SHORT COMMUNICATION

Immune system status in the patients after severe brain injury

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Abstract

Introduction: **Extracranial complications occuring after severe brain injury definitely aggravate clinical status and debase Glasgow Outcome Score (GOS). The immune system disorders could cause for example pneumonia and other inflammatory complications – urinary infection, coagulopathy, etc.**
Material and methods: **We have admitted and observed a group of 8 patients with various degree of brain injury and we have demonstrated some changes of immune system parametres after the insult.**
Results: **Most of the patients had a significant loss in cell mediated immunity parametres, especially T-lymphocytes (CD3+, helper cells) levels were decreased, whereas B-lymphocytes levels were increased. Humoral parametres and acute phase proteins levels were also changed. C-reatcive protein level increased in all cases. However the levels of C3 and C4 were lower. The level of IgE antibodies were high and they even got higher. They achieved the values typical for atopic reaction or parasitic diseases.**
Conclusion: **Patients with immune system disorders have more extracranial complications. Patients with lower Glasgow Coma Scale after admission have often immune system disorders. However the prognostic value of monitoring of immue system disorders seems to be low.** ***(Tab. 2, Fig. 3, Ref. 9.)***
Key words: brain injury, immune system disorders, extracranial complications.

The severity of craniocerebral trauma is especially determined by the primary brain damage and the development of secondary ischemia. There are a lot of other factors, which could affect the treatment results: the resuscitation urgency, hypoxia, aspiration, hypotension, age, chronical diseases, extracranial complications occuring during the stay on the intensive care unit, etc.

It is supposed, that immune system disorders could play an important role in pathophysiology of brain injury. However stress reaction developing after trauma generally, could raise the endogenic catecholamines release insofar that it affect the immunosupresion. It is possible, that immune system disorders could cooperate in the development of another extracranial complications, above all pneumonia and other inflammatory complications. A main task of our research is to determine a role of immune system disorders for the outcome of our treatment in patients with severe brain injury.

Patients and methods

We have admitted 8 patients with different severity of brain injury, always with various degree of brain contusion and other accsesory head injuries (hematomas, skull fractures, etc.). Age accesory of the examined patients was 19–73 years, median 32 years. They were treated by conservative or surgical way (Tab. 1).

The group was analyzed by a prospective study. Every patient underwent an investigation of cellular and humoral immune parametres, basic and differential blood count. These investigations were performed by biochemical laboratory and flow cytometry laboratory. All investigations were repeated every 3 days untill the patients were discharged. The study group was compared with a group of 23 healthy voulnteers and the results were statisticaly evaluated (Mann–Whitney U test, Wilcoxon Matched Pairs test).

Further we evaluated a clinical status changes during the hospital stay by the Glasgow Coma Scale (GCS) and we followed all complications occuring during our treatment.

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Tab. 1. Patients from the study group, their diagnosis, treatment and Glasgow Coma Scale after admission and before discharge.

	Study group					
	Age	Sex	Diagnosis	Treatment	GCS addmision	GCS discharge
1.	42	M	Contusio cerebri et hematoma intracerebrale (HIC) reg. l. sin. Pneumothorax	conservative	4	14
2.	21	F	Contusio cerebri bilaterale, HIC ad ganglia basale l.sin. Fractura orbitae et calvae	conservative	5-6	15
3.	43	F	Subdural hematoma (SDH) et HIC traumat. l. sin., fractura cruris aperta	surgical	6	exitus day 10
4.	73	F	SDH et HIC l. sin. Fractura calvae	surgical	5	exitus day 17
5.	19	F	Contusio et oedema cerebri, Fractura pelvis	conservative	10	15
6.	19	M	Contusio cerebri bil. Fractura basseos cranii Fractura vertebrae L4	surgical	3	15
7.	22	M	Epidural hematoma (EDH) l. sin. Contusio cerebri bilat.	surgical	4-5	15
8.	55	M	SDH l. sin. Fractura baseos cranii et calvae	surgical	3	exitus day 7

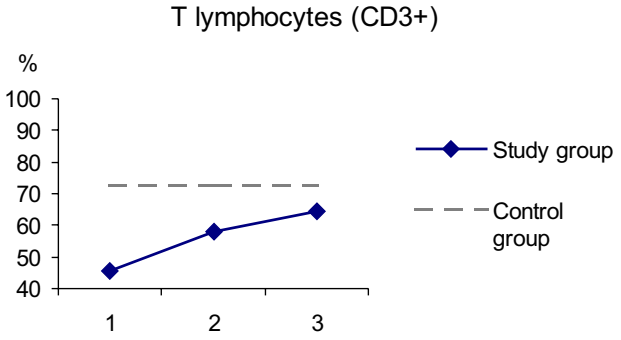

Fig. 1. T-lymphocytes (CD3+) directly after the insult (1), within the hospitalization (2) and directly before the discharge (3). It is obviously a significant decrease of CD3+ lymphocytes levels after the insult (p<0.01) and their gradual normalization (p<0.05).

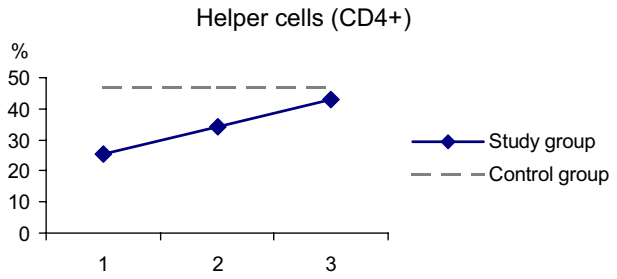

Fig. 2. Helper cells (CD4+) directly after the insult(1), within the hospitalization (2) and directly before the discharge (3). It is obviously a significant decrease of helper cells levels after the trauma (p<0.01) and their gradual normalization (p<0.05).

Results

According to the first results, all patients were slightly anaemic with haemoglobin levels under 120 g/l. Generally, the counts of white body cells were increased in all patients. Higher levels were caused by higher levels of granulocytes (5 patients over 90 %), whereas the counts of lymphocytes were mostly decreased. All patients except patient 1 had relatively low levels of T-lymphocytes (CD3+, p<0.01) and helper cells (CD4+, p<0.01). Gradually, it came to the increase of these parametres (p<0.05) (Figs 1, 2). The levels of cythotoxic/supressor lymphocytes (CD8+) were also decreased after the insult (p<0.01) (Fig. 3) as well as the CD4+/CD8+ ratio. Both of these parametres were eventually normalized, faster than CD3+ and CD4+ (p<0.05). The levels of monocytes (CD14+) were normal except for patient 3, he had higher levels. B-lymphocytes levels were increased in 5 patients, remaining 3 patients had normal values.

Immunoglobulines (IgA, IgG, IgM) and circulating immunocomplexes levels were normal or slightly increased. Only IgE values were in 6 patients multiple increased with a tendency to a further growth during the hospitalization (p<0.01) (Tab. 2). From observed acute phase proteins, only CRP levels were high after the admission, but they slightly normalized. Other monitored parametres did not show prominent deviations.

Except for patients 3, 4, and 8 who died, all other patients improved virtually to the full consciousness. Infectious complications have appeared in patients 4 and 8, in both cases a notable bronchopneumonia has occured (Enterobacter, Klebsiella and Pseudomonas aeruginosa). Patient 3 was getting better, the reason of her sudden death on the 7th day after the surgery was

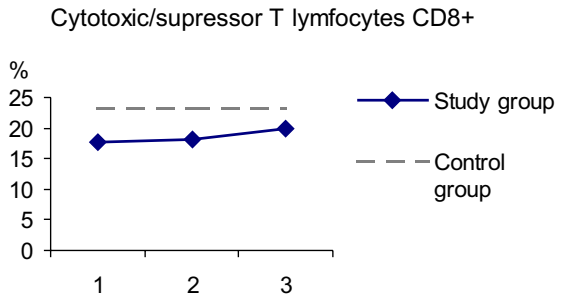

Fig. 3. Cytotoxic/supressor lymphocytes (CD8+) immediately after the insult (1), within the hospitalization (2) and right before the discharge (3). It is obviously a significant decrease of CD8+ lymphocytes after the insult ($p<0.01$) and their gradual normalization ($p<0.05$).

probably embolization from compound fracture of the crus. Except hemathemesis from oesophageal varices (patient 1) no more extracranial complications occured.

Discussion

Inspite the influence of craniocerebral injuries on immune system is well known, there are only few references in the literature. One of the most important articles is Quattrochi's et al publication (1990), which evaluated a group of 20 patients after severe brain injury. Within a few days after admission they have found out almost total anergy for all administered antigens during the in vivo skin tests. However authors were not engaged in humoral immunity factors. They pointed out the significant decrease of T-lymphocytes and helper cells. The levels of the activated T-lymphocytes (CD3+ DR) and cytotoxic/supresor lymphocytes remain unchanged. These results were confirmed also in our research. Conversely, it came to the significant decrease of the cytotoxic/supresor lymphocytes (CD8+), but their levels normalized quickly. A strong growth of the IgE immunoglobulines after the insult, with a tendency to a further increase was a surprising moment of our research. The values often achieved levels typical of atopic reaction, or parazitic infection. This finding can be explained probably by the acute stress reaction, as well as the growth of the granulocytes and CRP. Against this explanation is the IgE level growth over time. A wane of IgE levels with sequential tail of a stress reaction would be more expected (such as CRP levels).

Tab. 2. Monitored humoral and cellular immune system parametres.

Humoral factors	Cellular factors
IgG	leukocytes IgA granulocytes
IgM	lymphocytes
IgE	monocytes (CD14+)
CIKT	lymphocytes (CD3+)
CRP	helper cells(CD4+)
α1-antitrypsin	cytotoxic/supressor(CD8+)
orosomucoid	activated (CD3+/DR)
ceruloplasmin	CD4/CD8 ratio
praealbumin	B-lymphocytes (CD19+)

According to our results a possible relation between cellular immunity status and severity of contusion and GCS after admission exists. Patients with mild brain injury have got a normal (patient 1) or slightly reduced (patient 6) levels of T-lymphocytes and helper cells as opposed to the patients with severe injuries. Conversely, the decrease of the cellular immunity parametres probably does not tell anything about the prognosis of these patients, because in our study group the decrease of cellular immunity parametres occured both in patients with a favourable as well as with an unfavourable outcome. Moreover in 2 patients (4 and 8), who died due to a severe bronchopneumonia, the cellular immunity parametres improved almost to the normal values. An unanswered question remains if a sequential improving – normalization of the cellular immunity parametres is not only an immune system response to a simultaneous infection. However it does not eliminate a possibility of infections development after previous immunosupresion.

Finally, we could say, that craniocerebral injuries modify the reactivity of immune system. While one of its parts seems to be quite stimulated due to acute stress reaction (neutrophils, CRP, IgE), another part of the immune system parametres (T-lymphocytes, helper cells) sickens for immunosupression. This kind of immunosupression seems to be more important in patients with severe brain injuries and it could contribute to increased number of fatal infectious complications. It is possible that early initiated immunotherapy could provide better chances for patients after brain injury.

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