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Letter to the Editor

THE INFLAMMATORY RESPONSE IN MENINGITIS

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INTRODUCTION

Infections of the central nervous system (CNS) are diverse and come with high mortality. Such pathologies can include abscesses, encephalitis, and meningitis. Meningitis is a very ancient infectious disease which was already mentioned by Hippocrates and, in 1805, the first epidemic outbreak appeared in Europe (1). In 1806, the disease was identified in the United States and later appeared in Africa in 1905 (2). Meningitis is an acute inflammation of the meningeal membranes that surround the brain and spinal cord. The disease can occur after an infection caused by a microorganism. Bacterial meningitis can be very serious with a high risk of complications that can lead to death (3), while viral meningitis is normally less serious (4).

Patients with meningitis may present with purulent cerebrospinal fluid (CSF) and seizures, with the latter often occuring in children. The symptoms of meningitis may include headache, stiffness of the neck, nausea and/or vomiting, high fever, drowsiness, and convulsions (Table I). The most common cause of bacterial meningitis is Neisseria meningititis (Nm), which can produce convulsions and coma, and the prognosis is unfavorable for the elderly.

Table I. *Various forms of meningitis and some symptoms.*

Forms:
Acute bacterial meningitis, viral meningitis, non-infectious meningitis, recurrent meningitis, subacute and chronic meningitis
Symptoms:
Stiffness of the back of the neck, high fever, headache, nausea, vomiting, convulsions, seizures, drowsiness, focal neurologic deficits, papilledema, deterioration of consciousness, photophobia

Microglia and macrophages from the bone marrow are involved in the primary response to infection and release various cytokines including IL-1, tumor necrosis factor (TNF), and IL-6, and the chemokine IL-8 which attracts neutrophils to the inflammatory site (5).

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CNS infection causes damage and clinical syndromes, which can improve after adequate antimicrobial treatment. An efficient host immune response can cause the elimination of the pathogen with relief for the affected patient.

DISCUSSION

When pathogens invade brain tissue, they induce an immune response with secretion of inflammatory molecules, including cytokines. These reactions cause meningitis, a pathological state that is more frequent in newborns and young children. Meningitis causes increased vascular permeability, tissue damage, and disruption of the blood-brain barrier (BBB) which divides the peripheral circulation and the CNS.

Microglia are primary and relevant immune cells of the CNS which are important for the phagocytosis of bacterial microbial agents that can cause meningoencephalitis in children. In meningitis, these cells are altered and therefore unable to carry out their immunological role. The activation of microglia induces the production of cytokines such as IL-1, TNF, and IL-6, which contribute to meningeal inflammation.

The BBB is an obstacle for the penetration of microorganisms and foreign molecules into the CNS but allows the passage of small molecules such as oxygen and CO2. Newborns may become infected with Streptococcus B following delivery and should be treated promptly with antibiotics, including Ampicillin, Rifampicin and Cefotaxime, which are indicated for the treatment of serious bacterial infections. Furthermore, treatment with cortisone was found to be helpful, although in some circumstances it may not be indicated. Treatment with nonsteroidal anti-inflammatory drugs can also help, but in some cases, it has been noted that they do not increase survival for bacterial meningitis infection.

Bacterial meningitis can affect various age groups, and the pathogenic organisms vary based on the age of the patient. Immune-compromised individuals may be more susceptible to infections that cause meningitis. In addition to bacteria, fungi and viruses can also cause brain infections and therefore meningitis.

In a bacterial meningitis infection, IgA immunoglobulin proteases are disrupted, allowing the proliferation of the pathogenic bacterium (6). This brain pathology is usually caused by the following bacteria: Streptococcus pneumoniae (or Pneumococcus), Nm (or Meningococcus), and Haemophilus influenzae type b (or simply, Haemophilus). The bacteria that are produced travel by bloodstream until they reach the CNS and infect it. The infection induces inflammation and consequently, pathological signs appear. This disease is often not very contagious, but when it occurs, it can lead to encephalitis resulting in nausea, vomiting, headache, fever, epilepsy, cognitive impairment, seizures, and death. Convulsions occur in approximately 17% of adults with bacterial meningitis (7), while epileptic seizures, which can be detected with electroencephalogram (EGG), must be treated by the doctor based on the patient's characteristics.

CONCLUSIONS

Bacterial meningitis is an infection that affects the CNS with serious consequences that can cause mortality. It is an important topic in the field of infectious diseases due to its high degree of incidence and severity. The acute form of meningitis can have a rapid onset of symptoms, and identification of the bacterium can be done routinely in the laboratory. There are several bacteria that can cause meningitis and it can also be caused by viruses or fungi. Fortunately, the vaccine has dramatically reduced the incidence of this disease.

In bacterial meningitis in newborns, fever or hypothermia may be found in approximately 60% of cases (8). The disease can present itself within a few days following infection with the clinical signs mentioned above. The diagnosis should be made after isolating the pathogen in cultures of blood or CSF and after neuroimaging.

Often the signs of meningitis from bacterial infection can be confused with viral, fungal, and parasitic ones. Brain abscesses, CNS tumors, encephalitis, and other infections can also mimic bacterial meningitis.

Therapy should be timely and aggressive to avoid the patient's deterioration or death. Genetic studies are now underway for bacterial meningitis and new therapies utilize the inhibition of complement and metalloproteinases and anti-inflammatory cytokines that can block IL-1, TNF, and IL-6. However, further studies are needed to improve the treatment of meningitis.

Conflict of interest

The authors declare that they have no conflict of interest.

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