



BRIEF REVIEW OF VIRAL ENCEPHALITIS

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ABSTRACT

Encephalitis is a disease characterised by inflammation of the encephalon. An important element to take into account in this pathology is that it has several causes, among which viral and metabolic are the most important. This clinical picture generally manifests itself with headache, altered mental state, seizures, focal signs, movement disorders, and in some cases also manifested with meningeal or cortical signs, depending on whether it is multi-focal or focal. It is important to consider post-infectious or para-infectious processes in encephalitis. The most important thing is always to take into account onset, progression and speed, together with contact with sick people. In suspected viral encephalitis, aciclovir 10 mg/kg/every 8 hours for 14 days is recommended.

The aim of this literature review is to show how the treatment of viral encephalitis has changed over the years, considering possible elements that may improve or worsen the prognosis.

KEY WORDS: *viral encephalitis, central nervous system, herpes simplex virus.*

Encephalitis is defined as an inflammation of the brain parenchyma leading to neurological dysfunction which may be caused by infection or an autoimmune disorder. It is confirmed by the identification of inflammation of the brain tissue; it

should be noted that neuroimaging or pleural fluid studies are sometimes used to diagnose this pathology. Encephalitis is characterised by headache, decreased level of consciousness, focal seizures, papilledema, fever, lymphadenopathy,



arthralgias, myalgias, and a duration of 24 to 72 hours. One of the first diagnostic tests to be performed is a simple cranial tomography to rule out an increase in intracranial pressure; after this, and if there is no increase in intracranial pressure, a lumbar puncture can be performed (1). This pathology is important in relation to morbidity and mortality worldwide. Importantly, viral encephalitis can lead to central nervous system involvement, leaving the patient with a severe neurological prognosis. It is believed that the development of this long-term neurological disorder is due to neuroimmune alterations, primarily concentrated at the microglial level, and there is recent evidence that astrocytes play a role in the inflammatory response to the virus (2).

Viral encephalitis remains a global problem, and antiviral therapies remain one of the cornerstones to prevent neurological sequelae. Some patients may not have effective relief and may suffer serious sequelae. Within the central nervous system and microglia specifically, it has been determined that there is a rapid response to various central nervous system disorders including trauma, ischaemia and infections. Some studies have determined that microglia as a benefit and risk for encephalitis; the benefit that microglia can generate is that it detects infection and produces phagocytic activity including the production of type I interferon, thereby inducing autophagy or cytokine secretion. However, microglia causes damage at the membrane level and affects mostly the hippocampus, leading to long-term memory impairment and cognitive dysfunction (3)(4).

As is well known, viral encephalitis is characterised by encephalopathy, commissions, focal deficits and neurological sequelae; in some cases severe complications often lead to death of the patient. This is usually caused by the herpes virus, although other pathogens have been shown to cause this condition. Recent studies in neuroimaging and molecular biology allow more accurate diagnosis of the aetiology, although their benefits need to be confirmed based on clinical guidelines and interpretations. Despite the administration of acyclovir as therapy, in addition to basic care, the consequences remain dismal in 2/3 of patients presenting with herpetic encephalitis, requiring admission to intensive care units, most often in addition to acyclovir treatment, which can be combined with immunomodulatory therapies, including immunoglobulins and corticosteroids (5).

A study called genomic sequencing is a very powerful laboratory technique that allows the detection of various spectra of pathogens that are present. It is clear that this test is being applied for the detection of viruses, especially in cases of suspected infection where the aetiology of the virus is unclear. This technique has been used in patients presenting with encephalitis, especially immune encephalitis (6).

It should be noted that in viral encephalitis, identification of the causative pathogen remains a challenge, and 50% of cases remain undetected. As mentioned above, sequencing techniques have an important value, although their use as a routine diagnostic remains uncertain (7).

A study conducted in 2020 states that the symptoms mostly present in patients with encephalitis, whether viral or

autoimmune, include behavioural and mental disturbances, amnesia, motor disorders, autonomic disturbances, speech disturbances, seizures and altered consciousness (8).

There are certain points of view in relation to reactive cerebral autoantibodies; these do invite importance due to the fact that they mediate alteration in the central nervous system. It is necessary to mention that these have much to do with the generation of pathogenesis. It is important because with this we can analyse the different pathogens that can cause encephalitis, especially the herpes simplex virus. The status of a nervous system disorder of viral origin is determined by neurovirulence. While the patient with a viral infection may recover from neurological dysfunction, some may suffer from post-viral encephalitis, which may be reported within weeks or months after infection. In some cases these reactive brain autoantibodies have been detected in parallel with the onset of the disease, suggesting that autoimmunity is present in encephalitis as an early event. However, it has not yet been established that the virus-associated autoimmune reaction has pathological effects in early stages of the disease (9).

Depletion of microglia, and the colony-stimulated factor 1 receptor blocking signalling pathway, leads to increased viral replication one with severe neurological alterations and increased mortality. Although the mechanism remains undefined, microglial T-cell interactions, together with phagocytosis of infected neurons, apparently play a role. Paradoxically, the production of inflammatory cytokines was increased in several instances following a viral infection in which a depression of brain microglia was generated, suggesting that: Cells that are different from microglia mediate the inflammatory response or that microglia have a regulatory function. Under known circumstances, the antiviral response of microglia contributes negatively to long-term neurological sequelae, although few studies have focused more on this aspect. Moreover, defects in microglia function have been identified as contributing to susceptibility to encephalitis or its sequelae (10).

During homeostasis, the microglia is in most immune cells in the central nervous system. Microglia is characterised by the maintenance of brain cell function and integrity. During virus-induced encephalitis, the microglia are essential for the defence and protection of neurons. The activation of the microglia and antiviral defences are not regulated by neurons, but by milestones and other brain cell types; the microglia also has three mental effects caused directly or indirectly by altered neuronal integrity, all leading to long-term sequelae; understanding the function of the microglia in the brain as it is infected by viruses is essential for the development of current treatments for viral encephalitis. Thus, microglia are immune cells that reside in the central nervous system, plus they have several functions at the brain level related to health, disease. Their response during encephalitis depends on whether or not the inflammation is triggered by a sterile infection or contamination, and obviously depends on the type of infecting pathogen (11).

Rituximab is an antecedent monoclonal antibody 20, which is used in various autoimmune pathologies and in diseases in which there is B-cell malignancy. In the case of viral



encephalitis, it has been used as a maintenance therapy; however, prolonged use of rituximab leads to decreased B-cell function, which contributes to non-neutropenic infections, such as a viral infection causing encephalitis; however, non-neutropenic infections and bacterial infections are common in patients with a common variable immunodeficiency. Rituximab may therefore result in a dose-dependent activation of T-cells, which increases the risk of other infections (12)(13).

Conclusions

Throughout the study carried out in this literature review, the role of some structures and especially some important elements of the central nervous system involved in increasing or decreasing the presence of neurological sequelae, such as the microguide. It is important for us to bear in mind that viral encephalitis has a variable course, there is the possibility of neurological sequelae. It is important to mention this aspect because the techniques and management of this pathology are constantly evolving.

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