IL-1β (fmol/ml)
		at start	most decreased		
1	6	250	28	156.8	42.6
2	10	263	16	145.2	32.8
3	6	344	426	30.6	18.2
4	6	151	78	84.6	91.4
5	6	698	149	65.3	21.0
6	5	309	101	107.6	45.8

[a]All patients listed received IFNs daily, except for patient 6 who received it every other day.

[b]Patients 2 and 6 received IFN-α, and the other patients received IFN-β.

between the two patient groups. From these experience, we suggest that in CH(C) some cytokines, especially TNF-α, may be an index to predict the improvement of serum ALT abnormality during IFN therapy. To date, quantitative assay for HCV has not been available, and thus whether IFN has any effects on HCV is next to be determined.

References

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