IMPACT OF CYTOKINES ON THE PATHOMECHANISM OF ALCOHOLIC NEUROPATHY

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Abstract. *Alcohol abuse is the most frequent cause of polyneuropathy in adults. This polyneuropathy is morphologically heterogeneous with a va-riable degree of lesion in axons or myelin. The pathogenesis is complex and it is not clear why in some patients the lesion is limited to axonal degeneration only while in others it develops into demyelinating polyneuropathy [3]. The main problem of the latter concerns the possible impact of immunological factors on this type of myelin lesion [2]. To elucidate these questions we evaluated the expression of some cytokines, i.e. tumour necrosis factor alpha (TNF-α), monocyte chemotactic protein-1 (MCP-1) and growth-regulated oncogene alpha (GRO-α), known also under the term cytokine-induced neutrophil chemoattractant-1 (CXCL1) in the blood serum of patients with alcoholic polyneuropathy. TNF-α is a pleiotrophic cytokine that plays a crucial role in immunological and defence reactions [1]. It has an impact on cell infiltration by promoting adhesion molecules and chemokine agents. MCP-1, as a strong monocyte chemoattractant factor, exerts an effect on differentiation of ThO lymphocytes into Th2 cells, by playing the role of a key factor in inflammatory processes [7]. GRO-α is another chemokine acting as a growth stimulator involved in inflammatory reactions and tumorigenesis [4,6].*

Keywords: *alcohol, polyneuropathy, myelin, chemokine, immunological factor, diagnostics, inflammation.*

Material and methods. The studied population of polyneuropathy consisted of 31 with an alcohol abuse history. All study subjects presented with signs and symptoms of polyneuropathy.). The alcoholic polyneuropathy group there were 8 females and 23 males with a mean age of 54.5 (range 30-60 years). In both types of polyneuropathy the typical motor and sensory disturbances in upper and lower extremities, with a predominance of the latter ones, were present. The type of polyneuropathy, i.e. the involvement of either axon or myelin, or both, was evaluated by means of electrophysiological methods (electromyo-graphy and velocity of nerve conduction). The subjects with alcoholic polyneuropathy were divided into two groups, one with a case history of less than 9 years and another one with a clinical course longer than 10 years. The control group consisted of 20 healthy subjects (mean age 49.1; range 23-78 years). TNF-α, MCP-1 and GRO-α levels in blood serum were measured in duplicate with the ELISA immunoassay test, with the aid of Quantikine human TNF-α, MCP-1 and GRO-α kits (R&D System, USA). For statistical comparison of differences between the polyneuropathy group and control subjects, the nonparametric Mann-Whitney U-test was used.

Results

The expression of TNF-α in serum of polyneuropathy did not differ from that seen in the control material. The level of MCP-1 in serum was higher (though insignificantly) in patients with the demyelinating form of alcoholic than presented by control patients. The serum level of GRO-

α was significantly higher in both patients with alcoholic polyneuropathy than the levels seen in the sera of control subjects.

Discussion

The pathogenesis of alcoholic polyneuropathy seems to be somewhat less complex than the diabetic one. It includes a direct toxic effect of alcohol abuse, indirect by metabolic and exotoxic changes in parenchymous organs, mainly in the liver, as well as malabsorption and maldigestion [5].

In both studied types of polyneuropathy, there is one question that still remains open: why in some cases with this disease there are only some axons that display typical signs of polyneuropathy, while other ones develop the demyelinating form of changes. The next question deals with the impact of immunological events on this process. Skundric and Lisak [2] underline the clinical aspects of the problem, emphasizing that lack of success in preventing polyneuropathy, even after normalisation of the former, impaired glucose metabolism. This observation suggests an involvement of immunological mediators, which once activated may act notwithstanding the favourable effect of hyperglycaemia treatment.

Some authors point to the role of TNF-α in the mechanism of diabetic polyneuropathy. Satoh et al. [1] claim that under conditions of chronic hyperglycaemia, the production or expression of TNF-α is increased in vascular and neural tissues. This in turn leads to increased microvascular permeability and hypercoagulability, resulting in the development of polyneuropathy. Another author [1] found in his material of patients with diabetes mellitus an elevated level of TNF-α. However, we were unable to confirm these findings. In our study material, the expression of TNF-α in blood serum of either type of polyneuropathy study did not differ from that found in control subjects.

The other cytokine investigated in our study, MCP-1, presented only minor changes, i.e. an insignificant increase in serum level in patients with alcoholic polyneuropathy. However, these results cannot suggest an impact of MCP-1 in the studied polyneuropathies., neutrophil-activating peptide-2 (NAP-2) and interleukin-8 are potent chemotactic agents for human neutrophils. Although these chemokines bind to similar, but not identical, receptors, the mechanism governing their signal transduction is very similar [4].αAdverse results of GRO-α expression were found in our study. Surprisingly enough, the GRO-α levels were higher in the total group of alcoholic polyneuropathy In the literature, there are only a few studies available that deal with the role of GRO-α in primary and secondary inflammatory processes. GRO-α, the growth-regulated oncogene acting in some neoplastic and inflammatory processes [6], promotes tumour growth, metastases and infiltration by leukocytes. A host CXC receptor-2 dependent pathway is involved in this mechanism. An interesting point concerning the biological activity of GRO-α was emphasized by Wang et al. [4]. The authors found in their experimental studies that proteinase-activated receptors 1 and 2 induced the release of GRO-α from rat astrocytes, and this action was capable of protecting nerve cells from apoptotic death. The role of GRO-α in the studied polyneuropathies is by no means entirely clear. However, the presented results do imply that GRO-α may contribute to unravelling the mechanism leading to alcoholic polyneuropathy.

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