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The clinical significance of level changes of hs-CRP, IL-10 and TNF for patients with MS during active and relieving period

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Abstract. – OBJECTIVE: To investigate the clinical significance of the change of the level of hs-CRP, interleukin-10 (IL-10) and tumor necrosis factors (TNF-α) for patients with multiple sclerosis (MS) during the active and the relieving period.

PATIENTS AND METHODS: 36 patients with MS during the active stage and the relieving stage after therapy (experimental group) were compared with 10 healthy people at the relieving period, considered as control group. Immunoturbidimetry was used to examine levels of hs-CRP while the level of IL-10 and TNF-α were tested by enzyme-linked immunosorbent assay (ELISA).

RESULTS: Levels of hs-CRP, TNF-α and IL-10 in the serum and cerebral spinal fluid (CSF) were different for MS patient at different stages. Levels of hs-CRP, TNF-α and CSF IL-10 at attacking stage were higher than those at the relieving stage (p <0.05, p <0.01 or p <0.001). The levels of IL-10 in the serum at relieving stage were higher than in the CSF (p <0.05). The levels of TNF-α and IL-10 of MS patients at relieving stage in the serum and CFS were higher than those of healthy people (p <0.05 or p <0.01).

CONCLUSIONS: The significantly increased levels of hs-CRP, TNF-α and CSF IL-10 in the serum and CSF reflect MS at attack stage. The levels of TNF-α and IL-10 in the serum and CSF at the relieving stage of MS patients were higher than those of healthy individuals, suggest that at relieving stage, MS may be still developing. Finally, the increased level of hs-CRP in the serum can be used as an evidence to diagnose MS at the active stage.

Key Words:
Multiple sclerosis, hs-CRP, IL-10, Tumor necrosis factors.

Introduction

Multiple sclerosis (MS) is an autoimmunity disease, but its pathological mechanism is still unclear. Our hospital enrolled 36 patients, and evaluated the levels of hs-CRP, IL-10 and TNF-a in the serum and cerebrospinal fluid (CSF) at the active stage and relieving stage, aiming to further explore the pathogenesis of MS in terms of cellular and molecular immunity and provide evidences for diagnosis.

Patients and Methods

Patients

Reference materials are in line with the standard of diagnosis, such as, McDonald et al[1].

Active stage: new symptoms and old symptoms which are worse lasting at least 24 h after relieving or stabilizing for at least 3 months.

Relieving stage: symptoms and signs improved lasting at least 3 months.

Exclusive Criteria: patients combined with autoimmunity disease, tumor, currently infection, tissue damage and using sex hormone alternative therapy or antagonist.

Clinical Data

MS active stage group: 36 patients (28 males and 8 females) aging from 16 to 50 (34.6±14.7) years old, at the active stage of MS were admitted and enrolled in the Service of Neurology of our hospital from January 2004 to December 2007. The time from the onset to admission was 11.0 h ~ 7 d, and the mean time was 53.6±29.4 h.

Group at relieving stage: Patients into active stage after therapy and being in a relieving state.

Control group: Selected 10 healthy people (6 males and 4 females), aged from 18 to 52 years old (36.1±15.8) at the same stage.

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Observation Indicators and Methods

4 mL of blood samples were taken from the elbow vein of fasting patients at the active stage in the early morning before treatment. As well, 3 mL of CSF were taken through lumbar puncture. 4 mL of blood samples and 3 mL of CSF were similarly taken from both patients at the relieving stage and healthy control peoples. Blood samples were further centrifuged 15 min at the speed of 3000 r/min, and the separated serums were stored in a refrigerator at -30°C, and tested in batches. hs-CRPs stored in kits (Orion Diagnostica, Espoo, Finland) were measured by immunoturbidimetry, while IL-10 and TNF-α stored in kits (Immun Otech Co., Marseille, France) were tested by enzyme-linked immunosorbent assay (ELISA).

Statistical Analysis

Statistical package SPSS10.0 (SPSS Inc., Chicago, IL, USA) was used. Quantitative data was presented by mean ± standard deviation ($\overline{x} \pm S$). Paired t-test was used to evaluate difference inter-group and between active stage and relieving stage. $p < 0.05$ was considered as statistically significant.

Results

Concentration changes of hs-CRP, IL-10 and TNF-α in MS patients at different stages and in healthy patients (see Table I)

In MS patients, the levels of serum hs-CRP were very significantly higher ($p < 0.01$) at active stage compared to those of CSF at the active stage, or those of serum and CSF at the relieving stage (Table I). As well, the levels of hs-CRP in the CSF of MS patients at active stage were also higher than those of MS patients at relieving stage (Table I) and those of healthy people ($p < 0.05$), while both MS patients and healthy people at the relieving stage shared similar levels of hs-CRP (Table I).

The levels of IL-10 in the serum of MS patients at the active stage was lower than those in the CSF and serum at the relieving stage ($p < 0.01$ or $p < 0.05$). The levels of IL-10 in the CSF of patients at the active stage were higher than those of MS patients at the relieving stage, and those of healthy people ($p < 0.01$). However, the levels of IL-10 in the serum and CSF of MS patient at relieving stage were significantly higher than those of healthy patients ($p < 0.05$ or $p < 0.01$).

Finally, the levels of TNF-a in the serum of MS patients at the active stage were significantly higher than those in the CSF of MS patients at active stage and those in the serum of MS patients at relieving stage ($p < 0.05$ and $p < 0.01$, respectively). Meanwhile, the level in CSF for MS patients at the active stage was higher than MS patients at relieving and healthy group ($p < 0.05$ or $p < 0.01$). The level in the CSF for patients at relieving stage was significantly higher than the level of healthy people ($p < 0.05$).

Discussion

MS is determined as an inflammatory and demyelinating autoimmunity disease in the central nervous system. Its pathological character is anomalous0ly myelinoclastic and gliosis in the white matters of central nervous system. The pathogenesis of MS is still unclear, but it has been confirmed at the animal trial in terms of immunology. Currently, our knowledge is underscoring the unbalanced function of Th1 and Th2 cells, which leads to a series of immunoreaction, including excitation of megalophages and secretion of multiple cytokines (CK). CK has played an important role in the attack-relieving mechanism of MS. Pro-inflammatory cytokines (such as TNF-α) and Sup-inflammatory cytokines (such as IL-10) are mediating the development of inflammation. Kinds of CK involving diseasing of MS and the expression levels are closely associated with the development and prognosis of diseases. TNF-α is a pro-inflammatory CK secreted by Th1 cells. Pro-inflammatory CK can form a positive feedback loop in accordance with cascade mode; then, the immunoreaction in the body can be magnified layer upon layer, which will directly and indirectly harm myelin and oligodendroglial cells by influencing ion channel. Finally, it leads to the incidence of MS.

Levels of TNF-α is positively associated with the damage of oligodendroglia cells[2,3]. In the research, the levels of TNF-α in the serum and CSF for MS patients at active stage is higher than those at the relieving stage, suggesting that TNF-α had played important roles in the pathogenesis of MS. As well, the increased levels of TNF-α in the serum and CSF, especially in the CSF, sustained the active attack of MS. At the relieving stage, the significantly higher levels of TNF-α in the CSF than those of healthy people suggest that MS is still developing at the relieving stage.

However, IL-10 is a powerful sup-inflammatory CK secreted by Th2 cells, which can decrease the expression of pro-inflammatory CK and transfer induced immune function into immune

Table I. Concentration change of hs-CRP, IL-10 and TNF-α for MS patients at different stages ($\bar{x}$±S).

Group		hs-CRP (mg/L)		IL-10 (ng/L)		TNF-α (ng/L)	
		serum	CSF	serum	CSF	serum	CSF
MS Stage	Active	18.38±6.86 $^{**▲▲§}$	6.32±4.63$^{▲§}$	32.35±11.65$^{**▲§}$	86.14±22.37$^{▲▲§§}$	42.47±13.54 $^{*▲▲§}$	68.45±16.47$^{▲§§}$
	Relieving	6.75±2.73	2.44±0.45	49.68±14.97§§	23.68±8.97§	24.32±9.53	29.33±11.22§
Healthy people		4.38±2.13	1.73±0.31	11.35±4.92	12.73±5.23	20.87±8.18	17.45±6.74

Comparing with CSF for MS patients at active stage: t=2.33, $^{*}p$<0.05, t=2.91, 2.80, $^{**}p$<0.01; comparing with MS patients at relieving stage t=2.27, 2.42, 2.37, $^{▲}p$<0.05, t=2.90, 2.84, $^{▲▲}p$<0.01; comparing with healthy people t=2.24, t=2.36, t=2.33, t=2.19, t=2.37, $^{§}p$<0.05, t=2.84, $^{§§}p$<0.01.

tolerance function[4]. The levels of IL-10 in the CSF and serum of patients at the active stage were significantly increased and higher in the serum relatively to the CSF. In MS patients at the relieving stage, the levels of IL-10 in the serum were significantly increased, but IL-10 in CSF of patients at the relieving stage was lower than those observed in attacking stage. Serum and CSF levels of IL-10 of MS patients at relieving stage were higher than those in healthy people. These data suggested that, as sup-inflammatory CK, IL-10 might play an important role in MS patients at active and relieving stage. The increased levels of IL-10 at the relieving stage indicate the presence of inflammation in MS patients. Furthermore, CRP, a serum β globulin composed of 206 amino acid residues synthesized by the liver and produced through the stimulation of IL-6, can activate alexin, eliminate external pathogenic factors and harmful cells, and provide a condition for tissue repair[5]. In recent years, ELISA and latex immuno-enhancement scattering or transmission turbidimetric technique had increased the detectability of CRP to > 0.15 mg/L, namely hs-CRP. Consecutively, the increased level of hs-CRP indicates the existence of chronic inflammation or autoimmune diseases in the body. In the study, the levels of hs-CRP in the serum and CSF of MS patients at relieving stage increased significantly, with serum levels higher than those of CFS which may have a relation with blood-brain barrier. The level of hs-CRP in the serum suggests that MS is at an active stage. The measurement of hs-CRP is crucial for classifying and diagnosing the MS.

Conclusions

Different states of MS reflect different levels of hs-CRP, TNF-a and IL-10 in the serum and CSF. At attacking stage, the levels of hs-CRP, TNF-α or IL-10 in the serum and CSF of MS patients were significantly increased with the particularity that the levels in the serum and CSF of TNF-α or CSFIL-10 were also higher than those in healthy people, suggesting that at relieving stage, MS might still be developing. Therefore, increasing levels of serum hs-CRP can be treated as one of the diagnostic evidences[6].

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Conflict of Interests

The Authors declare that they have no conflict of interests

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