Anti-thyroid autoimmunity and psychic disorders*

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Thyroid hormones are essential for normal brain development and function, also regulating some processes in immune system. The vicious effect of hypothyroidism for central nervous system displayed in myxoedema is known for many decades, but there is a CNS disorder related to autoimmune thyroid disease and not merely dependent on hypothyroidism. That is Hashimoto's encephalopathy (steroid-responsive encephalopathy of autoimmune thyroiditis) — an enigmatic combination of cognitive, mood and motor disorders with psychotic symptoms, which pathogenesis is still unclear. The article describes natural history of this entity, its epidemiology, clinical and laboratory manifestation, and compares several existing theories of its pathogenesis with appropriate pros and contras. Vascular, dyshormonal and non-vascular autoimmune links of Hashimoto's encephalopathy pathogenesis are discussed in intermingled discourse. The attempt to construct a synthetic concept of Hashimoto's encephalopathy pathogenesis is given. The experience of authors based on investigation of clinical, endocrine and immunological parameters of 17 cases of autoimmune thyroiditis with schizophrenia-like manifestations is described, correlations are explored between immunoendocrine and psychic manifestations of disease.

Keywords: autoantibodies, Hashimoto's thyroiditis, Hashimoto's encephalopathy, steroid-responsive encephalopathy associated with autoimmune thyroiditis, schizophrenia, autoimmune encephalitis, psychosis

The versatile clinical manifestations of the Hashimoto's chronic autoimmune thyroiditis often include psycho-neurological disorders [1]. The thyroid hormones are necessary for the development and function of central nervous system (CNS). In 1850, a British surgeon Thomas Blizzard Curling reported the association of the thyroid aplasia and oedemata with retarded brain development in two children [2].

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The injection of thyroid hormones can reverse the changes caused by hypothyroidism as regards to the brain organogenesis and functions of learning and memory, because their mechanisms are thyroid-dependent ones [3–7]. Some studies showed that thyroid hormones are key signals regulating neuronal plasticity associated with learning, and changes in the expression of transthyretin carrying these bioregulators may serve as a characteristic correlate of memory consolidation [8]. It has been demonstrated that phagocytic behavior of microglia in rat brain also is thyroid-sensitive [9].

Although hypothyroidism disturbs significantly the ontogenesis and functions of central nervous system, causing in severe cases of myxoedema profound impairment of cognitive abilities and even psychosis, the behavioral, motor and other psychoneurological disorders accompany euthyroid and slightly hypothyroid cases and periods of Hashimoto's disease as well, thus constituting the picture of so called "Hashimoto's encephalopathy". In 1966 Lord W. B. Brain et al. described a new disease, which they called "Hashimoto's encephalopathy" (HE). It was a case of a 48 years old man with Hashimoto's thyroiditis in euthyroid condition, who had twelve attacks of psychoneurological disorder during seventeen months [10]. He had such symptoms as hemidysaesthesia, aphasia, hemiplegia, hemianopsia, confusion, paresthesiae, periods of agitation and depression, tremor, hallucinations and stupor.

HE is a fairly rare neuroendocrine syndrome, and also an autoimmune disease of the brain. It is known as steroid-reactive(or steroid-responsive) encephalopathy, associated with autoimmune thyroiditis (SREAT). Efforts of treating HE with glucocorticoids, in most cases have a positive effect [11–12]. HE has a lot of clinical manifestations that mimic an assortment of neurological and psychiatric disorders. The most frequent psychoneurological symptoms are: cognitive dysfunction, tremor, altered consciousness, transient aphasia, seizures, myoclonus , gait disorder/ataxia, transient aphasia and focal deficit, stroke-like episodes [12–17].

The entity, although discussed and explored for more than 50 years since its initial descriptions, remains an enigma of Thyroidology and Psychiatry, because its aetiology and pathogenesis are obscure.

The lecture describes the development of current views on the role of thyroid in ontogeny and functions of brain, as well as classical and newest ideas/data on the aetiology and pathogenesis of Hashimoto's encephalopathy. The synopsis of the world case reports and research:

— literature on this disorder is added with authors' own results obtained by study of 17 cases of Hashimoto's thyroiditis with schizophrenia-like clinical manifestations. The relation of the disease to adjuvant-like aetiological factors is discussed. Three major mechanistic concepts of Hashimoto's encephalopathy are detailed, namely cerebral vasculitis theory, hormone dysregulation theory and concept, explaining the disease *via* direct action of the autoantibodies against various thyroid (thyroperoxidase, thyroglobulin, and TSH-receptor) and several extrathyroid antigens (towards alpha-enolase and other enzymes, gangliosides, MOG-protein, and onconeuronal antigens);
— all of them expressed in the brain [18]. The lecture demonstrates that all above mentioned concepts intermingle and prone to unification, suggesting the unified scheme of pathogenesis for the Hashimoto's encephalopathy. The clinical manifestations, criteria, forms, course, treatment and prognosis of Hashimoto's encepha-

lopathy and its comorbidity to other diseases — are also discussed in brief. The relation between Hashimoto's encephalopathy and non-vascilitis autoimmune encephalomyelitides of paraneoplastic and non-paraneoplastic origin is emphasized. Authors' original case reports of autoimmune encephalitides accompanying Hashimoto's thyroiditis are embedded. The key unresolved task in Pathophysiology of Hashimoto's encephalopathy is a creation of valid animal model for this nosological entity. Authors' attempt to create a mice model of the disease using IgG from patients is described.

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