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TRAUMATIC ENCEPHALOPATHY

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Abstract. Chronic traumatic encephalopathy (CTE) formerly known as dementia pugilistica is a neurodegenerative disease that occurs after repetitive mild traumatic brain injury. CTE has been found most often in professional athletes involved in contact sports (for example, boxing) and in non-athletes who have experienced repetitive head impacts. The clinical features include impairments in cognition, behavior, mood and motor functioning. There are also distinctive microscopic and gross changes that are associated with tauopathy. We present contemporary diagnostic criteria for CTE and approach to treatment include glutaminergic transmission modulation.

Key words: traumatic brain injury,chronic traumatic encephalopathy, athletes' encephalopathy

In 1928, Martland N. described a degenerative disease of boxers (punch drunk syndrome), which develops as a result of repeated traumatic brain injuries without a skull fracture and is manifested by confusion, bradykinesia, tremor and gait disturbance [9]. In 1949, Critchley M. first introduced the term “chronic traumatic encephalopathy (CTE) [9]. For several decades, CTE was considered a disease unique to boxers. Only in 2005 Omaly B.I. et al. first described a clinically and pathomorphologically similar neurodegenerative brain disease caused by cranial vault trauma in a professional football player [10]. Since then, more and more descriptions of the development of CTE in non-athletes have accumulated in the literature.

Chronic traumatic encephalopathy (CTE), formerly known as boxer's dementia, is a long-term progressive neurodegenerative disease that develops as a result of repeated mild traumatic brain injury (most often in the form of a concussion) [1, 2, 4, 5]. CTE is most often associated with contact sports (boxing, football, ice hockey, rugby, American football, professional wrestling, mixed martial arts), but it also occurs in other professional fields, in particular in equestrian sports (steeplechase), circus clowns, military personnel, as well as in patients with epilepsy and patients with mental retardation, shaking and banging their heads [1, 2, 4, 5, 8]. . Recently, CTE has been diagnosed more and more often, almost always in men [1]. Clinically, CTE manifests itself as impairment of cognitive, behavioral, affective and motor functions [7]. Pathomorphologically, micro- and macroscopic changes in the brain associated with the accumulation of hyperphosphorylated tau protein in neurons and astrocytes are revealed [8]. A key symptom of CTE is long-term participation in contact sports resulting in mild traumatic brain injuries [1]. Clinically, CTE is characterized by progressive impairment of cognitive, affective, behavioral and motor functions [7]. Behavioral and affective disturbances are the most common clinical manifestations in CTE [6]. 1. Of the cognitive functions, memory and regulatory functions are primarily impaired [9]. Decreased memory is found in approximately half of patients with pathomorphologically confirmed CTE [7]. At the same time, short-term memory decreases in isolation while long-term memory is preserved: patients experience difficulties in remembering new information [5, 7]. Regulatory dysfunction is manifested by a decrease in speech activity, slower thought processes, difficulties in judgment and decision-making, and decreased self-control [7, 9]. In later stages of the disease, language skills and visuospatial functions decline [7]. 2. Affective disorders are detected in 30% of patients with CTE [1]. The most common affective disorders include depression and despair [3, 5]. In particular, McKee A.S. et al. (2011) found depression in 28% of patients with a pathologically confirmed diagnosis of CTE [1]. Less common are suicidal thoughts and attempts, anxiety, agitation, apathy, and extremely rarely, dementia with mild euphoria and bipolar disorder [1, 7]. 3. The most common behavioral disorders

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are irritability and aggression. Less common are impulsiveness, paranoid ideas, decreased intuition, disinhibition, risky behavior, sexual disinhibition, deterioration of relationships with friends and family members, obscene speech and the use of physical force, and abuse of any drugs [3, 5]. 4. Of the motor disorders in CTE, parkinsonism is typical, manifested by tremor, hypomimia, rigidity and instability when walking. As CTE progresses, some patients develop dysarthria, dysphagia, coordination disorders, and statolocomotor ataxia [7]. Movement disorders are more common in boxers (73% of boxers with CTE) than in American football players (13% of players with CTE) [8]. Some patients, in addition to CTE, have motor neuron disease (MND), which manifests itself with paresis, atrophy, spasticity and muscle fasciculations, primarily in the muscles of the shoulder girdle, neck, arms and bulbar group. As a rule, manifestations of MND manifest themselves earlier, and only then do patients develop cognitive, behavioral and affective disorders [7]. In rare cases, according to pathomorphological data, in addition to CTE, patients are diagnosed with neurodegenerative diseases such as progressive supranuclear palsy (PSP) and Alzheimer's disease (AD) [2, 4, 5]. Other symptoms of CTE include chronic pain, including headache, which usually occurs in the early stages of the disease [7]. A decrease in cognitive (namely, difficulty in making decisions) and behavioral (risky behavior) functions in patients with CTE is especially pronounced in managing finances: there is a tendency to make thoughtless and non-profitable financial investments, which worsens the socio-economic status of patients up to the point of bankruptcy [1 , 5, 7]. As a result, it becomes difficult for a patient with CTE to support their family, personal connections are lost, which leads to depression and suicidal thoughts. Patients commit violent, criminal or risky acts, and are sexually disinhibited. In the later stages of the disease, many patients with CTE are characterized by alcohol or drug dependence and demonstrative religiosity [1, 5]. As a rule, the symptoms of CTE are characterized by a certain stage of appearance. Thus, at the first stage, patients experience affective disorders, as well as memory loss, which is confirmed in tests of visual memory and reproduction [1]. The second stage is characterized by unpredictable behavior and a decrease in the patient’s social status [1, 5]. At the third stage, motor disorders appear, usually with elements of parkinsonism, as well as cognitive impairment, reaching the level of dementia. Speech, visual impairment and ataxia are possible [1, 5]. General criteria for STE To make a diagnosis of STE, the following five criteria must be present: 1. A history of repeated head impacts, differing by type of injury (a) and source of exposure (b): a) types of injury: I) mild TBI or concussion. In the absence of a history of other repeated traumatic brain injuries, a minimum of four mild TBIs or concussions is required, II) moderate/severe TBI. In the absence of a history of other repeated traumatic brain injuries, a minimum of two moderate or severe TBIs or concussions is required, III) asymptomatic (subconcussive) head injury; b) source of exposure: I) participation in high-risk contact sports (including boxing, American football, ice hockey, lacrosse, rugby, wrestling, football) for at least six years, of which two years at a level not less, than in a sports college, ii) military service (including combat or non-combat exposure to explosions and explosives), iii) other significant repeated blows to the head (including domestic violence, professional activities such as police officers kicking down doors), iv) for moderate/severe TBI: any cause (eg, motor vehicle accident). 2. Exclusion of another neurological disorder with similar clinical manifestations (including residual symptoms of a single TBI or persistent post-concussion syndrome), although a concomitant diagnosis of drug dependence, post-traumatic stress disorder, mood/anxiety disorders, or other neurodegenerative disease (eg, AD or pvFTD) may be present. 3. Clinical manifestations persist for at least 12 months. 4. The presence at the time of examination of at least one of three clinical signs. 5. The presence of at least two additional signs. II. Main clinical signs of STE It is necessary to have at least one of the following three criteria: 1) cognitive impairment identified from anamnesis or during neuropsychological tests that assess episodic memory, regulatory functions and/or attention; 2) behavioral disturbances, such as short temper, physical and/or verbal violence, identified from history or examination; 3) affective

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disturbances, such as sadness, depression and/or despair, identified from history or examination. III. Additional clinical signs of STE At least two of the following nine criteria must be present: 1) impulsivity: the appearance of gambling addiction, increased or unusual sexual activity, drug dependence, excessive or unusual purchases, etc.; 2) anxiety: anxious mood, agitation, obsessive, compulsive or obsessive-compulsive behavior identified from history or examination; 3) apathy - loss of interest in previous hobbies, motivations and emotions or a decrease in goal-directed behavior, identified from anamnesis or upon examination; 4) paranoia: delusional beliefs of suspicion of something, persecution by someone and/or unreasonable jealousy, identified from anamnesis or upon examination; 5) suicidal tendencies: suicidal thoughts or attempts identified from anamnesis or upon examination; 6) headache: chronic severe headache at least once a month for at least 6 months; 7) motor disorders: dysarthria, dysphagia, bradykinesia, tremor, rigidity, gait disturbance, falls and other signs; 8) deterioration of condition: progression of symptoms and signs recorded during repeated (at least a year later) testing and clinical examination; 9) latent period of manifestation: as a rule, the first clinical signs appear at least two years after TBI [8]. Depending on the main clinical sign Montenigro P.H. et al. STE is divided into 4 types: 1. Behavioral/affective version of STE [8]. The patient has behavioral/affective disorders and the absence of cognitive ones. 2. Cognitive version of STE. The patient has cognitive impairment and the absence of behavioral/affective impairment. 3. Mixed version of STE. The patient has cognitive and behavioral/affective disorders. 4. A separate variant of STE with dementia is identified, when progressive impairment of cognitive functions leads to a decrease in daily activity. Patients lose the ability to self-care and become functionally dependent on other family members. Several options for the course of STE are possible: 1. Progressive course: progression of symptoms over two years. 2. Stationary course: no progression of symptoms for two years. 3. Fluctuating course: with periods of deterioration and improvement of the condition. As in the case of other neurodegenerative diseases, such as AD, and in the case of CTE, it is currently impossible to make a definitive diagnosis intravitally, but it can be assumed with varying degrees of probability in the form of a possible, probable or unlikely diagnosis. To do this, it is necessary to check the presence of potential biomarkers of the disease in the patient. It should be noted that the search for new, more specific biomarkers for CTE is currently underway, so in the very near future the list of possible biomarkers of the disease will be supplemented and refined. Currently, the following biomarkers of CTE are identified: 1) cyst of the transparent septum, cavity

Verge or fenestration according to neuroimaging data;

2) normal level of amyloid in the cerebrospinal fluid;

3) increased levels of tau protein in the cerebrospinal fluid;

4) PET with florbetapir or flutemetamol does not reveal any pathological

amyloid accumulation [8];

5) detection by PET with a new ligand T807, which selectively binds to tau protein, paired helical strands of tau protein,which indicates the deposition of tau protein.

This biomarker is at the experimental development stage [8, 10];

6) thinning of the cortex according to MRI, which indicates neurodegeneration;

7) generalized cortical atrophy of the cortex, thalamus, hippocampus and/or amygdale according to MRI or CT.

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