Brain contusion: morphology, pathogenesis, and treatment

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Key words: brain contusion, pathogenesis, secondary neuronal damage, intensive care, surgery.

Summary. Focal cerebral contusions can be dynamic and expansive, leading to a delayed neurological deterioration. In head – injured patients, the rise in intracranial pressure (ICP), subsequent to uncontrollable swelling, is the only and the most frequent cause of death. Studies show that brain swelling, after traumatic brain injury (TBI), is caused by brain edema rather than cerebral blood volume (CBV). CBV is reduced in proportion to cerebral blood flow (CBF) reduction, following a severe TBI. Cerebrovascular damages, leading to subsequent reductions in regional CBF, may play an important role in secondary cell damages following TBI. The histological examination revealed the formation of microthrombosis in the contused area, extending from the center to the peripheral areas within 6 hours after injury. In the pericontusional zone and surrounding parenchyma, vasoresponsivity may be nearly three times normal, which suggests hypersensitivity to hyperventilation and other phenomena.

Glutamate is the most widely distributed excitatory neurotransmitter in the mammalian brain. However, when glutamate is present in excessive quantities, it may overactivate specific ion channels, especially the N-methyl-D-aspartate channel. A shift of potassium into the extracellular space will result in rapid swelling of astrocytes, which absorb quantities of potassium to preserve ionic homeostasis. This process may cause rapid cytotoxic edema, which is probably, a major factor in causation of posttraumatic raised ICP. The presence of a focal contusion and primary or secondary ischemic events were the clinical features most strongly correlated with high dialysate of glutamate. Raised ICP was significantly more common, and outcome was worse in patients with high levels of glutamate.

Contusion is a key factor in the development of blood brain barrier (BBB) permeability. BBB endures at least 7 days post TBI. Biphasing opening of the BBB, following head trauma and a possible second wave of secondary brain damage, was confirmed. Brain tissue pO₂ monitoring might become an important tool in the treatment regime for TBI patients.

Histologically the loss of CA3 pyramidal cells in the hippocampus was observed ipsilaterally in the cortical contusion and bilaterally in diffuse axonal injury. Aggressive, early hyperventilation after TBI augments neuronal death in CA3 hippocampus.

Due to high mortality associated with such cerebral contusions, a standard practice has evolved into evacuating contusions in patients who had deterioration in the level of consciousness, lesions more than 30 sec and CT suggestion of raised ICP.

Severe head trauma is one of the prevailing causes of death in the developed countries. According to statistics, 100,000 people die from trauma in the United States every year. Severe head injuries constitute ½ of these deaths. Hundreds of thousands of head trauma survivors suffer from long-term disabilities (1). After severe and moderate head injuries, parenchymal damage is detected in over 55% of cases (2). For over 50% of patients, contusion foci are located in surgically favorable frontal and temporal lobes. Until quite recently, little emphasis has been placed on the analysis of reasons of the neurological state deterioration after hospitalization. In 1993, Stein et al. proved that the deterioration of the neurological state of hospitalized patients is an indication of poor outcome (1). By implication, the main task of a surgeon is to avoid or
reduce secondary neuronal damage, which, in effect, causes the deterioration of the neurological state (1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16). It is thus necessary to reduce ICP or to maintain cerebral perfusion pressure (CPP) at 60-70 mm Hg. Neurological state is classified as deteriorated when Glaskow Outcome Scale (GCS) is reduced by 2 scores and the pupils are asymmetric (>1 mm) as well as areactive. These symptoms indicate the need to introduce correctives in treatment. Without any changes in treatment, mortality rates increase from 9.6 % to 56.4%, whereas good results, according to GCS, decrease from 68 to 29 % (1). It has been proved that subsequent neurological state deterioration is caused mainly by brain parenchyma damage.

BC or BC with hematoma comprises approximately 60% of the totality of intracranial injuries (3, 4, 5, 6, 7, 8, 16, 17, 18). Contusions leading to the neurological state deterioration are more common in the age group of over 40 (56 %). Sometimes initial brain damage seems mild or moderate immediately after the injury (2). In patients with BC, neurological deterioration, on average, manifests 6 hours after the trauma (77.5 %), while neurological worsening caused by extracerebral hematomas occur up to 6 hours after the injury (19). For children and young people, GCS score <9 on admission was predictive of either severe neurological state deterioration or death caused by multiple contusion, brain swelling, and brain herniation, i.e. a complex of symptoms indicative of a dynamic, progressive nature of head injury (11). In 1998, Firsching et al. performed magnetic resonance image (MRI) scanning of over 100 severely head-injured patients of poor neurological state immediately after the trauma and detected primary brain stem contusion (pons), which was not visible on CT. In the majority of cases, these patients exhibited poor outcome (20).

Studies on the subject emphasize the importance of an in-depth knowledge of pathogenesis for adequate clinical management of BC. Recent findings throw new light on pathogenesis and secondary neuronal damage. BC used to be defined as traumatic necrosis followed by reabsorption. Such a view defies the progressive nature of the injury, though its dynamics is implied in the commonly acknowledged fact of reabsorption. The currently used definition of BC points out that it is a dynamic and expansive process inevitably leading to the deterioration of the neurological state (21). Dynamic processes are most pronounced in neurons, glial tissue, and blood vessels. In the early stages, microscopic examination reveals perivascular hemorrhage, astrocytic swelling, changes in the myelin, infiltration of the macrophages, apoptosis, phagocytosis, and atrophy (12). The majority of neuro-researchers distinguish the following zones in the severely injured brain: contusional, pericontusional (synonyms - perilesional, hypoperfusional, ischemic, edemic). Very important is hypoperfusional zone, which is very dynamic and apt to expansion in cases of inadequate treatment (8, 12, 17, 22, 23).

Several pathophysiological processes triggered by BC are of special significance, and disturbances in cerebral blood flow are among them. Severe head injury causes disturbances both in hemispheric and regional cerebral blood flow (CBF). Examinations show that CBF in the contusion foci is 4.7 ml/100g/min., and it is 16-18 ml/100g/min. in the hypoperfusional zone. In the normal brain, CBF is >50 ml/100g/min. (24). Ischemic threshold is commonly considered to be 18-20 ml/100g/min. Disturbances in blood vessel sensitivity are frequent in hypoperfusional zone and are related to the increase and, even more so, to the decrease of arterial blood pressure (ABP), the increase of ICP, the decrease of CPP, and changes in ventilation (12, 18, 24, 25). In hypoperfusional zone, blood flow decreases 3 hours after the injury, while the probability of blood vessel thrombosis significantly increases after six hours postinjury (26). Adequate treatment and permanent multimodal monitoring enable to prevent expansion of the hypoperfusional zone into the normal brain for approximately 10 days postinjury and even longer periods. An important fact to be pointed out is the absence of reperfusion in this zone (18). Lebedev reports cases of hypoperfusional zone re-reduction (27). Erratic clinical management brings about the increase of this zone and its expansion into the normal brain, which causes an irretrievable brain damage. Hypoperfusional zone can encompass approximately 15% of brain hemisphere. The aggressive expansion of the volume of the contusion focus increases the secondary neuronal damage. In patients with poor outcome, hypoperfusional zone can be very extensive and encompass a large bulk of brain hemisphere (3, 4, 5, 24, 28, 29). Cerebral autoregulation is an ability to maintain normal CBF despite changes in CPP; BC is likely to cause severe damage in cerebral autoregulation. Cerebral autoregulation is based on active variations of cerebrovascular resistance. ABP, ICP, and CBF measurements provide important data about cerebral autoregulation. We perform ICP and ABP slow wave simultaneous measurements to investigate their correlation.

Very important for brain contusion pathogenesis is the increase of glutamate, its coagonist aspartate, and
structural amino acids (threonine and valine) in parenchyma microdialysis probes or in cerebrospinal fluid (CSF). Glutamate is an excitatory neurotransmitter in brain. Evidence has been provided on its significant role in “the causation of both acute and chronic neuronal damage.” Recent studies state that “many of the normal physiological processes of the cortex and the hippocampus, in particular, are thought to depend on this neurotransmitter function of glutamate.” The increase of glutamate significantly activates ion channels, N-methyl-D-aspartate channel, in particular. In a random manner, sodium and calcium penetrate into cells while potassium enters the extracellular space. “When this process is rapid, it can result in massive accumulation of intracellular calcium with rapid neuronal death - “fast excitotoxicity.”” Such dynamics leads to a fast neuronal death that can occur during the first day after the trauma. In case of delayed entry of calcium, neuronal death can be traced within the period of 5-7 days after the injury (7). The penetration of potassium into the extracellular space causes a rapid swelling of astrocytes. This can, in turn, lead to “cytotoxic edema,” which is thought to cause the increase of intracranial pressure. The investigation of morphological changes has provided more insight into the mechanism of astrocyte swelling (7, 12, 16). The implementation of the microdialysis technique revealed a rise of glutamate in the extracellular space after severe head injury and stroke. The blockage of glutamate by N-methyl-D-aspartate channel antagonists decreases the secondary damage of neuronal cells. It has been detected that the biggest amounts of this neurotransmitter are found in cases of brain contusion (>20 mmol/L), subdural hematoma and diffuse injury (<20 mmol/L), and epidural hematoma (about 3 mmol/L). These findings suggest that the more severe brain damage, the higher the increase of glutamate (7). Posttraumatic increase of glutamate in the cerebrospinal fluid is indicative of neuronal and glial damage as well as cytotoxic rather than vasogenic edema (31).

In a lot of cases, BC is accompanied by the following parallel states, which can cause brain ischemia: hypoxemia (PaO2 <60 mm Hg), hypotension at mean arterial blood pressure (MABP) <50 Hg (for >30 min. prior to resuscitation), hemispheric CBF <20 ml/100g/min., herniation (fixed dilated pupil), and CPP <50 mm Hg for >30 min. (7).

It has been detected that ischemia is an important factor influencing the increase of glutamate, which is >80 mmol/L, in cases of brain contusion, and 5-20 mmol/L in the absence of brain contusion. This implies that brain contusion is crucial for the behavior of glutamates and for the increase of structural amino acids (threonine and valine) resulting from neuronal death (7, 16). Following this study, it can be suggested that the combination of ischemic events and brain contusion causes a more severe secondary neuronal damage.

The data lead to an assumption that the rise of glutamate in brain microdialysate is followed by the increase of ICP, decrease of CPP, progressive damage in hippocampus, brain stem, cerebellum, and, inevitably, in the pericontusional area. The increase of glutamate >20 mmol/L is suggestive of poor outcome. When glutamates increase up to 50-100 mmol/L, neuronal death can be detected within several hours due to their overexcitation. Studies on animals and humans indicate that contusion in one hemisphere leads to neuronal death not only in the focus of BC but also in the brain stem, cerebellum, and, especially, in the ipsilateral hippocampus. In cases of contusion in both hemispheres, neuronal death occurs in bilateral hippocampus, brain stem, and cerebellum (3, 4, 5, 7, 8, 13, 14, 15, 18, 20, 21, 26, 28, 32, 33, 34, 35). Secondary hippocampus damage can evoke posttraumatic epileptic seizures because hippocampus modulates epileptogenic activity (36, 37, 38). The rise of the neurotransmitter glutamate causes increased hyperglycolysis, which, in turn, affects a further increase of this neurotransmitter and, in this way, enhances the activity of this destructive circle. If CPP remains <70 mm Hg for more than 1 hour, the level of glutamate increases, and brain becomes very vulnerable. The increase of the glutamate concentration is not even; the highest levels of glutamate have been detected within 9 days postinjury. It has to be pointed out that even in cases of normal CPP (80-110 mm Hg), the occurrence of an epileptic seizure causes a significant increase of glutamate (30-60 mmol/L (39). The above-described processes can be defined as a chain reaction to be interrupted by a careful clinical management.

Clinical testing of “Selfotel,” the NMDA receptor antagonist, did not come to expectations. “Selfotel” proved to be ineffective at high levels of glutamate (e.g. increase of 50 times normal). Data on 693 patients demonstrate that satisfactory results were seen only in patients with epidural and subdural, i.e. extracerebral hematomas, in cases of mild brain parenchyma damage (40). The use of “Selfotel” for the treatment of animals with brain contusion demonstrates better results (28).

The damage of brain blood barrier (BBB) is also very important (4, 5, 14, 41, 42). Approximately a
decade ago, the majority of neurosurgical research emphasized the vasogenic origin of posttraumatic brain swelling. At present, many leading scholars in the field, such as Marmarou, Bullock, Schröder, and others, highlight the importance of cytotoxic brain edema (7, 12).

A closely related problem is the decrease of BBB. In literature on the subject, different data on the BBB damage time are reported. Baldwin et al., for example, indicates two stages. During the first stage, BBB decreases in brain cortex and hippocampus 1 hour after the injury. After 3 hours, BBB returns to the initial level. During the second stage, BBB decreases in brain cortex and hippocampus 1-2 days postinjury (5). Soares et al. detected the decrease of BBB in brain cortex and hippocampus 2-12 hours postinjury followed by its restoration to the initial state within a three-day-period (19). Holmin et al. report on the decrease of BBB 2 days after the injury, reaching its maximum 5-6 days postinjury. BBB restores to normal within 16 days (41). The decrease of BBB causes not only vasogenic edema but also inflammatory processes, which, in turn, can cause secondary neuronal damage (41, 42).

Katayama et al. reveal one more aspect of the pathogenesis of the BC focus volume increase. They detected a rapid increase of osmolarity in the BC focus due to the neuronal cell disintegration, homogenization, and metabolic disturbances. Such “mass” is inclined to reabsorb liquids; a process that can be referred to the increase of osmolarity in this mass, provided CBF remains sufficient (26).

The increase of ICP and the decrease of CPP will be mentioned only in passing because this subject is not the primary intent of the present study. In order to maintain optimal CPP and to retain optimal brain oxygen saturation, it is essential to manage ICP. When ICP is >20 mm Hg, it is considered pathological, and, when ICP is over 40 mm Hg, it is very dangerous. ICP is one of the main indicators of poor outcome, though there is an alternative view foregrounding the significance of CPP. The decrease of ICP is essential for the increase of CPP. Regardless of CPP, the initial ICP of >20 mm Hg yields a poorer outcome than that of <20 mm Hg. With ICP greater than 20 mm Hg, it is very difficult to maintain CPP in the range of 70-80 mm Hg. The increase of CPP at the expense of the increase of MABP does not yield good results. CPP should not be allowed to decrease below 60-70 mm Hg (1, 43). Until quite recently, ICP was believed to be uniform in the entire skull cavity. Lately, however, not only supra-infratentorial but also interhemispheric gradients of ICP have been detected in patients with BC (44). These findings help to explain the deterioration and differences of CPP and brain parenchyma oxygen saturation in different brain locations (22, 31, 35).

ICP and CPP monitoring does not reflect brain oxygen consumption. Recent management schemes propose the estimation of direct parenchyma saturation for oxygen. This method offers higher accuracy (>90%) compared with that of the oxygen blood saturation method in jugular bulb (accuracy 46%) and excludes risk factors such as vein sinus thrombosis (45).

In the brain contusion focus, pO2 is constantly below hypoxic threshold (decreases by 70%) and is not affected by hyperventilation (HV), a fact that is indicative of the brain death zone. In the pericontusional zone, pO2 decreases, while the reaction of blood vessels to HV, ABP, and ICP as well as CPP changes is significantly disturbed. In the normal brain, both pO2 and blood vessel reactivity is not impaired (34). Aggressive HV (PaCO2 21 mm Hg) radically reduces hypoperfusional zone saturation (by ½) even when CPP is above 60 mm Hg. This is due to the changes in the reactivity of blood vessels in the pericontusional zone and severe vasoconstriction (24, 31, 34, 35). BC is thus a very aggressive process triggering many pathological mechanisms that, in turn, activate new processes, many of which still need further investigation (37).

With regard to the stated above, it would be pertinent to recapitulate BC-induced changes in brain and the body: changes in ABP, the decrease of regional and hemispheric CBF, the increase of contusion focus osmolarity, the expansion of water into contusion focus, the increase of ICP, the decrease of CPP, the occurrence of brain ischemia, the increase of glutamate concentration and structural amino acids, the swelling of the glial tissue, the decrease of BBB, the triggering of inflammatory responses, the increase of platelet cells activating materials and free radicals, changes in brain pH, the possibility of brain hyperemia occurrence, and the decrease of brain saturation. Neuronal death is detected in the BC focus and the surrounding tissue as well as in the hippocampus, brainstem, and cerebellum (4, 5, 7, 12, 14, 16, 18, 24, 25, 26, 30, 32, 41, 42). There exists a controversial view on the role of brain hyperemia: some authors regard it as a negative factor while others point out its beneficial effects (33, 41).

These complex changes and the morphology of the dynamics of the hypoperfusive zone play an important role in the consideration of an effective surgical treatment. During surgical treatment, a histological exami-
nation of the pericontusional zone was performed by an electronic microscope. The examination revealed that, in extracellular spaces, swelled astrocytes externally compress blood microvessels obstructed by red cells and white cells. The fact that the blood vessel endothelium is not impaired confirms the astrocytal origin of blood microvessel compression (7, 46). Lebedev claims that astrocytes exhibit changes during the first minutes after the trauma (27).

Neuronal death caused by brain contusion occurs at different time intervals in different locations. In brain cortex, it can occur 24 hours postinjury, while maximum apoptosis is observed on 7th day after the trauma. In hippocampus, it occurs within 48 hours and in thalamus within 14 days (8). Baldwin reports cases of neuronal death in hippocampus 24 hours postinjury and states that BC causes the death of 41% of neurons in this zone (5). A question then poses itself whether and how this posttraumatic chain reaction can be interrupted and what clinical management can yield best results.

As it has already been stated, brain contusion is a dynamic and expansive process having pronounced effects not only in the vicinity of the contusion focus but also in more remote areas such as hippocampus and the brain stem. Inadequate treatment and the absence of monitoring enhance these effects. The recommended optimal MABP is 140-70 mm Hg and the optimal CPP range is between 105-70 mm Hg (22). Some authors recommend maintaining CPP above 70 mm Hg, and they hold that the decrease of CPP under 30 mm Hg can double the contusion focus (1, 22, 29). Some authors explore the influence of MABP on the dynamics of the BC volume. For example, the rise of MABP up to 140 mm Hg increases the contusion volume by 15%, while the fall of MABP up to 50 mm Hg doubles the contusion volume (22).

The problem of HV as a means of minimizing ICP also needs to be considered. For approximately 20 years, HV has been a commonly used technique for the reduction of ICP. Recent research emphasizes negative effects of aggressive HV and points out a high degree of risk involved in its use (47). It has been indicated that the use of HV in the clinical management of BC can cause a 40% increase of neuronal apoptosis in hippocampus at PaCO2 <25 mm Hg after 5 hours. This occurs only in cases of BC. The expansion of contusion focus has also been detected, and this is referred to vasoconstriction, especially in the pericontusional zone, reduced CBF, alkalosis, and increased negative effects of glutamate (9). As it has already been stated, the increase of the contusion focus, along with its penetration into the normal brain, is determined by the expansion of the pericontusional zone due to highly distorted and raised vasoreactivity (6, 12, 40). In recent studies, the majority of researchers claim that conservative treatment of BC is ineffective. BC focus is a zone of dead brain, an urgent removal of which can hinder its expansion into the normal brain (46). In many countries, patients with BC undergo surgical treatment. The main criteria for surgical treatment are the following: the deterioration of conscious, according to the GCS; contusional focus of >30 cc; the symptoms of increased ICP (compressed brain ventricles, compressed or invisible basal cisterns, and the midline shift on CT (21, 48). The present survey of literature on BC provides sufficient evidence to claim that surgical treatment can reduce the secondary neuronal damage and improve short-term as well as long-term treatment results.

Galvos smegenų sumušimo (kontūzijos) morfologija, patogenezė ir gydymo principai

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Raktažodžiai: galvos smegenų kontūzija, patogenezė, antrinis neuronų pažeidimas, intensyvioji terapija, chirurginis gydymas.

Santrauka. Galvos smegenų kontūzijų gydymas yra labai aktualus. Dėl chirurginio galvos smegenų kontūzijos gydymo indikacijų ilgai buvo diskutuojama, tačiau pastaraisiais metais pristatytas vieningas nuomonės įrodymas, jog kontūzinių žūdėjimų nėra stabiliškas, jie didėja, o dėl jų poveikio padidėja intrakraninių slėgis, atsiranda galvos smegenų įstrigimo pavojus. Kuo intrakraninių slėgis didesnis, tuo pacientų prognozė yra blogesnė. Be to, galvos smegenų kontūzija sukelia antrinių morfologinių neuronų pokyčių atokiose nuo kontūzino žūdiniu galvos
smeguñų vietose: hipokampe, galvos smeguñų kamiene. Tik žinodamas galvos smeguñų kontūzijos patogenezę ir skyręs reikiamą gydymą, gydytojas galės sumažinti antrinių neuronų pažeidimą, sukeltą galvos smeguñų kontūzijos, ir pasiekti geresnių gydymo rezultatų. Tikimasi, kad šiame straipsnyje pateikiamą literatūros apžvalga dėl rekomenduojamos galvos smeguñų kontūzijos gydymo taktikos galėtų tapti pagrindu diskusijai apie tokių pacientų gydymo koregavimą.

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Received 24 November 2000, accepted 30 January 2002