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Letter to the Editor

AUTOANTIBODY-MEDIATED ENCEPHALITIC SYNDROMES

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INTRODUCTION

In recent years, there has been increasing interest focused on the study of autoantibodies that attack neurons. Encephalitis is inflammation of the brain parenchyma that is characterized by neuropsychiatric symptoms and can be mediated by autoantibodies, viruses, vaccines, and other biological agents. In 'autoimmune encephalopathy', autoantibodies can attack neuronal proteins and receptors, resulting in psychosis, decreased levels of consciousness, and cognitive and memory deficits (1). This may produce psychiatric symptoms and movement alterations, convulsions, and severe amnesia, as well as inflammation of the vertebrae and optic nerves, effects which depend on the type of antibody (Table I).

Table I. *Some symptoms of encephalitis.*

• Confusion	• Seizures	• Agitation
• Depression	• Psychosis	• Drowsiness that can lead to coma and death
• Fatigue	• Paralysis	• Personality changes or confusional state
• Headache	• Numbness	• Short-term memory loss
• Fever		

Current therapies present a number of side effects which could overlap with the pathological effects caused by autoantibodies, and therefore, more specific therapies are needed. This paper reports the mechanism of action of autoantibodies in the brain and their biological and pathogenic effects in relation to inflammatory and immunotherapeutic processes.

DISCUSSION

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Autoantibodies are key proteins that cause autoimmune diseases (Table II). They form immune complexes with self-antigens and recruit and activate inflammatory immune cells upon complement activation. When immune complexes are deposited in blood vessels, they cause vasculitis; while if they are deposited in the tissues, they recruit neutrophilic granulocytes and macrophages which release hydrolytic enzymes that cause tissue damage (2).

Table II. *Some symptoms resulting from the attack of autoantibodies in the brainstem.*

a) Eye movement abnormalities	b) Dysphagia	c) Dysarthria	d) Ataxia (facial)
e) Vertigo	f) Hearing impairment	g) Reduced consciousness	h) Hypoventilation

Antibodies are immune system proteins that are produced by B cells and plasma cells and are capable of distinguishing self-cells, tissues, and organs from non-self cells. The aggression of antibodies towards foreign microorganisms allows the human body to remain healthy. When this system no longer works, the organism enters a pathological state.

Autoantibodies are also proteins, and they derive their name from the fact that instead of acting against foreign antigens (such as viruses, bacteria, fungi, protozoa including amoebae, etc.) that react against their own tissues. The action of autoantibodies, a dysfunction of the immune system, can cause tissue hyperreactivity with inflammation (3). Autoantibodies can destroy cells and tissues, creating organ dysfunction and thus producing an autoimmune disease. The autoimmune disease that is generated by autoantibodies is classified based on the type of organ or tissue affected.

Autoantibodies can affect a single organ, such as the thyroid, joints, the immune system, or brain, or more rarely, the disease can be multi-organ. Clinical manifestations may include pain, fever, muscle weakness, fatigue, allergy, or general deterioration of the organism. The diagnosis of an autoimmune disease involves clinical analysis with the search for antineuronal nuclear antibody (ANNA) and extractable nuclear antigen (ENA), which are antigens that can interact with particular antibodies, triggering an immune response.

When autoantibodies react with brain tissue, they can generate encephalitic syndromes (4) (Fig. 1). Encephalitis is inflammation of the brain which can also affect the spinal cord, and it can be caused by various agents such as viruses, bacteria and their products, proteins, antigens, and autoantibodies. It can cause diverse symptoms with a wide range of severity (5).

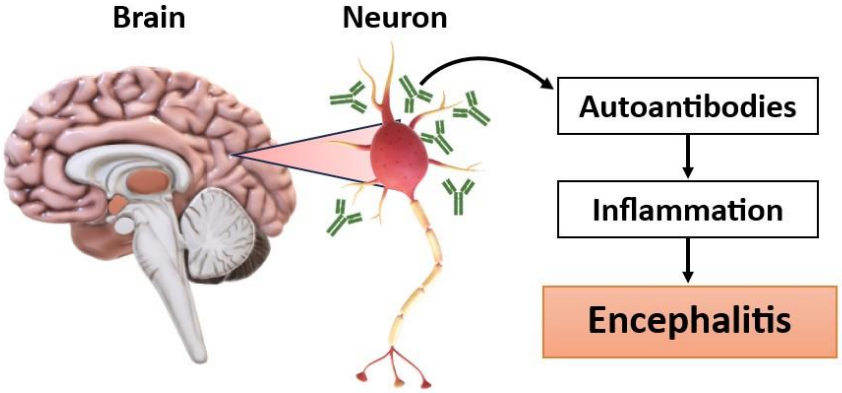

Fig. 1. *In the brain, autoantibodies can attack neurons, causing inflammation and encephalitis.*

The diagnosis of encephalitis is often made after performing magnetic resonance imaging (MRI) of the brain and a lumbar puncture. If the encephalitis is caused by a viral agent, therapy involves the use of antivirals which, by lowering the viral load, also reduce inflammation.

Autoantibody-mediated encephalitis is a type of autoimmunity against the CNS with serious and sometimes long-lasting neurological damage (5). This acute onset disease, which progresses in a period of days to weeks, may have a correlation with epilepsy and other neurologic dysfunctions (6). The syndromes can be different but are both caused by autoantibodies that attack neuronal antigens (which can be extracellular or intracellular). One of the receptors to which the autoantibody binds may be N-methyl-d-aspartate (7), which can cause convulsions, inflammation, psychosis, and

mood disorders in the affected subject. Autoantibody encephalitis may be mediated by damage to voltage-gated potassium channels and this effect is treatable with immunotherapy (8).

CONCLUSIONS

The study of autoantibody-mediated encephalitis has advanced greatly in the past decade, with *in vivo* and *in vitro* models helping to further the understanding of this disease. However, there are still many questions to be answered about the mechanisms and research must continue to advance the diagnosis process and identify new therapeutic approaches.

Conflict of interest

The authors declare that they have no conflict of interest.

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