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RESEARCH ARTICLE

To The Question of Septic Encephalopathy: Clinical and Morphological Parallels

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ABSTRACT

To date, the study of septic encephalopathy is relevant, since it is a big problem, in which many aspects of diagnosis, treatment, and occurrence are still being discussed and not fully understood. Adaptation of patients with complications after sepsis is a big problem in all clinical areas, both in economic and social aspects. Of course, the study of this problem is at the junction of several specialties.

KEYWORDS:
septic encephalopathy, sepsis, neurosurgical patients

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INTRODUCTION

For many years, the problem of sepsis has been a global social and economic issue that is not easy to cope with, since patients who have had sepsis are not always able to fully recover, with further adaptation in society [1,2,3,25,29]. Despite high technologies and a large number of antibacterial drugs, it has not yet been possible to reduce mortality. Pay attention to septic encephalopathy [1,2,3]. Septic encephalopathy is a diffuse dysfunction of the brain that develops in patients with infection, accompanied by a systemic inflammatory response, but without clinical and/or laboratory evidence of direct brain infection. This symptom was included in the new clinical qSOFA scale among the most important criteria for sepsis, arterial hypotension, tachypnea [3,5,6,8,24]. With the onset of the development of septic encephalopathy, brain dysfunction is associated, leading to the development of a critical state [4,9,21]. The brain has an important role to play in regulating the effects of bacterial and inflammatory factors, as well as regulating the immune system [12,13,23,30,32].

According to the literature, more than 70% of patients with sepsis have symptoms of encephalopathy [10,11,15,20,37]. Of course, methods that help identify septic encephalopathy are of great importance. An important point is the fact that mortality directly correlates with the severity of septic encephalopathy, which plays a decisive role in the early diagnosis of this pathology [14, 16, 22, 31]. One of the initial signs of sepsis is impairment or confusion of consciousness. EEG, CT, MRI, etc. play a huge role in the diagnosis of sepsis. Not the last place is occupied by a biochemical blood test, which has a wide range of indicators (preseptin, procalcitonin, C reactive protein, etc.), but none of the

methods is specific for the detection and diagnosis of septic encephalopathy [21,22,23, 34]. Septic encephalopathy remains a diagnosis of exclusion, and is diagnosed only after other infectious, metabolic, or toxic causes have been ruled out [1,2,3,38,39,40].

At the current stage, the study of septic encephalopathy is relevant, since it is a social problem in which diagnosis, mechanisms of occurrence, and approaches to treatment are still being discussed and not fully understood [3, 11,17,19,41].

Of course, this problem is being studied at the intersection of several specialties. The clinic uses several scales for the diagnosis of septic encephalopathy (CAM-ICU, ICDSC, FOUR, GCS) [3,9,26,29,36]. But they are considered as insufficiently sensitive for the diagnosis of septic encephalopathy. Pathomorphological changes in the substance of the brain have been studied to a greater extent in experiments on animals, in the clinical and morphological aspect they are extremely few [3,7,18,33,35].

Aim

To develop algorithms for complex diagnosis and prediction of the outcome of sepsis-associated encephalopathy for etiopathogenetic personalized treatment, taking into account clinical, pathomorphological and biochemical manifestations.

MATERIALS AND METHODS

Investigated 86 sectional cases (from 26 to 79 years old), divided into 4 groups: 1 - control group (patients without pathology associated with the brain, without cancer), group 2 - aneurysmal lesion of cerebral vessels, group 3 - cerebral infarction, group 4 - persons with sepsis. In the 2nd (12 people) and in the 3rd (10 people) groups, patients who had surgical interventions, sometimes repeated. Autopsies were performed at several bases of city hospitals, including the RNHI named after Prof. A.L. Polenov, city of St. Petersburg in the period from 2011-2019.

The morphological method of research was carried out with fixation of pieces of sectional material. Areas of brain tissue were fixed in 10% neutral formalin, embedded in paraffin. From each block, from 2 to 4 sections were made at different levels, which determined the possibility of a wide study of the material obtained. Morphological examination included histological, histochemical, immunohistochemical methods. Histological examination was carried out with the staining of sections with hematoxylin and eosin, histochemical - using the Spielmeier method, Nissl's method, Gendengain's method, Mallory's method, immunohistochemical - using clonal antibodies CD 4, CD 20, CD8, tumor necrosis factor alpha, interleukins 1, interleukins 6, interleukins 6, interleukins 8.

RESULTS

4 cases were taken from the 2nd group of patients with a systemic inflammatory response in patients with arterial aneurysms in the acute period of aneurysm rupture, complicated by the development of grade II-III vasospasm. Age range 42-61 (Hunt and Hess scale III-IY, WFNS scale SAH III-IY, Fisher CT scale III-IY.) Localization of the aneurysm: fork of the right SAH, right PMA-PSA, left PMA-PSA. Surgical intervention in the acute period of rupture of the aneurysm (5-10 days). All 4 patients were initially admitted to multidisciplinary hospitals in the city of St. Petersburg.

In particular, the clinical course was marked with II-III grade cerebral vasospasm, confirmed by angiographic data (AH in endovascular surgery, SCT AH). Early need for inotropic therapy to maintain optimal PMD. Early, from 2-3 days of vasospasm verification, the development of endotheliitis with the formation of capillary leakage syndrome, peripheral edema, polyserositis. When examining neuroresuscitators with arterial aneurysm, SAH in the acute period of aneurysm rupture, laboratory studies were carried out (clinical and biochemical blood test, coagulogram (PTI, APTT, TB, fibrinogen concentration, AT III, XIIa-3L activity, blood and cerebrospinal fluid lactate, CBS, C-reactive protein, CECs (circulating endothelial cells), Pro-inflammatory cytokines (IL-1β, IL-6, IL-8, TNFα), anti-inflammatory cytokines (IL-10), PCT test (semiquantitative and quantitative), endogenous intoxication level (definition of VSNMM according to M.Ya. Malakhova), Na-uretic peptide, ACTH, STH, prolactin, cortisol, TSH, T3, T4. We also monitored systemic hemodynamics (blood pressure (BP), cardiac index (CI), stroke index (ISV), global end-diastolic volume index (GCVI), stroke volume variability (VVV), left ventricular contractility index (LVLV), index total peripheral vascular resistance (IOPSS), intrathoracic blood volume index (IVGOK), extravascular lung water index (IVSVL), pulmonary vascular permeability index (IPLS)).

The bacteriological method was also introduced to laboratory blood tests during the life of patients and posthumously.

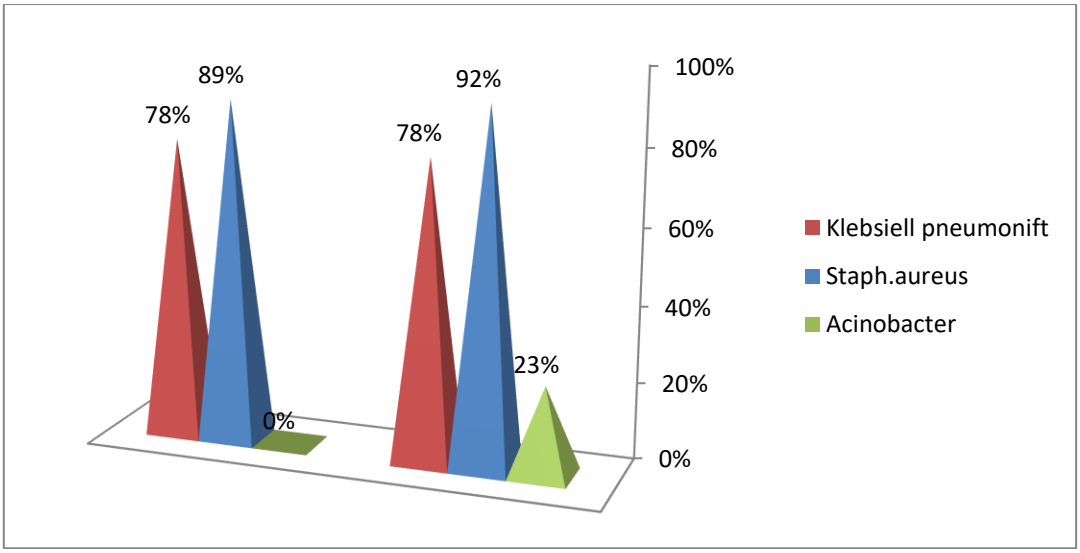

Fig.1: Monitoring of bacteriological research.

During intravital and postmortem bacteriological examination of blood, a mixed infection was inoculated, in which Staph was in the lead. Aureus and Kleb. Pneumoniae.

Currently, the main markers associated with the presence of infection in the body are C-reactive protein (CRP), interleukin-6 (IL-6), procalcitonin (PCT), preseptin (P-SEP), as well as a new biological marker neutrophil CD 64.

Patient K., 56 years old. Diagnosis: Aneurysmal vascular disease of the brain. Saccular arterial aneurysm of the left PMA-PSA. SAH from 30.08.2010. Operation: 01.09. CPT, clipping of the PSA saccular aneurysm neck against the background of temporary clipping of both A1 segments of the PMA. Fischer SAH 4 points.

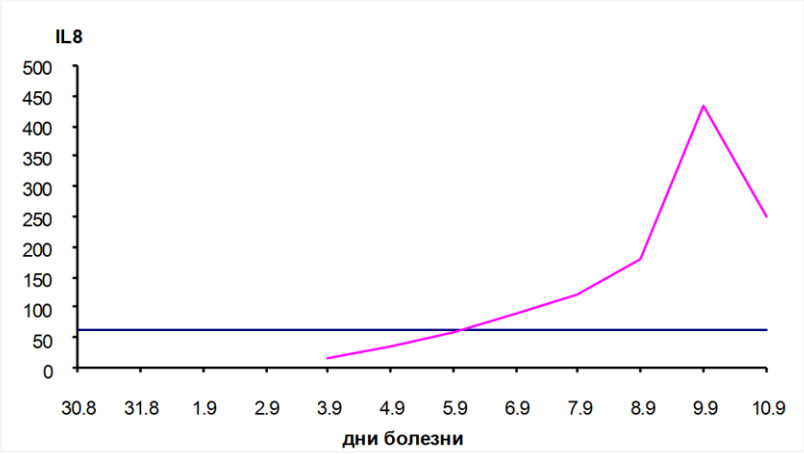

Fig.2: Dynamics of proinflammatory cytokines in patient K.

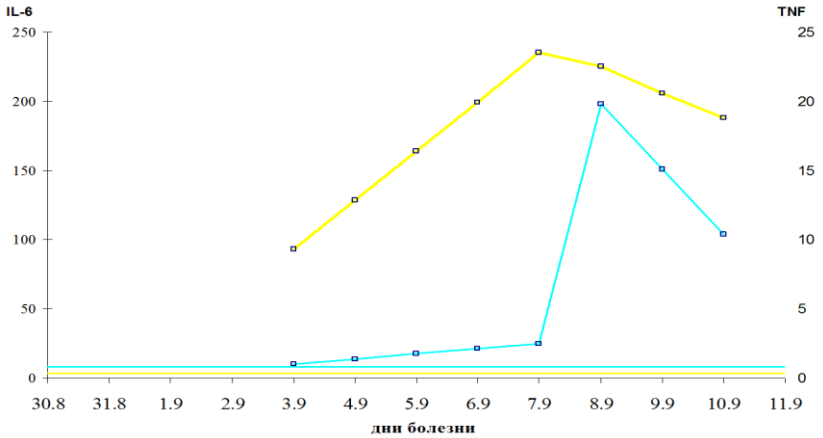

Fig.3: Dynamics of proinflammatory cytokines in patient K.

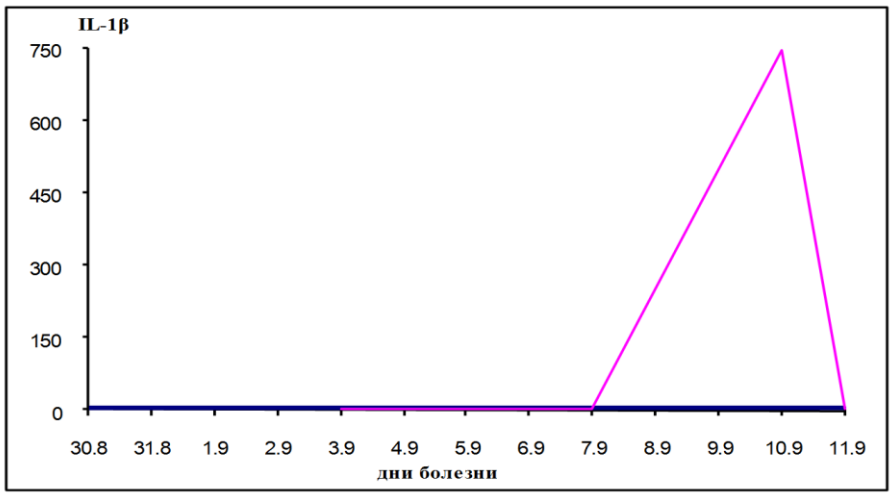

Fig.4: Dynamics of proinflammatory cytokines in patient K.

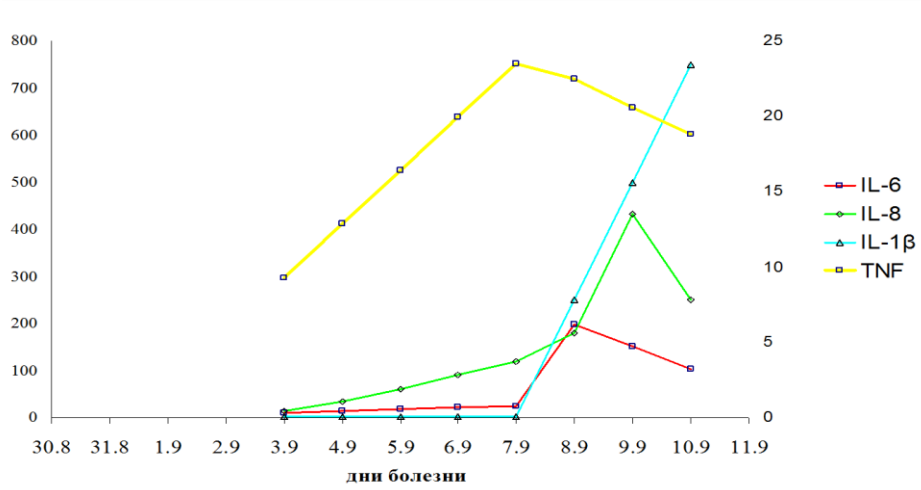

Fig.5: Hyperergic variant of the systemic inflammatory response

Patient B., 62 years old.

Diagnosis: Aneurysmal brain disease. Aneurysm of the fork of the right SMA. SAH of aneurysmal genesis from 02.02.2011. according to Fischer 3 points. Operation: CPTCH, clipping of the neck and body of the aneurysm of the right SMA. Repeated temporary clipping of AA. The P/O period was complicated by the course of vasospasm.

Complementary methods of surgical treatment, monitoring and therapy

Installation of an external drainage system according to Arendt in the left c. Kocher and an ICP sensor on the third day after 1 clipping operation AA. ICP monitoring: Spiegeelberg ICP sensor (N level ICP throughout the study period). Craniocerebral hypothermia by apparatus (t 33-35oC).

Patient B. Circulating endothelial cells. Concomitant diseases: Type II diabetes mellitus.

Fig.6: Circulating endothelial cells of patient B.

Patient B. Dynamics of acute phase
C-reactive protein. The procalcitonin test was negative throughout the entire period of treatment in the ICU.

Fig.7: Dynamics of acute phase C-reactive protein.

Blood in the right Sylvian cleft after AA rupture stimulates the insular cortex, which results in sympathetic cardiovascular effects (visible ECG changes)

Sympathetic activation can stimulate a systemic inflammatory response, including molecular adhesion mechanisms and cytokine synthesis, leading to cerebral vasospasm and poor clinical outcome.

Patients with SAH and the development of SIRS are more likely to develop cerebral vasospasm.

From the point of view of pathological physiology, it is known that it is manifested by a violation of perception, consciousness, attention, which is a multifactorial manifestation of damage to the central nervous system. It is known that astrocytes are the main homeostatic cells of the central nervous system (central nervous system), form multifunctional homeostatic barriers, and limit damage to nervous tissue. Astrocytes detect, produce and integrate inflammatory signals between immune cells and brain matter cells, thus regulating the brain's immune response. According to the literature, in septic encephalopathy astrocytes are present both in a state of "increased activity" and with dystrophic changes. It is believed that the balance between these conditions determines the further outcome of the inflammatory process and the development of neurological results. Age-related changes in astroglia and the rate of its aging are of great importance in septic encephalopathy. Septic encephalopathy is the leading factor in the clinical

course, prognosis and outcome of sepsis. At the cellular level, homeostatic control is carried out by neuroglia, which is also responsible for homeostasis of the central nervous system. Systemic inflammation disrupts mitachondrial function, involving in the process neuroglia with activation of glia, which is involved in the immune response of the nervous tissue to inflammatory damage and in septic encephalopathy. Astrocytes are a barrier to the spread of infectious agents, while maintaining the integrity of the blood-brain barrier (BBB).

Pathological anatomy

In the histological examination of the groups: 2nd - patients with aneurysmal lesions of the cerebral vessels, 3rd - with cerebral infarction, 4th - persons with sepsis (surgical, obstetric, etc.) and those who died from sepsis, there is no clear gradation in the definition of signs of septic encephalopathy. In histological preparations of all groups with sepsis, there were changes of the same type, which did not have a specific picture.

It is known that the severity of sepsis in elderly patients is justified by concomitant pathology, as well as a decrease in the immune system.

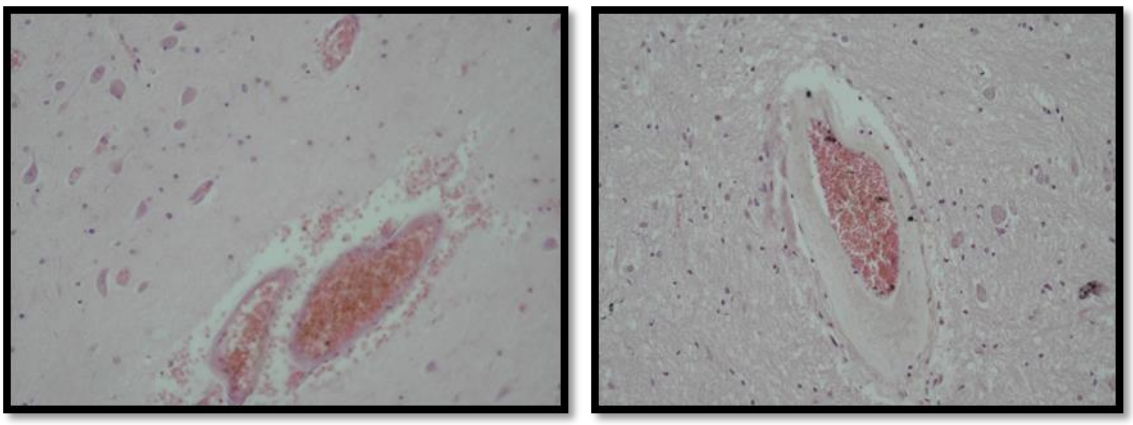

Fig.8, 9: Staining with Hematoxylin and eosin, x 10. Leukocytosis with destructive thrombovasculitis, damage to microvessels in the substance of the brain.

In the study of micropreparations with plain staining, by histochemical method, there were signs of purulent ventriculoencephalitis, leukocytosis with destructive thrombovasculitis, damage to microvessels in the brain substance.

The main pathological changes in the substance of the brain in septic encephalopathy include heart attacks, petechial and small focal bleeding, septic-embolic abscesses, septicopyemia. The most pronounced changes are noted in the hippocampus, cerebral cortex, varying degrees of severity of pericellular and perivascular edema.

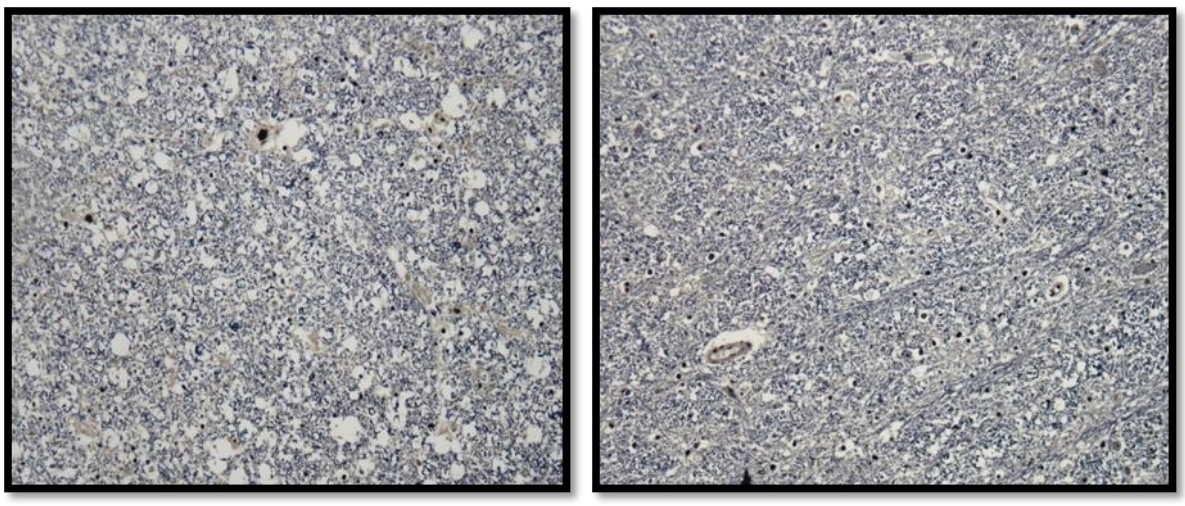

Fig. 10.11: Spielmeier's stain, x 10. Edema and swelling of the brain substance with the formation of microcystic areas.

Micrograph of brain tissue obtained using a Synapt-G1 mass spectrometer, x10.

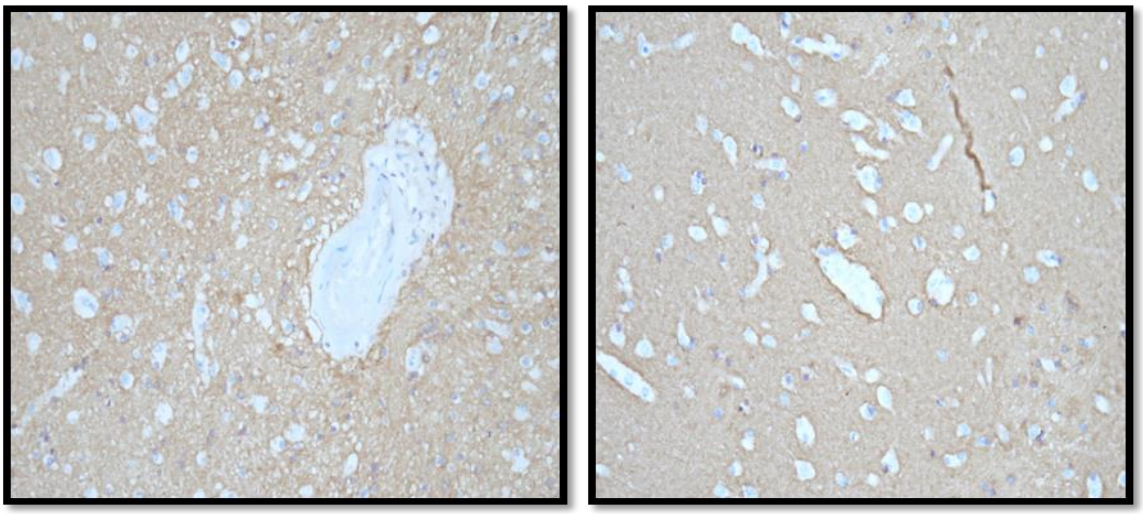

Fig.12, 13: Marker CD56. X20. Cell-effector cells of cellular immunity responsible for antiviral immunity with a mild response to the inflammatory response.

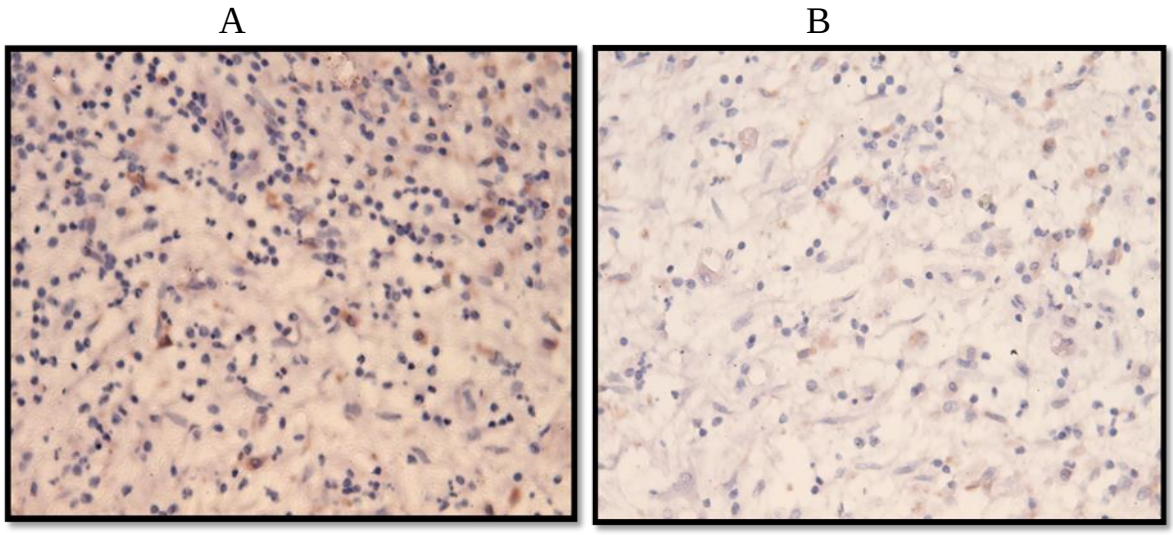

Fig.14, 15: Marker CD 8, x20 (A). Weakly expressed expression of T-lymphocytes in the substance of the brain. CD 68 marker, x 20 (B). Weakly expressed macrophage reaction.

It is known that the severity of sepsis in elderly patients is justified by concomitant pathology, as well as a decrease in the immune system.

CONCLUSIONS

The earliest and most sensitive marker of systemic inflammation is acute phase C-reactive protein. Daily monitoring of the CRP level allows you to navigate in the intensity and direction of the development of the systemic inflammatory response in a neuroresuscitation patient.

Evaluation of the dynamics of the severity of endothelial damage determined by the CEC complexes, along with CRP, indicates the effectiveness of the intensive therapy and the sanogenetic orientation of the systemic inflammatory response.

The levels of pro- and anti-inflammatory cytokines and their temporal dynamics reflect a high risk of developing multiple organ failure both in the presence of a bacterial infection and

without a bacterial origin.

Methods of extracorporeal detoxification (ultrahemofiltration, low-flow veno-venous hemofiltration) can be proposed as pathogenetic methods of intensive therapy with pronounced clinical and laboratory (CRP, CEC, pro, anti-inflammatory cytokines) signs of systemic inflammation.

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